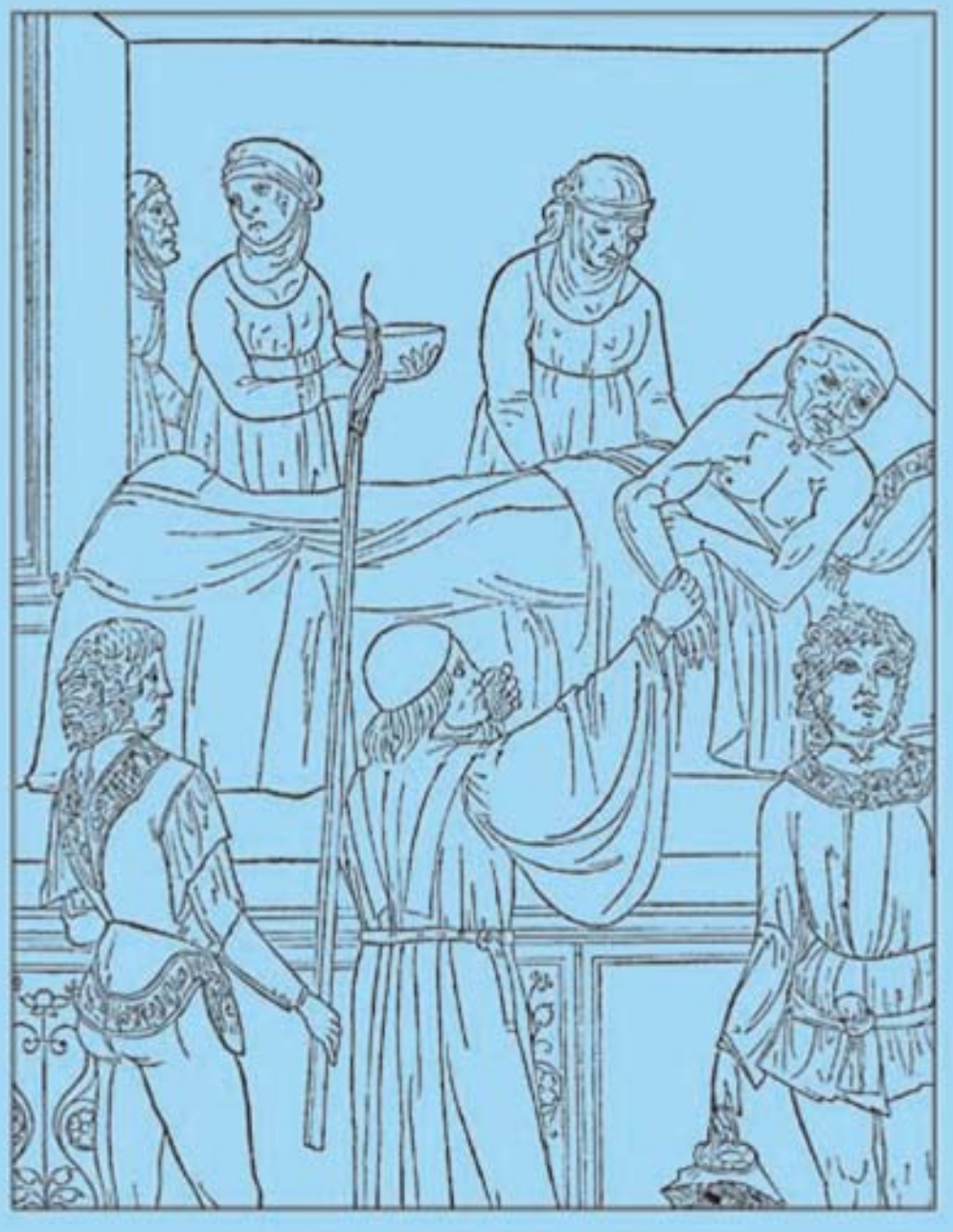
Tarascon Pocket Urologica

From the publishers of the *Tarascon Pocket Pharmacopoeia*®



Pamela Ellsworth, MD

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ABBREVIATIONS

↑: increased
↑ ↑: very high
↓: decreased
+/−: and/or, with/without
?: question
AAA: abdominal aortic aneurysm
ab: antibody
ABC's: airway, breathing, circulation
abnl: abnormal
abx: antibiotics
accts: accounts
ACE: angiotensin converting enzyme
ACTH: adrenocorticotropic hormone
AFB: acid fast bacillus
AIDS: Acquired immune deficiency syndrome
Approx: approximately
assoc: associated
asxic: asymptomatic
AUA: American Urologic Association
BCG: bacillus Calmette-Guerin
bid: twice a day
BMT: bone marrow transplant
BOO: bladder outlet obstruction
BP: blood pressure
btn: between
BUN: blood urea nitrogen
bx: biopsy
cAMP: adenosine 3', 5'-cyclic monophosphate
CBC: complete blood count
CFU: colony-forming units
cGMP: guanosine 5'-cyclic monophosphate
chemo: chemotherapy
CHF: congestive heart failure
CIC: clean intermittent catheterization
CIS: carcinoma in situ
cm: centimeter
CNS: Central nervous system
CT: computed tomography
CV: cardiovascular
CVA: costovertebral angle
CX: complications
DDX: differential diagnosis
DM: diabetes mellitus
DRE: digital rectal exam
DX: diagnosis
dz: disease
ED: erectile dysfunction
Epidem: epidemiology
ESR: erythrocyte sedimentation rate
ESWL: extracorporeal shock wave lithotripsy
f/up: follow-up
g or gm(s): gram(s)
GC: Gonorrhea
GFR: glomerular filtration rate
GI: gastrointestinal
GU: genitourinary
HA: headache
HC: hemorrhagic cystitis
Hct: hematocrit
Hgb: hemoglobin
h/o: history of
H&P: history and physical (exam)
hr: hour
HPV: human papillomavirus
HTN: hypertension
HU: hounsfield unit
hx: history
IC/PBS: interstitial cystitis/painful bladder syndrome
id: identify
IDSA: Infectious Diseases Society of America
INH: isoniazid
IVP: intravenous pyelogram
KOH: potassium hydroxide
KUB: kidney, ureter, bladder
LFTs: liver function tests
LHRH: luteinizing hormone-releasing hormone
LUTS: lower urinary tract symptoms
mcg: microgram
MEN1: multiple endocrine neoplasma type 1
mets: metastases
mg: milligram
ml: milliliter
mm: millimeter

mos: months
mRCC: metastatic renal cell carcinoma
MRI: magnetic resonance imaging
neg: negative
nl: normal
NSAIDS: nonsteroidal anti-inflammatory drugs
N/V: nausea/vomiting
OAB: overactive bladder
Path: pathology
PBO: placebo
PCR: polymerase chain reaction
Pg: picogram
pheo: pheochromocytoma
PO: per oral, orally
pos: positive
PSA: prostate specific antigen
pt(s): patient(s)
PT: prothrombin time
PTH: parathyroid hormone
PTT: partial prothrombin time
PUF: Pain, Urgency, and Frequency (symptom scale)
PVR: post-void residual volume
qd: once daily
qhs: every bedtime
qid: four times a day
RCC: renal cell carcinoma
RF: retroperitonal fibrosis
r/o: rule out
RX: treatment
sens: sensitivity
SMOS: Smith-Lemli-Opitz syndrome
soln: solution
SSX: signs and symptoms
SUI: stress urgency incontinence
SX: symptoms
TB: tuberculosis
TCC: transitional cell carcinoma
tid to qid: three to four times a day
Tm/S: trimethoprim sulfamethoxazole
TNM: Tumor-Node-Metastasis cancer staging system
TUR: transurethral resection
TURP: transurethral resection of the prostate
UA: urinalysis
UPJ: ureteropelvic junction
US: ultrasound
UTI: urinary tract infection
UUI: urinary urgency incontinence
UVJ: ureterovesical junction
VHL: von Hippel-Lindau (syndrome)
VUR: vesicoureteral reflux
VCUG: voiding cystourethrogram
WBC: white blood cells
wk(s): week(s)
XGP: xanthogranulomatous pyelonephritis
XRT: radiation therapy
yr(s): year(s)

DISEASES OF THE ADRENAL

Cushing Syndrome

- **Definition**: Hormonal disorder caused by prolonged exposure of body's tissues to high levels of cortisol.
- **Cause**: (1) Secondary to excess glucocorticoids such as prednisone use; (2) increased glucocorticoid production from a pituitary adenoma, Cushing disease (accts for 70% of Cushing syndrome cases excluding those caused by glucocorticoid use; (3) ectopic ACTH production which may be secondary to benign or malignant tumors that can produce ACTH – lung cancer (small cell and carcinoid) is most common, men 3× greater risk, thymomas, pancreatic islet cell tumors, medullary carcinoma of thyroid; (4) adrenal tumor — 4× more common in women, most are benign.
- **Epidem**: Rare, affects adults age 20–50 years, most cases not inherited, rare inherited forms include primary pigmented micronodular adrenal disease – small cortisol producing adrenal tumors in children and young adults, MEN1 (multiple endocrine neoplasia type I) – may have Cushing syndrome due to pituitary, ectopic production, or adrenal tumor.
- **SSX**: Upper body obesity, rounded face, increased fat around neck, with slender arms and legs, skin that is fragile, thin, bruises easily and that heals poorly, purple or pink stretch marks on abdomen, thighs, buttocks, arms and breasts, and weakened bones. Fatigue, weak muscles, hypertension, increased thirst and urination secondary to increased glucose, irritability, anxiety or depression, fatty hump between shoulders. Women with Cushing may have excess hair growth on neck, face, chest, abdomen and thighs, and irregular or no menses. Men with Cushing have decreased fertility, decreased or absent desire for sex, and sometimes ED.
- **DX**: H&P, lab tests. Three most common tests used to diagnose Cushing syndrome are: (1) 24-hr urinary free cortisol test; (2) measurement of midnight plasma cortisol or late night salivary cortisol; or (3) low dose dexamethasone suppression test. Tests that may be used to identify cause of Cushing syndrome include: (1) high dose dexamethasone suppression test – high doses of dexamethasone usually suppress cortisol levels in patients with pituitary adenomas but not in those with ectopic ACTH-producing tumors; (2) Corticotropin releasing hormone stimulation – differentiates patients with pituitary adenomas from those with ectopic ACTH production or adrenal tumors.
  - ➢ Imaging: MRI of the brain to look for pituitary ademona if clinical suspicion.
  - ➢ Lab: Petrosal sinus sampling – higher levels of ACTH in the sinuses than in forearm indicate a pituitary adenoma. Similar levels of ACTH in petrosal sinuses and forearm indicate ectopic ACTH production.
- **RX**: Varies with etiology.
  - ➢ Pituitary tumor – surgical removal – transphenoidal adenomectomy
  - ➢ Radiation to pituitary gland – indicated for surgical failures and in pts who are not surgical candidates
  - ➢ Drugs to control production of excess cortisol include: ketoconazole, mitotane, aminoglutethimide, metyrapone
  - ➢ Ectopic ACTH production – need to remove all of the cancerous tissue that produces the ACTH; if this fails, bilateral adrenalectomy and replacement therapy as needed
  - ➢ Adrenal tumors – surgical removal

Conn Syndrome

- **Definition**: Characterized by overproduction of the mineralocorticoid hormone, aldosterone, by the adrenal gland. Aldosterone causes increase in sodium and water retention and potassium excretion leading to arterial HTN.
- **Cause**: Adrenal hyperplasia (bilateral accts for 70% cases, unilateral accts for 20% cases), adrenal carcinoma, or secondary to an aldosterone-secreting adrenal adenoma ($<$ 5% cases). Rare forms include disorders of the renin-angiotensin system.
- **Epidem**: Most common cause of secondary HTN.
- **SSX**: HTN, muscle cramps and weakness, headache, metabolic alkalosis; unlike secondary causes of hyperaldosteronism there is little edema.
- **DX**:
  - ➢ Chem: low serum renin/aldosterone ratio ($<$ 0.0005) – may be confounded by antihypertensive drugs; elevated sodium, potassium $<$ 3.7 suspicious. Adrenal vein sampling for lateralized aldosterone and cortisol levels
  - ➢ Saline infusion test: 2 L NaCl IV over 4 hr decreases serum aldosterone to $<$ 10 ng% in normals
  - ➢ Captopril test: 25 mg PO $\times$ 1 decreases serum aldosterone levels to $<$ 50% at 2 hrs in normals
  - ➢ Imaging: CT or MRI used to differentiate adenoma from bilateral hyperplasia (CT sens 71–100%, specificity 22–100%)
- **RX**: If adrenal adenoma – surgical removal, although HTN persists in 45% pts who undergo surgical RX.
  - ➢ If bilateral adrenal hyperplasia – spironolactone or eplerenone (has 25–50% less mg per mg potency than spironolactone). Side effect of treatment in men is gynecomastia
  - ➢ Prognosis is good with appropriate treatment
- **CX**: If not adequately treated can lead to poorly controlled HTN and increased rate of stroke, heart disease, and renal failure

Addison's Disease

- **Definition**: Primary adrenal insufficiency with lack of production of cortisol and aldosterone. Affects 1 to 4 of every 100,000 people in all age groups and both sexes.
- **Cause**: Can be grouped into 3 categories: (1) adrenal dysgenesis, (2) adrenal destruction, and (3) impaired steroidogenesis. Adrenal dysgenesis includes: congenital adrenal hypoplasia, mutations of steroidogenic factor-1, and ACTH unresponsiveness. Adrenal destruction includes autoimmune polyglandular syndrome, adrenoleukodystrophy, adrenal hemorrhage, adrenal metastases, adrenal infections, and amyloidosis. Impaired steroidogenesis includes congenital adrenal hyperplasia, mitochondrial disorders, Smith-Lemli-Opitz syndrome (SMOS), and enzyme deficiency in cholesterol metabolism.
- **Epidem**: Automimmune related in 80% cases – adrenal insufficiency occurs when at least 90% adrenal cortex is destroyed; polyendocrine deficiency syndrome, types 1 and 2 – type 1 is inherited and occurs in children, type 2 (Schmidt syndrome) usually affects young adults; TB can destroy the adrenal glands; less common causes include chronic (most commonly fungal) infections, cancer metastases to the adrenals, amyloidosis, prior bilateral adrenalectomy, AIDS associated infections, adrenal bleeds, and genetic defects
- **SSX**: Chronic worsening fatigue, muscle weakness, loss of appetite, weight loss, nausea/vomiting, diarrhea, low blood pressure, orthostatic SX, irritability and depression, craving for salty foods, hypoglycemia, headache, sweating and irregular/absent menses

in women, hyperpigmentation of the skin with darkening most visible on scars, skin folds, pressure points, and mucous membranes. Addisonian "adrenal crisis" – sudden, severe worsening of sx with sudden, penetrating pain in lower back, abdomen or legs, severe nausea/vomiting, dehydration, low blood pressure, loss of consciousness. May be fatal.

- **DX**: May be difficult to DX in early stage.
  - ➢ Lab: ACTH stim test – most commonly used; normal response after ACTH injection is increase in blood and urine cortisol. Those with Addison's disease or long-standing secondary adrenal insufficiency have little or no increase in cortisol levels.
  - ➢ CRH stim test – useful if ACTH stim test is abnormal. Pts with Addison's disease produce high levels of ACTH but no cortisol. Pts with secondary adrenal insufficiency have absent or delayed ACTH responses. A delayed ACTH response points to hypothalamus as a cause.
  - ➢ Imaging: CT abdomen +/− MRI brain
- **RX**: Replacing/substituting hormones that the adrenal is not producing.
  - ➢ Cortisol replaced with hydrocortisone, prednisone, or dexamethasone
  - ➢ Aldosterone replaced with the mineralocorticoid fludrocortisone (florinef)

Pheochromocytoma

- **Definition**: Catecholamine-secreting tumor that arises from chromaffin cells – tumors arising from the adrenal medulla account for 85.9% of pheochromocytomas. May arise in extra-adrenal sites most commonly in the organ of Zuckerandl (75% of extra-adrenal sites). Extra-adrenal sites along sympathetic nerve chain overlying distal aorta, within ureter or bladder.
- **Cause**: May be malignant (10%) or benign tumor.
- **Epidem**: Occurs in 2–8 per million. Peak incidence during 4th and 5th decades, men = women
  - ➢ Often called the "10% tumor" – 10% malignant, 10% bilateral, 10% extra-adrenal, 10% familial, 10% involve children, 10% or slightly less recur, 10% associated with MEN syndromes, in pts presenting with stroke 10% will be found to have a pheochromocytoma
  - ➢ With familial syndromes more likely to be bilateral and benign. Familial disorders assoc with pheo include: Von Hippel-Lindau (10–30%), hereditary paraganglioma (10–20%), MEN 2 (50%), and neurofibromatosis.
- **SSX**: Classic triad of SX: headache (72%), sweating (69%), and palpitations (51%). Other SSX include: sweating, tachycardia, palpitations, chest pain, feeling of anxiety, nervous shakes (tremors), nausea, weight loss, heat intolerance, visual blurring, polydipsia, dyspepsia, constipation, dizziness, shock, paresthesias or pain in arms, seizure, pallor, flushing, polyuria, papilledema, orthostatic hypotension, psychiatric disorders, dilated cardiomyopathy, stroke, Raynaud phenomenon, palpable mass.
- **DX**: Elevated levels of catecholamines (norepinephrine, epinephrine, and dopamine) in blood or urine and elevated urinary metanephrines in 95–99% affected individuals. Plasma free normetanephrine level $>$ 1.4 nmol/L, and plasma free metanephrine levels of $>$ 0.5 nmol/L indicative of a pheochromocytoma. Also can check 24-hr urine catecholamines and metanephrines (epinephrine, norepinephrine, and dopamine). Clonidine suppression test may be helpful for distinguishing btn high levels of plasma metanephrine caused by release of sympathetic nerves and that caused by release from a pheo. Clonidine 0.3 mg po administered with plasma norepinephrine level checked before and 3 hrs after administration, normal individuals suppress to $<$ 300 pg/mL, whereas pheo remains high at 1000–2000 pg/mL.

- ➢ Imaging: US – inexpensive, but least accurate. CT – quick, good for identifying adrenal abnls. MRI – pheos often enhance, better for identifying extra-adrenal pheos

- **RX**: Surgical removal (often laparoscopically) after adequate preoperative preparation. Phenoxybenzamine hydrochloride (dibenzyline) 20–30 mg initially, increasing by 10–20 mg/day until BP is stable and there is mild postural hypotension. Pts usually require daily dose of 40–100 mg. Propranolol used when cardiac arrythmias are prominent, but only can be used when effective alpha-blockade established. Dose is 20–40 mg PO tid to qid. Alpha-methyltyrosine (metyrosine) decreases catecholamine synthesis and is used in pts with cardiomyopathy and resistance to alpha-blockers. Dose is 0.5 to 1.0 g PO 3 to 4 times per day in well-hydrated patient. Side effects include: crystalluria, sedation, diarrhea, anxiety, and psychiatric disturbance.

Adrenocortical Carcinoma

- **Definition**: Malignant neoplasm of the adrenal.
- **Cause**: Approximately 60% of patients present with SSX related to excessive hormone secretion, but hormone testing demonstrates that 60–80% of tumors are functioning.
- **Epidem**: Affects only 1–2 persons per one million population; occurs in adults, mean age at diagnosis is 22 yrs. Only 30% of malignancies are confined to the adrenal at time of diagnosis.
- **SSX**: Nonfunctioning carcinomas may have SSX related to local invasion by tumor or mets. With nonfunctioning carcinoma most common SSX is abdominal pain; may also have weight loss, nausea, myalgia, palpable abdominal mass. If functioning, may have SSX of Cushing syndrome, feminization, and hyperaldosteronism.
- **DX**: In-phase and out-of-phase T1 weighted imaging MRI may be most effective noninvasive method to differentiate benign from malignant adrenal masses. Lab evaluation to determine if functional vs. nonfunctional. Most common sites of mets are the peritoneum, lung, liver, and bone.
  - ➢ Imaging: CT of abdomen to stage. MRI may be useful, as noted above.
- **RX**: Treatment varies with stage.
  - ➢ Stage 1 – T1 (tumor $\leq$ 5 cm, invasion absent), N0, M0
  - ➢ Stage II – T2 (tumor $>$ 5 cm, invasion absent), N0, M0
  - ➢ Stage III – T1, N1 (+ nodes), M0
    - ° T2, N1, M0
    - ° T3 (tumor outside adrenal in fat), N0, M0
  - ➢ Stage IV – T3, N1, M0
    - ° T4 (tumor invading adjacent organs), N1, M0
    - ° Any T, any N, M1 (distant mets)
  - ➢ Complete surgical removal of the tumor is treatment of choice for pts with stage I, II, and III tumors. Lymph node dissection is indicated for those pts with stage III with enlarged regional nodes. Adjuvant radiation therapy has not been shown to be of benefit for stage I and II tumors. For pts with stage III adrenocortical carcinoma with localized but unresectable disease, radiation therapy 4200–5000 rad over 4 weeks is an option. Mitotane in doses as high as 10–12 g/day is an option in those patients unable to undergo complete resection. Standard treatment options for pts with stage IV adrenocortical carcinoma include chemotherapy with mitotane, radiation therapy to bone mets, and surgical removal of localized metastases, particularly those that are functioning. Another option is participation in a clinical trial.

- ➢ Prognostic factors include completeness of resection and stage of disease. Overall 5-year survival for tumors resected for cure is approx 40%.

Adrenal Adenoma

- **Definition**: Benign neoplasm of the adrenal gland.
- **Cause**: Approximately 80% are nonfunctioning. Large tumors more likely to be malignant – suspicion for malignancy in tumors > 4 cm.
- **Epidem**: Women > men, prevalence increases with age.
- **DX**: H&P
  - ➢ Lab evaluation to determine if functioning – may include urinary and plasma-free metanephrines, plasma aldosterone-to-renin ratio, urine 17-ketosteroids, overnight 1-mg dexamethasone suppression test
  - ➢ Imaging: CT scan. If pheo suspected, consider MRI.
- **RX**: Depends on whether or not mass is functional.
  - ➢ If work-up indicates lesion is likely an adrenal adenoma, follow-up with periodic CT scans may be performed.
  - ➢ If suspect malignancy (i.e., > 4–6 cm) then surgical removal indicated.
  - ➢ If lesion increasing in size significantly, may require removal to ensure that it is not malignant.

DISEASES OF THE KIDNEY

Acute Pyelonephritis

- **Definition**: Inflammation of the kidney and pelvis from bacterial infection
- **Cause**: Gram-negative rods in 95% cases, most commonly *E. coli*. Other etiologic causes include aerobic gram-neg bacteria, *Staphylococcus saprophyticus*, and enterococci. In elderly patients, *E. coli* is a less common (60%) cause. The increased use of catheters and instruments among these pts predisposes them to infections with other gram-neg organisms such as *Proteus*, *Klebsiella*, *Serratia*, or *Pseudomonas*.
- **Epidem**: Most commonly, secondary to ascent of bacteria from lower UTI. Hematogenous acute pyelonephritis occurs most often in debilitated, chronically ill patients and those receiving immunosuppressive therapy. Metastatic staphylococcal or fungal infections may spread to the kidney from distant foci in the bone or skin. Women > men. Increased incidence in those with DM, sickle cell disease, congenital urinary tract anomalies, and papillary necrosis.
- **SSX**: fever, flank pain, nausea, frequency, urgency, dysuria, CVA punch tenderness, adominal/back pain
- **DX**: Labs – UA and culture. On urine dipstick the combination of the leukocyte esterase and nitrite tests (with a positive result on either) for UTI is more specific but less sensitive than either test alone. Urine cultures positive in 90% cases. The consensus definition of pyelonephritis established by the Infectious Diseases Society of America (IDSA) is a urine culture showing at least 10,000 colony-forming units (CFU) per mm^3 and symptoms compatible with the diagnosis. Lower counts (1000–9999 CFU/mm^3) are of concern in men and pregnant women.
  - ➢ Imaging: Radiographic imaging is not necessary in all cases. Consider imaging in complicated cases or if symptoms do not improve with antibiotic therapy. Renal US and/or CT scan to rule out abscess formation, pyonephrosis, or other anomalies. Helical CT findings suggestive of acute pyelonephritis include striated or wedge-shaped perfusion defects, loss of corticomedullary differentiation, renal enlargement, and perinephric stranding.

- **RX**: Outpatient oral therapy is successful in 90% of selected patients with uncomplicated acute pyelonephritis who can tolerate oral intake, will be compliant with the treatment regimen, will return for early follow-up, and have adequate social support. Pregnant women with fever > 38°C, severe nausea, vomiting, recurrent upper urinary tract UTI, signs of sepsis including tachycardia, rigors or hypotension, immunocompromise, significant medical conditions such as DM or previous renal disease, h/o substance abuse, concurrent preterm labor, and noncompliance should be hospitalized and treated with IV abx and hydration.

Indications for Hospitalization

Absolute	Relative
Persistent nausea/vomiting with poor fluid intake	Age > 60 yrs
Suspicion of sepsis	Anatomic urinary tract anomaly
Urinary tract obstruction	Immunocompromised (i.e., DM)
Progression of SX	Poor compliance

For outpatient treatment use oral fluoroquinolone or Tm/S pending sensitivities for 14 days. For those admitted, initial IV abx, ampicillin plus aminoglycoside pending sensitivities for 14–21 days. Repeat urine cultures 5–7 days posttreatment to ensure resolution. Ten to 30% pts with acute pyelonephritis will have a relapse after 14-day treatment.

Emphysematous Pyelonephritis

- **Definition**: Acute necrotizing parenchymal and perirenal infection by gas-forming organisms
- **Cause**: *E. coli* is most frequently identified organism, but also may be associated with *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Aerobacter aerogenes*, *Citrobacter*, and rarely yeast.
- **Epidem**: Adults > children; female > male. Roughly 70–90% cases involve diabetics. May also occur in pts with urinary tract obstruction associated with stones or papillary necrosis and significant renal impairment; 10% cases are bilateral.
- **DDX**: acute pyelonephritis
- **SSX**: fever, vomiting, flank pain, urgency, frequency, dysuria, CVA tenderness
- **DX**: Lab: UA, culture, CBC, electrolytes, bun, creatinine, glucose
  - ➢ Imaging: Diagnosis is made by demonstrating intraparenchymal gas on radiographic evaluation. US may show strong focal echoes that suggest intraparenchymal gas. CT scan may be helpful in localizing gas and demonstrating extent of infection.
- **RX**: Initial RX is fluid resuscitation, IV antibiotics, and relief of obstruction if present. If no improvement, then surgical or percutaneous drainage or nephrectomy.

Renal Abscess

- **Definition**: Abscess involving the renal parenchyma.
- **Cause**: Retrograde ascent of bacteria from lower urinary tract infection. Most commonly gram-negative organisms.
- **Epidem**: Most common predisposing factors are DM (47%), renal calculi (41%), and ureteral obstruction. Association between vesicoureteral reflux and renal abscess rarely noted.
- **SSX**: fever, chills, malaise, urgency, frequency, dysuria, abdominal or flank pain, weight loss

- **DX**: Often there is a delay in diagnosis.
  - ➢ Labs: CBC, blood cultures, UA, urine culture
  - ➢ Imaging: CT scan and US have 82–90% accuracy of diagnosis. CT findings will vary with evolution of abscess – initially may show renal enlargement with focal, rounded areas of decreased attenuation. After several days there may be a thick, fibrotic wall around the abscess. With chronic abscess there is obliteration of tissue planes, thickening of Gerota's fascia, and low-attenuation parenchymal mass surrounded by an inflammatory wall of slightly higher attenuation that enhances with contrast due to the increased vascularity of the abscess wall.
- **RX**: Traditional treatment is open or percutaneous drainage and antibiotics. Stable, immunocompetent pts with renal abscesses $<$ 3 cm may be treated with 6 wks of IV antibiotics. Factors that predict a less favorable outcome to antibiotic therapy alone include abscess diameter $>$ 3–5 cm, involvement with more than 1 organism, presence of gram-neg bacilli, duration of treatment $<$ 4 wks, and use of aminoglycoside as only antibiotic.

Renal and Ureteral Tuberculosis (TB)

- **Definition**: Infection of the kidney and/or ureter with *Mycobacterium tuberculosis*.
- **Cause**: Blood-borne mets. Previous pulmonary infection may occur many years before development of renal/ureteral disease. Rarely may develop secondary to bacillus Calmette-Guerin (BCG) therapy for TCC
- **Epidem**: Prevalence rate of 1.2–2.6% in Western world and 15–20% in developing countries. Men:women ratio is 2:1, most commonly affects pts 20–40 yrs, but increasing incidence amongst older pts. Most common site of ureteral involvement is distal ureter at UVJ. Renal TB is most common site of extrapulmonary TB among Caucasians. Ureter involved in 50% pts with GU tract TB.
- **SSX**: The most common symptoms of GU tract TB, in descending order of frequency, include increased frequency of urination (during the day initially but at night later in the disease course), dysuria, flank pain, suprapubic pain, blood or pus in the urine, and fever.
- **DX**: Lab – TB skin test (+) in about 90% cases. CBC, ESR, chemistries, C-reactive protein. Serial (usually 3) early morning urine collection for AFB smear is a specific (89–96%) but less sensitive (52%) tool. Serial urine cultures considered criterion standard for evidence of active disease, sensitivity 65% specificity 100%. Polymerase chain reaction (PCR) is highly sensitive (87–100%), specific (92–99.8%), and fast (available within 6 hrs).
  - ➢ Imaging: KUB may demonstrate calcifications in region of kidney(s) and ureter in about 50%. Renal US may show cystic or cavitary lesions, cortical scarring, hydronephrosis and abscesses in the kidney. CT may be helpful in assessing the extent of the disease and, if performed with contrast, will reveal if kidney is functioning or not and function relative to contralateral kidney.
- **RX**: Standard treatment is rifampin, INH, pyrazinamide, and ethambutol for 2 months, then rifampin and INH for 4 more months unless resistance to either agent exists; if so, obtain a follow-up sensitivity report. In patients who are HIV-positive, continue treatment for a total of 9 months. In pts with impaired renal function can use Rifampin, isoniazid, pyrazinamide, ethionamide, and prothionamide in normal doses because they are either eliminated in the bile or broken down to metabolites

that are not excreted by the kidney. However, Ethambutol causes optic neuritis, which may be irreversible, and reduced doses should be given according to the glomerular filtration rate (GFR). In addition, Streptomycin and other aminoglycosides are ototoxic and nephrotoxic and should be avoided if possible in patients with impaired renal function.

Xanthogranulomatous Pyelonephritis

- **Definition**: A chronic inflammatory condition of the kidney resulting in diffuse renal destruction, a grossly enlarged and nonfunctioning kidney associated with nephrolithiasis.
- **Cause**: Thought to start with obstruction (stone or sloughed papilla) followed by infection (proteus most common organism) that leads to destruction of tissue and deposition of lipid material by histiocytes. Granulomatous process then occurs. Xanthoma cells present – are lipid-laden macrophages.
- **Epidem**: Most cases are unilateral. Peak incidence is sixth and seventh decades, but may occur in children also. Women > men; 15% have DM.
- **SSX**: fever, chills, flank pain, palpable mass, malaise, frequency, urgency, dysuria
- **DX**: Lab – UA and culture, CBC may demonstrate anemia, hepatic dysfunction in up to 30% pts.
  - ➢ Imaging: CT preferable – allows for determination of extent of disease – low density fluid-filled areas within renal parenchyma and findings indicating perinephric extension are suggestive of XGP.
- **RX**: Open nephrectomy often performed; however, in skilled hands with limited disease, may be performed via hand-assisted laparoscopic approach. If drainage is attempted first, must watch closely as disease may progress and develop into a renal-cutaneous fistula.

Malacoplakia

- **Definition**: A rare lesion involving the urothelium of bladder, ureters, and renal pelvis that is characterized by mottled yellow and gray soft plaques and nodules that consist of numerous macrophages and calcospherites.
- **Cause**: Exact etiology is unknown. Appears to be related to abnormal intracellular killing by phagocytes, particularly macrophages. Electron microscopic studies revealed intact bacteria or bacteria in varying states of degradation within phagolysosomes of the malacoplakic macrophages. Michaelis-Gutmann bodies arise within the phagolysosomes.
- **Epidem**: Woman to man ratio of 4:1. Peak incidence after age 50 yrs. Most pts have persistent UTI, *E. coli* being most common organism. Forty percent of pts have intercurrent systemic illness, carcinoma, AIDs, or autoimmune disease. Bilateral renal involvement in 64% with renal disease.
- **SSX**: renal – flank pain, nausea, vomiting, abdominal pain, palpable mass. Bladder – frequency, urgency, dysuria
- **DX**: Michaelis-Gutman bodies are pathognomonic. Percutaneous renal biopsy may be helpful in establishing DX.
  - ➢ Lab: UA and culture, CBC (anemia present in 82%, increased WBC in 60%)
  - ➢ Imaging: US demonstrates multiple irregular masses, renal enlargement, distorted echogenicity; CT demonstrates poor enhancement, lack of excretion, renal enlargement, multiple mildly enhancing, heterogeneous solid masses.

If bladder involved, CT demonstrates circumferential bladder wall thickening, multiple lobules, large masses.

- **RX**: Long-term antibiotics. Quinolones effective in 80–90% pts. Other agents such as Tm/S, which assist intracellular killing of bacteria may be used. Vitamin C and bethanechol may be helpful by increasing cGMP-cAMP ratio, which improves macrophage function. Nephrectomy for unilateral disease leads to 90% cure rate. For bladder lesions, treatment is transurethral resection of the lesion in addition to antibiotics.

Aspergillosis, Blastomycosis, Coccidiomycosis, Cryptococcus, Histoplasmosis

	Aspergillosis	Blastomycosis	Coccidiomycosis	Cryptococcus	Histoplasmosis
Cause	Aspergillus fumigatus, A. flavus, A. niger	Blastomyces dermatitidis	Coccidioides immitis	Cryptococcus neoformans	Histoplasma capsulatum
Epidemiology	Second to candida as opportunistic org in pts with malignancy, DM, immosuppression	Airborne in rotted wood dust. Great Lakes and Southeastern United States; GU involvement in 10–30% with systemic disease. Epididymis > prostate > kidney	Airborne spread (inhalation) of mycelial stage-infective spores. Worst in wet season. Increased prevalence in DM, steroid use, AIDS, immunocompromised	Ubiquitous fungus. Airborne, birds probable vector. Increased inicidence in immunocompromised and AIDS pts	Bat and bird vectors via airborne spores. Midwest and southern US
SSX	Fever, chills, flank pain, tenderness, hematuria	Frequency, hesitancy, urinary retention, nocturia, epididymal induration, large fluctuant prostate	That of disseminated disease, boggy or indurated prostate, scrotal swelling, indurated epididymis, draining sinus	Renal abscess: hematuria, pyuria, proteinuria Prostatic abscess: urinary retention, voiding difficulties Penis: may have exophytic mass	Prostate: obstructive voiding SX Epididymis: induration and fluctuance

	Aspergillosis	Blastomycosis	Coccidiomycosis	Cryptococcus	Histoplasmosis
DX	Urine fungal culture or tissue bx	Skin test – pos in < 40% cases Tissue – fungal stain "broad-neck" yeast forms in infected tissue	Culture and sensitivity of draining sinus; tissue bx—coccidiodal spherule	Urinalysis and culture. With renal infection only 40% have (+) culture. Tissue bx for culture and stain	Tissue bx with methamine silver may id org; disseminated dz, peripheral blood smears may show intraleukocytic budding yeast. In disseminated dz – anemia, thombocytopenia, (+) marrow cx and stain; comp-fix ab titer (+) in 96% with dissem dz. Immunodiffusion ab titer + in 87%, RIA for ag + in urine (90%) and blood (50%)
RX	IV amphotericin B or itraconazole. Endourologic rx if obstructing bezoar present; nephron-sparing surgery or nephrectomy for refractory cases	Mild or moderately severe disease, itraconazole may be used, if seriously ill, with CNS involvement, are immunocompromised rx with amphotericin B. Ketoconazole has been used in renal transplant pts.	Isolated lesions, such as epididymal, may be treated with excision alone; systemic disease treat with amphotericin B	Renal: IV amphotericin B – poor prognosis Prostate: fluconazole Penile: excisional bx, amphotericin B	Systemic amphotericin B: 0.5 mg/kg body wt IV × 2 wk total of 35–40 mg/kg/ body weight initial course. Ketoconazole 400 mg qd × 6 mos cures 85%

org = organism; bx = biopsy; GU = genitourinary; CNS = central nervous system; id = identify; dz = disease; cx = complication; ab = antibody; RIA = radioimmunoassay.

Retroperitoneal Fibrosis

- **Definition**: A chronic inflammatory process, usually of unknown cause, in which fibrous tissue surrounds the large blood vessels in the lower lumbar area, and may encase the ureters causing ureteral obstruction, occurring most commonly at the level btn the last lumbar and first sacral vertebrae.
- **Cause**: Proposed causes include retroperitoneal hemorrhage, urinary extravasation, trauma, perianeurysmal inflammation, XRT, surgery, inflammatory bowel disease, collagen disease, fat necrosis, malignancy, infections, methysergide (Sansert)-induced, and rarely associated with Reidel thyroiditis. In pts with AAA, RF thought to be secondary to a hypersensitivity reaction to antigens leaking into retroperitoneum from atheromatous plaques.
- **Epidem**: Incidence is 1 in 200,000. Men:women ratio of 2:1 to 3:1, peak incidence btn 40–60 yrs of age
- **SSX**: malaise, lumbar pain, anorexia, asthenia, low grade fever, edema, anemia, lower extremity edema, varicocele, hdyrocele
- **DX**: hx important to identify possible causative factors
  - ➢ Labs: elevated ESR in 94%, check serum electrolytes, BUN, creatinine
  - ➢ Imaging: CT or MRI helps establish diagnosis – demonstrates extent of disease
  - ➢ Path: bx must be obtained to rule out malignancy.
- **RX**: Varies with etiology. If sansert related, stop sansert. Favorable responses to different treatments including corticosteroids, tamoxifen, azothioprin, methotrexate, cyclophosphamide, penicillamine, used alone or in combination, with or without concomitant use of double J stent. Surgical RX (open or laparoscopic) consists of bilateral ureterolysis, even in the presence of unilateral disease. Surgical RX assoc with 90% long-term success rate.

Benign Renal Masses

	Adenoma	Oncocytoma	Angiomyolipoma	Lipoma	Juxtaglomerular Cell Tumor
Definition/cause	Benign small renal tumor derived from poss distal renal tubule origin	Benign adenoma composed of oncocytes ? distal tubule in origin	Benign renal tumor composed of 3 histologic components: blood vessels, adipocytes, and smooth muscle	Benign tumor composed primarily of fat cells	Benign neoplasm of juxtaglomerular cell origin
Epidemiology	? truly benign vs. malignant	Exact incidence unknown – approx 3–7% of prev dx'd RCCs felt to be oncocytomas	May occur as isolated phenomenon or as part of syndrome assoc with tuberous sclerosis – 80% angiomyolipomas occur in pts with tuberous sclerosis. Often bilateral and large. Tuberous sclerosis prevalence is btn 1 in 5000 and 1 in 15,000	Rare, noted in middle-aged women	2/3 occur in young women in their reproductive yrs, average 21 yrs at dx; women to men is 1.7:1, most $<$ 5 cm, often around 2.5 cm
DDX	RCC	RCC	Malignant and nonmalig-nant renal masses	liposarcoma	RCC, Wilms tumor, hemangiopericytoma, renal artery stenosis
SSX	Asxic – incidental finding	Hematuria, flank mass	Often asxic – sudden increase in pain may be	Flank pain, palpable renal	Blurry vision, HA, nocturia, HTN, fatigue

Benign Renal Masses (cont'd)

	Adenoma	Oncocytoma	Angiomyolipoma	Lipoma	Juxtaglomerular Cell Tumor
SSX (cont'd)			related to spontaneous bleed; may cause GI SX if large	Flank mass, +/− hematuria	
DX	CT scan – similar to RCC but < 3 cm no calcification	May have central scar on CT/MRI Path—large eosinophilic cells with granular cytoplasm	Lab: Hgb/Hct if severe pain CT – presence of fat within lesion characteristic of AML	CT – fatty renal mass confined within capsule	CT demonstrates tumor but cannot differentiate from other renal masses. Hypovascular mass on arteriography also rules out renal artery stenosis
Rx	Surgical excision ? partial nephrectomy	Consider partial nephrectomy if < 4 cm, well encapsulated, confined to one pole of kidney	Need to screen for tuberous sclerosis Indications for intervention: ? malignancy, spontaneous hemorrhage causing significant SX, pain, hematuria, risk of rupture. Selective embolization or nephron-sparing surgery if possible	Surgical excision	Surgical excision via partial or total nephrectomy depending on size and location of the lesion

Asixic = asymptomatic; RCC = renal cell carcinoma; HA = headache; ? = question.

Fibroepithelial Polyp

- **Definition**: Rare benign urothelial proliferative lesion.
- **Cause**: May be congenital or secondary to chronic irritation/infection.
- **Epidem**: Most (80%) occur in boys, 70% on left side, 62% at UPJ, remainder distributed in prder of frequency in posterior urethra, distal and mid ureter. Can occur at any age, men to women ratio is 3:2. Vary in length, usually 20–50 mm, but up to 135 mm.
- **SSX**: flank pain, dysuria, frequency, hematuria, hydronephrosis
- **DX**: Lab: urine cytology to rule out TCC
  - ➢ Imaging: CT scan helpful in identifying ureteral tumors and associated hydronephrosis if ureteral obstruction present
  - ➢ Other: cystoscopy, +/− retrograde studies/ureteroscopy helpful in identifying lesions – identification of a stalk is hepful in differentiating fibroepithelilal polyp in ureter from ureteral carcinoma.
- **RX**: Endoscopic resection of urethral polyps. Ureteroscopy and biopsy of ureteral lesions to confirm DX. Ureteral polyps can be removed endoscopically if stalk is visible, less commonly requires open excision. No recurrences noted if completely excised.

Renal Cell Carcinoma

- **Definition**: Cancer that develops in the lining of the renal tubules
- **Cause**: Smoking, obesity, HTN, RX for HTN, unopposed estrogen therapy, occupational exposure to petroleum products, heavy metals, and asbestos associated with increased risk. Hereditary RCC in adults include von Hippel-Lindau (VHL) assoc, VHL (3p26), tuberous sclerosis (9q34, 16p13), hereditary papillary RCC (7q34), hereditary leiomyoma RCC (1q42-43), hereditary renal oncocytoma, translocation from chromosome 3 to chromosome 2, 6, 8 or 11, lynch type 2 (2p16, 3p31), and medullary carcinoma kidney (11p). Four histopathophysiologic types of RCC identified:
  - ➢ Clear cell carcinoma (75–85% of tumors): Assoc with deletion of one or both copies of chromosome p, arises from proximal tubular epithelium
  - ➢ Chromophilic (papillary) (14% tumors): usually small tumors; often multifocal and bilateral. Assoc with monosomy 7 and 17. Two subtypes, type I basophilic and type II eosinophilic. Type I is often diagnosed at a lower stage and lower grade than type II, and has a better prognosis. Type I appears to be more common than type II, but metastases appear to occur more commonly with type II.
  - ➢ Chromophobic (4%): Most arise from intercalated cell of collecting duct. Better prognosis than clear cell usually. Assoc with hypodiploid number of chromosomes and multiple chromosome losses, but not 3p.
  - ➢ Collecting duct (Bellini's duct) tumor: rare, clinically aggressive
- **Epidem**: Accts for about 3% of all adult cancers. Approximately 32,000 new cases are diagnosed and 12,000 people die from the disease annually. Occurs most often in people btn ages 50 and 70. Affects men to women 2:1. Incidence and survival rate increasing. One third cases have mets at presentation and 50% of those resected for cure are expected to relapse during course of disease. Common sites of mets: lung, bone, liver, adrenal, brain
  - ➢ At least 4 hereditary syndromes assoc with RCC: (1) von Hippel-Lindau (VHL) syndrome (RCC occurs in 40% of those with VHL), (2) hereditary papillary RCC (HPRC), (3) familial renal oncocytoma associated with Birt-Hogg-Dube syndrome (BHDS), and (4) hereditary RCC.

- **SSX**: Abdominal pain (40%), malaise, palpable flank or abdominal mass (30–40%), hematuria (50–60%), fever, night sweats, weight loss, new-onset varicocele, malaise, hypercalcemia.
  - ➢ Paraneoplastic syndromes: hypercalcemia, erythrocytosis and nonmetastatic hepatic dysfunction (Stauffer syndrome). Polyneuromyopathy, amyloidosis, anemia, fever, cachexia, weight loss, dermatomyositis, increased ESR, and hypertension also assoc with RCC
- **DX**: Assess for HTN, supraclavicular adenopathy, flank or abdominal mass with bruit.
  - ➢ Approx 30% pts with RCC have met disease, organs involved include: lung (75%), soft tissues (36%), bone (20%), liver (18%), cutaneous sites (8%), CNS (8%)
  - ➢ Lab: UA, CBC with diff, electrolytes, BUN, creatinine, LFTs, calcium, ESR, PT/PTT
  - ➢ Imaging: CT scan chest, abdomen, pelvis with/without contrast – imaging procedure of choice for diagnosing and staging RCC. MRI useful in those with renal insufficiency
- **Staging**: Two systems used, Robston staging SX and TNM.
  - ➢ Robson classification:
    - ° Stage I – tumor confined within capsule of kidney
    - ° Stage II – tumor invading perinephric fat but still contained within Gerota fascia
    - ° Stage III – Tumor invading renal vein or inferior vena cava or regional lymph node involvement or both
    - ° Stage IV – tumor invading adjacent viscera or distant metastases
  - ➢ **TNM classification**
    - ° Primary tumor (T)
      - ▪ Tx –primary tumor cannot be assessed
      - ▪ T0 – no evidence of primary tumor
      - ▪ T1 – tumor 7 cm or smaller in greatest dimension, limited to the kidney
      - ▪ T2 – tumor larger than 7 cm in greatest dimension, limited to kidney
      - ▪ T3 – tumor extends in to major veins or invades adrenal gland or perinephric tissues but not beyond Gerota fascia
      - ▪ T3a – tumor invades adrenal gland or perinephric tissues but not beyond Gerota fascia
      - ▪ T3b – tumor grossly extends into renal vein or vena cava below the diaphragm
      - ▪ T3c – tumor grossly extends into renal vein or vena cava above the diaphragm
      - ▪ T4 – tumor invading beyond Gerota fascia
    - ° Regional lymph nodes (N)
      - ▪ Nx – regional lymph nodes cannot be assessed
      - ▪ N0 – no regional node metastasis
      - ▪ N1 – mets in a single regional node
      - ▪ N2 – mets in more than 1 regional lymph node
    - ° Distant metastasis (M)
      - ▪ Mx – distant mets cannot be assessed
      - ▪ M0 – no distant mets
      - ▪ M1 – distant mets

- **RX**: Surgical resection is the only known effective RX for localized RCC.
  - ➢ Radical nephrectomy via an open, laparascopic, or hand-assisted laparascopic approach. Radical nephrectomy involves complete removal of the Gerota fascia and its contents include resection of kidney, perirenal fat, ipislateral adrenal gland with or without ipsilateral lymph node dissection. Some advocate that adrenal gland should not be removed unless there is a large upper pole tumor. Nephron-sparing surgery (partial nephrectomy) indicated for those with solitary kidney, bilateral tumors, and in select pts in whom contralateral kidney is threatened by assoc disease processes such as HTN and DM, and also may be considered in those with small ($<$ 4 cm) polar tumors with normal contralateral kidney. Local recurrence rate after partial nephrectomy is 4–10%.
  - ➢ Advanced RCC: Hormonal therapy and chemotherapy have had little effect. Biologic response modifiers yield better results and include interferon alpha (objective response in up to 30% in select pts) and interleukin-2 (response rates of 13.5–18.6%). A variety of new biologic response modifiers have been approved for the management of advanced RCC (Table).

Biologic Response Modifiers

	Temsirolimus (Torisel)	Sunitineb (Sutent)	Everolimis (Afinitor)	Sorafenib (Nexavar)
Mechanism of action	Mammalian target of rapamycin (MTOR) inhibitor. Torisel binds to an intracellular protein FKB12 and the protein-drug complex inhibits the activity of MTOR that controls cell division. Inhibition of MTOR prevents transcription of mRNAs and translational proteins required for cell cycle progression from G1 to S phase.	A kinase inhibitor	A kinase inhibitor – indicated for pts with advanced RCC after failure of RX with sunitineb or sorafenib	A tyrosine protein kinase inhibitor – targets the Raf/Mek?Erk pathway (MAP Kinase pathway)
Dose	25 mg IV infusion over a 30–60 min period once/wk. RX continues until disease progression or signif toxicity. Prophylax with IV diphenhydramine 25–50 mg about 30 min prior to each dose of torisel	Starting dose is 50 mg QD for a schedule of 4 wks of treatment followed by 2 wks off treatment. Can be taken with or without food. Dose increments of +/− 12.5 mg recommended based on individ safety and tolerability	10 mg PO QD with or without food. Treatment interruption and or decrease dose to 5 mg may be needed to manage AEs	400 mg (two 200 mg tabs) PO bid. May change to 400 mg once daily or every other side if significant AEs
Efficacy	49% increase in median overall survival with Torisel (10.9 mos, range 8.6–12.7 mos) compared to interferon alpha (7.3 mos, range 6.1–8.8 mos), median	In 2 trials evaluating efficacy in pts with cytokine refractory mRCC – objective response rates noted in 34% and 36% treated with sutent	Superior to PBO for progression-free survival 4.9 mos (range 4–5.5 mos) for afinitor compared to 1.9 mos (1.8–1.9 mos) for PBO	In a study of pts with mRCC randomized to placebo or sorafenib, the progression free rate was significantly higher with sorafenib (50%) compared

	Temsirolimus (Torisel)	Sunitineb (Sutent)	Everolimis (Afinitor)	Sorafenib (Nexavar)
Efficacy (cont'd)				to placebo (18%) and the progression free survival significantly longer for sorafenib (163 days) than placebo (41 days)
Adverse effects	Hyperglycemia, hyperlipidemia, immunosuppression, interstitial lung dz, rash, asthenia, mucositis, nausea, edema, anorexia	Fatigue, asthenia, diarrhea, nausea, mucositis, stomatitis, vomiting, dyspepsia, abdominal pain, constipation, HA, rash, hand-foot syndrome, skin discoloration, altered tase, anorexia, bleeding	Stomatitis, infections, asthenia, fatigue, cough, diarrhea	Diarrhea, rash/desquamation, fatigue, hand-foot skin reaction, alopecia, nausea, vomiting
Warnings/ precautions/ DDIs	Caution when using with potent CYP3A4 inducers and inhibitors	CYP3A4 inhibitors may increase sutent plasma conc therefore dose reduction to a min of 37.5 mg; CYP3A4 inducers such as rifampin may decrease sutent conc therefore increase dose to max of 87.5 mg recommended; LV ejection fraction decreases to below lower limits of nl have occurred, monitor thyroid function tests	For pts with Child-Pugh Class B hepatic impairment decrease dose to 5 mg QD, if strong inducers of CYP3A4 increase dose in 5 mg increments to max of 20 mg QD; due to significant increase in exposure co-admin with strong or moderate CYP3A4 inhib should be avoided	When used concomitantly with docetaxal, doxorubicin or fluorouracil will increase area under the curve of these agents. CYP3A4 inducers increase metabolism of sorafenib and decrease sorafenib concentrations CYP2B6 and CYP2C8 substrates – caution systemic exposure is expected to increase with co-admin of sorafenib

CYP3A4 = cytochrome P450 3A4; AEs = adverse events; HA = headache; mRCC= metastatic renal cell carcinoma; nl = normal; LV = left ventricle; mos = months; PBO = placebo.

Renal Sarcomas

- **Definition**: Malignant neoplasm of the kidney that originates in the connective tissue of the kidney.
- **Cause**: unknown
- **Epidem**: Accts for 1–3% of malignant renal tumors. Incidence increases with age. Women:men ratio of 1.4:1, 40–60 yrs of age, rarely bilateral. Leiomyosarcoma accts for 60% of renal sarcomas, other lesions include liposarcoma (19% of renal sarcomas) and osteosarcoma. Most renal sarcomas arise from renal capsule or pericapuslar tissue.
- **SSX**: flank pain, gastrointestinal SX, flank mass, hematuria, weight loss
- **DX**: Lab: UA
  - ➢ Imaging: CT – with leiomyosarcoma the tumor tends to displace and compress the kidney – fat density with liposarcoma and bone density may be seen with osteosarcoma
- **RX**: Leiomyosarcoma: Radical nephrectomy – early local and distal recurrence common. With advanced disease may see some response with ifosfamide-based chemotherapy. Osteogenic sarcoma and liposarcoma best treated with radical nephrectomy.

Secondary Tumors of the Kidney

- **Definition**: Metastatic lesions to kidney
- **Cause**: Kidney is a frequent site of metastases from both solid and hematologic malignancies, most commonly lymphoma and lymphoblastoma. More commonly identified postmortem.
- **SSX**: often asymptomatic – may have flank pain, hematuria.
- **DX**: Lab: UA
  - ➢ Imaging: Often incidental finding on CT scan. Bx may be useful in determining if lesion is primary RCC vs. metastatic lesion.
- **RX**: as per primary tumor (above)

Transitional Cell Carcinoma of the Renal Pelvis and Ureter

- **Definition**: Malignant neoplasm arising from the urothelium of the kidney, ureter, and bladder
- **Cause**: Increased incidence with Balkan endemic nephropathy and cigarette smokers. Other possible causes include: analgesics, coffee consumption, cyclophosphamide, occupational carcinogens (aniline dyes), inflammation due to stones or infection, familial cancer syndromes
- **Epidem**: TCC accounts for 90% of upper tract tumors; male:women ratio 3:1; Caucasians:blacks 2:1. When ureter is affected, most commonly affects distal ureter
  - ➢ Upper tract TCC occurs in 2–4% of pts with bladder TCC
- **SSX**: gross or microscopic hematuria in 75%, hydronephrosis if lesion is obstructing, flank pain in 30%
- **DX**: Lab: UA and culture, urine cytology (inaccurate with low-grade lesions), renal pelvic washings
  - ➢ Imaging: CT scan is helpful in identifying lesion and staging, soft tissue mass ave HU 46, range 10–70.
  - ➢ Endoscopic evaluation – cystoscopy to rule out assoc bladder tumors (30–75% pts with upper tract tumors have TCC of bladder at some time); retrograde studies may demonstrate filling defect; ureteroscopy allows for further evaluation of lesion; biopsy and or endoscopic removal if lesion is papillary and small.

- ➢ Staging – TNM classification
  - ° Tis – carcinoma in situ
  - ° Ta – epithelial confined, usually a papillary lesion
  - ° T1 – tumor invades lamina propria
  - ° T2 – tumor invades muscularis propria
  - ° T3 – invasion of peripelvic, periureteral tissue or renal parenchyma
  - ° T4 – involvement of contiguous organs
  - ° N0 – no nodal involvement
  - ° N1 – only one pos node $\leq$ 2 cm
  - ° N2 – only one pos node 2 cm $\leq$ 5 cm or mult pos nodes $<$ 5 cm
  - ° N3 – pos nodes $>$ 5 cm
  - ° M0 – no hematogenous or distant mets
  - ° M1 – hematogenous or distant mets

- **RX**: Tumor grade and stage are most important prognostic variables.
  - ➢ Treatment varies with location of lesion – surgical treatment is the mainstay if no evidence of metastases.
  - ➢ Renal pelvic tumor – nephroureterectomy plus cuff of bladder
  - ➢ Proximal and midureteral tumors – if low grade, low stage lesion may perform segmental resection and reapproximation. If multifocal or moderately to poorly differentiated, then nephroureterectomy plus cuff of bladder.
  - ➢ Distal ureteral tumors – low grade without multifocal lesions treatment is distal ureterectomy and ureteral reimplantation, if high grade or multifocal lesions then probably best served with nephroureterectomy with cuff of bladder.
  - ➢ Primary endoscopic management has been used in patients with solitary kidneys, bilateral disease and renal insufficiency. Results are best with low grade, low stage lesions and recurrence rates are higher than with open surgical treatment and, thus, pts require periodic surveillance.
  - ➢ The role of adjuvant and neoadjuvant chemotherapy for invasive upper tract TCC is not clearly defined.

Renal Cystic Disease

	Renal Cyst	Acquired Renal Cystic Disease	Autosomal-Dominant Polycystic Kidney Disease	Autosomal-Recessive Polycystic Kidney Disease
Definition	Simple renal cysts that are not connected to any part of the nephron	Cystic changes that occur in pts with end stage renal disease	Autosomal dominant form of polycystic kidney disease – charac by micro- and macrocysts derived from entire nephron	Autosomal recessive form of polycystic kidney disease – characterized by enlarged kidneys with microcysts
Cause	May originate initially from a portion of the nephron	Cystic changes may be due to tubular obstruction secondary to interstitial fibrosis, deposition of calcium oxalate, proliferation of renal tubular epithelium, renal ischemia or altered compliance of tubular basement membrane. Decreased clearance of mitogenic polyamines and increased production of renal growth factors in pts on hemodialysis and peritoneal dialysis may lead to cyst formation	2 genes identified: *PKD1* and *PKD2*. *PKD1* localized at 16p13.3 and *PKD2* at 4q13.23. *PKD1* accts for 90–95% cases, *PKD2* for 5% cases. Result of tubular epithelial cell hyperplasia. Expansion of cysts mediated by epidermal growth factor (EGF)	Cysts derived primarily from the colleting ducts. Also characterized by biliary dysgenesis leading to congenital hepatic fibrosis and dilatation of intrahepatic ducts
Epidemiology	May present at any time soon after birth to old age. Incidence increases with age, 20% by 40 yrs, 33% by 60 yrs. May be single or multiple, unilateral or bilateral, majority $<$ 2 cm, but can vary up to $>$ 10 cm	Incidence 34–79% in pts on hemodialysis and appears to increase with duration on dialysis. Also noted in pts with peritoneal dialysis and chronic renal insufficiency. Men:women 2.9:1. Incidence higher in pts with nephrosclerosis	Prevalence of 1:800. Accts for 9–10% of pts in United States on chronic hemodialysis. Most identified at 30–50 yrs but may be seen in children. Men more renal involvement than women. Assoc abnls: cysts of liver, pancreas, spleen and lungs,	Earlier the age at dx the more severe the dz. Often assoc with olighydramnios and pulmonary hypoplasia. Most common heritable renal cystic dz to manifest in childhood. As many as 50% newborns die within first hrs

	Renal Cyst	Acquired Renal Cystic Disease	Autosomal-Dominant Polycystic Kidney Disease	Autosomal-Recessive Polycystic Kidney Disease
Epidemiology (cont'd)			aneurysms (circle of willis). Berry aneurysms in 10–40%. Colonic diverticula and mitral valve prolapse	to days of life – of those that survive neonatal period, only 50% alive at 10 yrs of age
DX	Bosniak classification of renal cyst: I. single, benign, fulfills US or CT criteria of simple cyst II. benign cystic lesion that is minimally complicated, i.e., septations, small calcifications, infection, or high density III. more complicated lesion with xray features seen in malignancy ie more extensive calcification IV. cystic malignant tumors		Bilateral renal enlargement, 3 hepatic cysts, cerebral artery aneurysms, solitary cysts of arachnoid, pineal gland, pancreas, or spleen. CT may help detect cysts in other organs	US demonstrates enlarged, echogenic kidneys due to multiple small cysts
RX	Simple cysts typically do not require rx. If causes pain, obstruction or HTN may unroof cyst, sclerose or laparoscopically unroof either transperitoneally or retroperitoneally	For pts on hemodialysis of $>$ 3 yrs duration should have screening US or CT. Frequency of screening thereafter depends on presence/absence of cysts and nature of them	Monitor BP and follow renal function. RX HTN if present, supportive rx of renal failure. If upper tract infection need to use lipid-soluble abx such as fluoroquinolone or Tm/S. Cyst pain can be relieved with unroofing	No cure. Initial treatment is supportive. Rx HTN with ACE inhibitor and calcium-channel blocker

ACE = angiotensin converting enzyme; Tm/S = trimethoprim sulfamethoxazole.

Circumcaval (Retrocaval) Ureter

- **Definition**: The right ureter deviates medially behind the inferior vena cava to cross in front of it from a medial to a lateral direction, to course distally to the bladder.
- **Cause**: Embryologic abnormality related to persistence of subcardinal vein and failure of supracardinal system to develop. Virtually always affects the right side.
- **Epidem**: Incidence 1 in 1200 cadavers. Men:women ratio is 2.8:1. Usually present in 3rd or 4th decade of life
- **SSX**: asymptomatic or may present with SX of obstruction – flank pain, N/V, hydronephrosis
- **DX**: US: may demonstrate hydronephrosis and dilated proximal ureter
  - ➢ Imaging: CT may establish diagnosis by delineating course of ureter.
  - ➢ Retrograde ureteropyelography demonstrates S-curve of ureter usually at L3–L4 and the retrocaval ureteral segment.
- **RX**: if obstruction present, requires transection of ureter and reapproximation anterolateral to the inferior vena cava

Renovascular Hypertension

- **Definition**: A secondary form of HTN, caused by a narrowing of the renal artery.
- **Cause**: Atherosclerosis of renal arteries, renal artery fibromuscular hyperplasia, coarctation of the aorta, other intrinsic renal disease. Decreased blood flow to the renal juxtaglomerular apparatus causes renin production leading to angiotensin II, which causes arterial constriction that in turn increases aldosterone.
- **Epidem**: About 0.2–4% of all hypertensives. Onset of HTN before age 30 or after 55 yrs is a sign of poss renovascular HTN. HTN often difficult to control requiring 3 or more drugs.
- **SSX**: A systolic-diastolic bruit in the epigastrium, usually transmitted to one or both upper quadrants and sometimes to the back, is almost pathognomonic, but is present in only about 50% of patients with fibromuscular dysplasia, rare in patients with renal atherosclerosis. If HTN severe then may have HA, CHF SX, epistaxis. Hemorrhages and exudates in fundi in 30%.
- **DX**: Lab – hypokalemia, proteinuria, high renin concentration, azotemia when an ACE inhibitor is administered; peripheral plasma renin activity measured in am in a seated subject and indexed against Na^+ excretion – high rate of secretion present in about 75% pts with proven renovascular HTN.
  - ➢ Captopril test – most sensitive office screening test for DX renovasc HTN – all 3 criteria must be met: (1) stim plasma renin activity of 12 mcg/L (ng/mL) per hr, (2) absolute increase in plasma renin activity 10 mcg/L per hr, (3) increase in plasma renin activity of 150% or more, or of 400% if baseline value is $<$ 3 mcg/L per hr. Sensitivity and specificity ranges from 72–95%.
  - ➢ Imaging: Renal scan before and after captopril 50 mg PO shows decreased flow in affected kidney, 90% sens/specif – of limited use in pts with bilateral disease, stenosis of solitary kidney or renal insufficiency.
  - ➢ Duplex ultrasonography – high sens (96.7%) and specif (98%) for detecting renal artery stenosis in 50% when compared to angiography
  - ➢ Spiral CT or MRI have high sensitivity (98% and 96%, respectively) and specificity (94% and 74%, respectively) for detecting renal artery stenosis.
  - ➢ Angiography is the gold standard.

- **RX**: Percutaneous transluminal angioplasty (PTA). Factors assoc with decreased likelihood of improving BP or renal function after rx include: age > 65 yrs, male, severe atherosclerotic dz, proteinuria > 1 g/day, GFR > 40 mL/min, no abrupt or worsening HTN, duration of HTN > 10 yrs, DBP < 80 mm Hg, systolic BP < 160 mm Hg, nonsmoker, renal artery stenosis < 70%. In coarctation, pre-treat with propranolol to prevent postop HTN.

Urolithiasis

- **Definition**: The formation of urinary calculi, or the condition associated with urinary calculi.
- **Cause**: Key event in stone formation is supersaturation. Supersaturation is followed by crystallization, which is dependent on urine pH, temperature, and concentration of the major urinary ions. Once crystallization occurs, aggragation and retention must occur for a stone to form. Causes of stone formation include:
  - ➢ Hereditary causes: familial distal renal tubular acidosis (RTA), cystinuria, xanthinuria, glucose-6-phosphate deficiency, hypoxanthine-guanine phosphoribosyl transferase deficiency, phosphoribosylpyrophosphate overactivity, oxaluria, dehydroxyadenineuria
    - ° Dietary excesses: vitamin C, oxalate, purines, calcium
    - ° Sedentary lifestyle or immobilization
    - ° Medication: thiazides, triamterene, indinivir, glucocorticoids, calcium supplements, acetazolamide, sulfonamides
    - ° UTIs with urea-splitting organisms (i.e., proteus)
    - ° Myeloproliferative disorders
    - ° Gastrointestinal disorders: intestinal resection, jejunoileal bypass, chron's disease, malabsorptive disorders
    - ° Dehydration
    - ° Hypercalcemic disorders: hyperparathyroidism, sarcoidosis, histoplasmosis, hyperthyroidism, leprosy, malignancy, tuberculosis, coccidiomycosis, silicosis, pheo
    - ° Anatomic abnls that may predispose to crystal formation include: medullary sponge kidney, ureteropelvic junction obstruction, UVJ obstruction, calyceal diverticulum, vesicoureteral reflux, ureterocele, horseshoe kidney.
    - ° Decreased urinary stone inhibitors: citrate, magnesium, nephrocalcin, Tamm-Horsfall mucoprotein
- **Epidem**: Prevalence of 2–3%. Recurrence rate about 10% at one yr and 50% at 10 yrs for calcium oxalate stones. Peak incidence in ages 20s to 40s. Men:women ratio is 3:1. Prevalence higher in mountainous, desert, and tropical areas and during summer.
- **SSX**: Flank pain, renal or ureteral colic, hematuria, pyuria, hydronephrosis, vomiting, urinary frequency, flank/abdominal tenderness. Fever not usually present unless there is a UTI.
  - ➢ **DX**: Lab: UA (check pH, red cells, WBC, and assess for crystals) if UTI suspected culture.
  - ➢ First time stone former: The NIH Consensus Conference of 1988 recommended that a single stone former should undergo blood tests to detect primary hyperparathyroidism (serum calcium and if elevated a PTH), other causes of hypercalcemia, and decreased renal function (BUN and creatinine).

Recurrent Stone Former or Metabolically Active Disease (Stone Increasing in Size)

Fasting Blood	24 Hr Urine – at least one, ideally 3 consecutive, on a regular diet
Calcium	Volume
Parathyroid hormone if calcium elevated	pH
Magnesium	Creatinine
Creatinine	Phosphate
Uric acid	Calcium
Sodium	Citrate
Potassium	Uric acid
	Magnesium
	Cystine – only need to check on one
	Sodium
	Potassium
	Sulfate
	Ammonium

- ➢ Imaging: Noncontrast spiral CT scan is the imaging procedure of choice – identifies stone size, location, and presence/absence of hydronephrosis. May also differentiate btn stone makeup based on hounsefield units. KUB is limited by overlying bowel gas and may not identify small stones. Similarly, US may not identify small stones.

- **RX**: Acute management – relief of pain and obstruction if present – varies with pts clinical status, size of stone, and stone location. Majority of small stones < 4–5 mm will pass spontaneously, whereas obstructing ureteral stones > 6 mm seldom pass spontaneously.
  - ➢ Small stone, pain well controlled with oral pain meds or asymptomatic – treat with hydration, oral pain control, consider expulsive medical therapy with alpha-blocker (i.e. tamsulosin, terazosin or doxazosin, silodosin)
  - ➢ If pain is poorly controlled and/or stone is large, treatment varies with stone size and location.
  - ➢ If obstruction and UTI, abx and decompression either via ureteral stent placement or percutaneous nephrostomy indicated first, followed by RX of stone.
  - ➢ Renal calculi: ESWL is often first line RX except for Staghorn calculi, which usually require percutaneous nephrolithotomy with or without ESWL. ESWL effective for management of stones < 2 cm in diameter. Larger stones may necessitate placement of ureteral stent to prevent obstruction from Steinstrasse. Smaller cystine stones (< 1.5 cm) may be treated with ESWL. In select cases, ureteroscopy and laser stone treatment may be performed for renal calculi.
  - ➢ Ureteral calculi: Distal ureteral calculi often treated with ureteroscopy and laser treatment. Proximal calculi may be treated with ESWL or ureteroscopy and laser treatment
  - ➢ Uric acid stones may be treated medically with alkalinization of the urine.
  - ➢ Chronic management: prevention
  - ➢ In general, dietary recommendations include: limiting protein (max 1 g/kg/day) and sodium (100 mEq/day) intake and increasing urine output to < 2 L/day. Treat abnormalities present in 24-hr urine studies.

Urolithiasis: Treatment of Metabolic Abnormalities

	Hypercalciuria	Hyperuricosuria	Hyperoxaluria	Cystinuria	Hypocitraturia	Hypomagnesuria
Definition	> 4 mg/kg body wt/24-hr, > 300 mg/24-hr for male, > 275 mg/24-hr for female	> 600–700 mg/ 24-hr urine	> 40–50 mg/24-hr urine	> 400 mg/24-hr urine	< 300–320 mg/24-hr urine (if < 50 mg, it's RTA)	< 50 mg/24-hr urine
Type	Absorptive (I and II): Normal serum Ca^{2+}, low PTH; type II, normal fasting urine Ca^{2+} Renal leak: Normal serum $Ca^{2+/-}$, high PTH, increased fasting urine Ca^{2+} Resorptive: High serum Ca^{2+}, high PTH, high fasting urine Ca^{2+}	70% dietary, 30% over-production; hyperuricosuria may initiate calcium oxalate stone formation by epitaxy gouty diathesis: Acidic urine (pH < 5.5) ± hyperuricosuria. Overproduction may be due to myeloproliferative dz, glycogen storage dz, malignancy, diarrhea	5 causes: overindulgence, excess vitamin C, endogenous production, primary hyperoxaluria, inflammatory bowel dz	Cystine solubility is pH dependent. Increased solubility with pH > 7.5	Citrate is a stone inhibitor; citrate excretion decreased by metabolic acidosis, hypokalemia, infections	Magnesium is an inhibitor of calcium crystallization
Diffdx	Diff type I and II: low Ca^{2+}, oxalate, Na^{+} diet for 1 wk, check 24-hr urine; if urine Ca^{2+} > 200 type I, if < 200 type II Diff type II from renal leak: 2-hr urine for Ca^{2+} after 14–16 hr, overnight fast: > 30 mg Ca^{2+} is renal leak		45–60 mg/d: dietary 45–400 mg/d: endogenous 80–400 mg/d: inflammatory bowel dz			
Prevention	Absorptive type I: Sodium cellulose phosphate + magnesium gluconate 1–1.5 gm bid and low-oxalate diet or thiazides hydrochloro-thiazide (50 mg bid) and KCl. Absorptive type II: Diet restriction to 600 mg per day of Ca^{2+} and low-oxalate dietary ± thiazides or sodium phosphate or potassium phosphate (500 mg tid or qid). Renal leak: thiazides	Hyperuricosuric calcium oxalate stones: Allopurinol 300 mg/d, Na^{+} restriction (150 mEq/d) or potassium citrate 60 mEq/d in 3 doses. Gouty diathesis: Alkalinize urine with sodium bicarbonate or potassium citrate to keep pH 7. Low-methionine diet	Dietary excess: Restrict primary hyperoxaluria: pyridoxine 800–1000 mg/d in divided doses and/or magnesium gluconate 500 mg bid; enteric: calcium 0.25–1 gm qid or cholestyramine 8–16 gm/d in divided doses	Alkalinize urine to pH 7.5 with potassium citrate 30–60 mEq/d in divided doses; D-penicillamine 2 gm in 4 divided doses, start at 250 mg/d, increase gradually, or tiopronin 800 mg/d in 3 divided doses on empty stomach. Titrate tiopronin and D-penicillamine to keep cystine < 400 mg/d in urine. Captopril in isolated cases	Potassium citrate 60–120 mEq/d in divided doses or potassium phosphate and sodium phosphate	Magnesium gluconate 500 mg po bid, magnesium oxide, or magnesium hydroxide

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Renal Trauma

- **Cause**: May be blunt (i.e., from motor vehicle accidents, falls, blunt physical contact with external objects) or penetrating (knife wounds, gunshot wounds, or other penetrating objects).
- **Epidem**: Blunt trauma accounts for 90% of renal injuries. Renal injury is present in about 10% of abdominal traumas. Pre-existing renal anomalies (e.g., UPJ obstruction) may make renal injury more likely following trauma. 70% of renal trauma involves minor injuries: superficial renal lacerations, renal contusions, small subcapsular hematomas. Major renal injuries consist of deep parenchymal lacerations into the collecting system, renovascular pedicle injuries, and shattered kidneys.
  - ➢ Renal trauma grading system:
    - ° Grade 1
      - ▪ Hematuria with normal imaging studies
      - ▪ Contusions
      - ▪ Nonexpanding subcapsular hematomas
    - ° Grade 2
      - ▪ Nonexpanding perinephric hematomas confined to the retroperitoneum
      - ▪ Superficial cortical lacerations less than 1 cm in depth without collecting system injury
    - ° Grade 3
      - ▪ Renal lacerations greater than 1 cm in depth that do not involve the collecting system
    - ° Grade 4
      - ▪ Renal lacerations extending through the kidney into the collecting system
      - ▪ Injuries involving the main renal artery or vein with contained hemorrhage
      - ▪ Segmental infarctions without associated lacerations
      - ▪ Expanding subcapsular hematomas compressing the kidney
    - ° Grade 5
      - ▪ Shattered or devascularized kidney
      - ▪ Ureteropelvic avulsions
      - ▪ Complete laceration or thrombus of the main renal artery or vein
- **SSX**: hypotension, abdominal pain, hematuria (degree of hematuria does not predict severity of renal injury), flank hematoma
- **DX**: Labs: CBC, electrolytes, BUN, creatinine, urinalysis
  - ➢ Imaging: Renal imaging is indicated with all penetrating trauma to the flank, back, or abdomen. In adult patients with blunt trauma, renal imaging is indicated for gross hematuria or microscopic hematuria if assoc with shock. CT scan is the preferred imaging modality – delayed films may be necessary to determine if urinary extravasation present.
- **RX**: Routine trauma care should be administered – ABCs of trauma care (airway, breathing, circulation)
  - ➢ Minor trauma: observation and bed rest until urine clears and vital signs stable
  - ➢ Major trauma: surgery indicated for uncontrolled bleeding, renovascular injury, nonviable parenchyma, or significant urinary extravasation

Ureteral Injury

- **Cause**: External trauma or iatrogenic. Iatrogenic injury may occur with gynecologic procedures (hysterectomy, oophorectomy, bladder neck suspension), general surgical procedures (colectomy, appendectomy, vascular surgery), aortoiliac bypass surgery, urologic surgery (ureterolithotomy, pelvic laparoscopic procedures).
- **Epidem**: Iatrogenic injury occurs most commonly at the pelvic brim where ureter crosses the iliac artery and where it courses posterior to the broad ligament and ovarian vessels in females.
- **SSX**: abdominal and/or flank pain, fever, ileus, watery vaginal discharge, increasing creatinine
- **DX**: Labs: UA and culture, electrolytes, BUN, and creatinine
  - ➢ Imaging: CT scan may be useful in detecting ureteral injuries.
  - ➢ If not diagnosed promptly, may lead to (1) urinoma and need for percutaneous drainage, (2) nonfunctioning or hydronephrotic kidney, (3) ureteral stricture.
- **RX**: Varies with degree of injury and time since injury. With minor injury may pass JJ stent. If ureteral defect is large, will require exploration and repair. With iatrogenic suture ligation, may attempt laparoscopic suture removal and placement of JJ stent.

Bladder Infections

	Bacterial cystitis	Emphysematous cystitis	Candidal UTI	TB	Schistosomiasis
Cause	*E. coli* accts for 75–90% of acute uncomplicated cystitis in women, staph saprophyticus in 5–15%. Enterococci and aerobic gram-neg rods other than *E. coli* acct for remainder	Complication of UTI with gas formation in the bladder wall or lumen	Fungal infection of urinary tract	Mycobacterium tuberculosis; virtually always secondary to renal TB	Infection with the parasite trematode, *Schistosoma hematobium*
Epidemiology	Uncomplicated UTI is a UTI in setting of functionally and structurally normal urinary tract. Complicated UTI: pyelonephritis and/or structural or functional abnlty that decreases efficacy of abx RX	*E. coli* most common organism. Other organisms: *Proteus mirabilis, Nocardia, Candida, Enterobacter, Klebsiella, Streptococcus, Clostridium perfringens*. Risk factors include women, elderly age, debilitated with predisposing factors such as glucosuria particularly from DM, urinary stasis from lower urinary tract obstruction or neurogenic bladder, recent UTIs, an	*C. albicans* most common (51%), *C. tropicalis* (25%), *C. parapsilosis* (12%), *Torulopsis glabrata* (9%), others (3%)	Usually starts at or around one or both ureteral orifices	Transmission occurs throughout African continent and Far East and Middle-East. Free-swimming cercaria penetrate skin or are ingested, become schistosomula in blood and mature into adults in blood vessels. Oviposition occurs primarily in pelvic lower urinary tract, bladder most frequently affected, but can affect distal ureter and kidney

	Bacterial cystitis	Emphysematous cystitis	Candidal UTI	TB	Schistosomiasis
Epidemiology (cont'd)		immunocompromised state or steroid therapy. Assoc with enterovesical fistula, diverticulitis, Crohn's disease, carcinoma of rectum/sigmoid			
SSX	Dysuria, frequency, urgency, urge incontinence, hematuria	Frequency, urgency, nocturia, dysuria, suprapubic tenderness, pneumaturia	Dysuria, flank pain, nausea, frequency, stranguria, pyuria, hematuria, pneumaturia, vomiting, oliguria, anuria	Dysuria, urgency, frequency	Pruritic, macular rash at site of penetration 3–18 hrs after exposure, Katayama fever at onset of oviposition; active schistosomiasis may be associated with hematuria and terminal dysuria
DX	UA and culture of midstream urine with $> 10^5$ orgs, or $> 10^2$ orgs if symptomatic Imaging: not indicated in most pts. May be indicated if suspect obstruction, UTI fails to respond to appropriate abx, unusual organism	UA and culture KUB: thin radiolucent streaks or gas bubbles outlining bladder wall; air within bladder lumen with air-fluid level in upright position US: bladder wall thickening with gas appearing as small echogenic foci within bladder wall and lumen CT: gas within bladder wall or lumen; may reveal other pathology such as diverticulitis	Urine microscopic: candidal fungi with budding forms or pseudohyphae. Urinary casts containing fungi diagnostic for renal infection. $>$ 10,000 on clean catch or cath'd specimen. PCR rapidy and accurately identifies Candida Imaging: US may identify fungal material in collecting sx; CT scan demonstrates fungal	Same as for renal TB (see page 7)	ECP (eosinophil cationic protein), an indirect assessment of eosinophilia, appears to be useful marker of both infection and of assoc bladder morbidity, reflecting inflammatory status of bladder wall. Terminally spined eggs in urine sediment of active infections. Midday urine best. Rectal bx may show eggs. KUB may demonstrate calcifications within urinary tract, CT also. VCUG identifies

Bladder Infections (cont'd)

	Bacterial cystitis	Emphysematous cystitis	Candidal UTI	TB	Schistosomiasis
DX (cont'd)		Cystoscopy—gas bubbles within shaggy, erythematous bladder wall	accretions as mass with density lower than stone		vesicoureteral reflux which occurs in 25%
RX	Tailor abx to urine culture results. Uncomplicated UTI RX for 3 days, > 7 days in women with sx that persist, hx recent UTI, DM or pregnancy. Complicated UTI treat for 10–21 days. Young men with uncomplicated UTI RX for 7 days. Older men RX as if complicated UTI. Bladder anesthetics: phenazopyridine 100 mg to 200 mg tid for 2 days or Uristat (Ortho-McNeil) 2 tabs PO tid for 1–2 days	Abx, bladder drainage, control blood sugar if elevated	Candidal cystitis: Fluconazole (PO or IV) – 400 mg loading dose then 200 mg/day for 14 days Amphotericin bladder irrigations (50 mg Amphotericin B in 1 L water or D5W admin at 42 mL/hr successful in 82–90% pts. If significant fungal accretions in kidney may require placement of percutaneous nephrostomy tube for drainage. Gold standard for disseminated or invasive disease is IV amphotericin, although similar results with fluconazole in non-neutropenic pts	Rx same as for renal TB (see page 7). If UVJ obstruction occurs, may require surgery	Metrifonate rx of choice in endemic areas. Dose: 7.5–10 mg/kg body weight, 3 doses at intervals of 14 days. Praziquantel preferred drug in office practice. Single dose of 40 mg/kg. Other agents include hycanthone mesylate, niridazole, and oltipraz. F/up at 3 mos intervals for 1 yr to ensure cure or decrease in egg excretion. Surgery indicated if obstruction, stones, bladder cancer

C + S = culture and sensitivity; orgs = organisms; hx = history; D5W = 5% dextrose in water.

Hemorrhagic Cystitis (HC)

- **Definition**: Cystitis associated with hemorrhage.
- **Cause**: In children may be related to infection with adenovirus type 11 and 21. May be secondary to BK virus infection in immunocompromised pts and those undergoing BMT. Other causes include: acrolein (the urotoxic metabolite of cyclophosphamide and ifosfamide), XRT to the pelvis and bladder, and an allergic reaction. Medications that may cause HC include: penicillin, NSAIDS, allopurinol, danazol, and risperidone.
- **Epidem**: HC related to acrolein occurs in 4–40% pts, mortality rate up to 75%. Five to 11.5% of pts undergoing pelvic XRT have bladder CX, including HC. HC typically occurs 6 mos to 10 yrs following pelvic XRT. High dose busulfan also appears to be a risk factor for HC.
- **SSX**: grossly bloody urine, clots, suprapubic pain
- **DX**: Labs – CBC, coags, UA, and culture (r/o UTI)
  - ➢ Imaging: For suspected obstruction, evaluate upper tracts with US or CT.
- **RX**: Preventative RX may be useful in pts receiving cyclophosphamide/ifosfamide: hydration and diuretic to maintain high urine output also Mesna can decrease risk of HC.
  - ➢ Ribavirin may be effective in pediatric pts undergoing BMT with HC. BK virus related – superhydration and if ineffective may laser the bladder lesions and/or parenteral vidabarine. XRT and acrolein-related HC: (1) continuous bladder irrigation (CBI); (2) intravesical alum, silver nitrate, carboprost, tromethamine, and formalin have been used; (3) systemic therapy with epsilon aminocaproic acid (amicar) or sodium pentosan polysulphate; (4) electrocauterization of bleeding areas in bladder; (5) neodydium yag laser of bleeding sites in bladder; (6) hydrostatic distention; (7) hyperbaric oxygen; (8) hypogastric artery embolization; (9) urinary diversion.

Eosinophilic Cystitis

- **Definition**: Bladder inflammation associated with eosinophils in the urine sediment and bladder wall.
- **Cause**: Proposed etiologies include: allergic reaction, bladder tumor, bladder trauma, parasitic infections, and chemotherapeutic agents; may be caused by an antigen-antibody reaction, which leads to production of various immunoglobulins, which causes activation of eosinophils and initiates the inflammatory process. Primary antibody IgE, which when it binds to antigen, causes degranulation of mast cells and activation of eosinophils.
- **Epidem**: Men:women ratio 1.3:1, slight preponderance seen among children. Assoc etiologic factors include: TCC bladder, TUR prostate, intravesical mitomycin C, tramilast, parasitic infection, eosinophilic enteritis, recurrent UTI, VUR, ovarian teratoma, sutures, chronic granulomatous disease, various foods.
- **SSX**: urgency, dysuria, suprapubic tenderness, hematuria, less commonly urinary retention, nocturia
- **DX**: Lab – UA may show pyuria, microhematuria, and occasionally eosinophilia. Serum: eosinophilia may be seen.
  - ➢ Imaging: VCUG may demonstrate VUR, bladder wall thickening, and small bladder capacity
  - ➢ Cystoscopy and bladder biopsy: erythematous, velvety, raised lesions in bladder or edematous bladder mucosa with ulcers. Bladder bx: eosinophilic infiltrate scattered throughout lamina propria and muscularis
- **RX**: TUR bladder lesion. Some cases are self-limiting. If persists or recurrent, treat with oral abx, antihistamines, steroids.

Differential Diagnosis for Fistula

	Colovesical (CVF)	Vesicovaginal (VVF)
Definition	Communication between bladder and colon	Communication between bladder and vagina
Cause	May be the result of diverticular disease, colon cancer, bladder cancer, irradiation, Crohn's disease, and ruptured appendix.	In developed countries, abdominal hysterectomy is most common cause. Gynecologic surgery accts for 70–80% of VVFs. Less common causes include: erosion of pessary or vaginal diaphragm, erosion from foreign body, TB of bladder. In undeveloped countries VVFs are obstetric related.
Epidemiology	Most commonly associated with diverticulitis (50%). Fistula on left side of the dome is most likely related to diverticular disease, whereas that on the right side is likely to be assoc with Crohn's disease.	In undeveloped countries, prolonged, difficult labor leads to increased pressure on bladder and bladder necrosis. Many gynecologic procedure-related VVFs are secondary to unsuspected bladder injury and extravasation and urinoma formation, which then drains into vaginal cuff.
SSX	Urinary frequency and urgency, dysuria, pneumaturia, suprapubic discomfort, GI SX	Abdominal pain, distention, SX of bladder irritability, hematuria, painless watery discharge from vagina, ileus.
Diagnosis	Lab: urine culture may show multiple organisms growing. Imaging: CT appears to have highest sensitivity in diagnosing colovesical fistula. Cystoscopy and cystogram useful in identifying location of fistula.	Lab: UA, culture. BUN and creatinine on vaginal fluid – if BUN and creatinine values exceed that of serum, confirms DX. Imaging: cystogram may identify the VVF, IVP or retrograde studies should be performed to rule out an assoc ureterovaginal fistula. Cystoscopy to identify size, location and number, and to assess degree of bladder inflammation. May instill fluid/dye (methylene blue or indigo carmine) into bladder and examine vagina with speculum. If prior XRT, need to also assess bladder capacity and bx fistula to rule out cancer.
Treatment	Depends on underlying bowel disease and often involves removal of affected segment of bowel and bladder closure, either open or laparoscopically.	Conservative RX: bladder drainage and abx. If fistula tract is small can try fulgurating the tract cystoscopically (success rate of 7–12.5%). Surgery: timing varies with degree of bladder inflammation. Large fistulas repaired through transabdominal or transvaginal approach depending on surgeon's experience. Small fistula often repaired transvaginally. Contraindications to transvaginal approach: high vault fistula, narrow vagina, close proximity to ureteral orifice. Vaginal repair success rate 85–90%, less with XRT-related. With XRT-related need to wait 6–12 mos post-XRT. Transabominal surgery successful in 86–100% cases.

Bladder Calculi

- **Cause**: In adults, commonly associated with bacteriuria, infravesical obstruction, neurogenic bladder, augmented (ileal or colonic) bladder, and rarely may be secondary to calculi migrating from the upper urinary tract. Dietary causes in children in such areas as Thailand, Indonesia, North Africa, Middle East, and Near East.
- **Epidem**: Uric acid stones identified in 50% people with bladder calculi, also calcium phosphate stones. Usually a single stone, but may be multiple. Pediatric bladder stones in endemic areas are usually ammonium acid urate or calcium oxalate stones and are the result of low phosphate, high oxalate, and acid diet.
- **SSX**: Intermittent dysuria, may be severe at end of urination if stone impacts at bladder neck. Terminal hematuria, interrupted stream related to obstruction from stone.
- **DX**: Lab – urinalysis and culture
  - ➢ Imaging: May be seen on plain film of pelvis if calcium-containing. US may demonstrate hyperechoic mobile lesion with shadowing.
  - ➢ Cystoscopy confirms presence, number, and size of stone(s).
- **RX**: Endoscopic or open stone removal depending on stone size. In adults, important to treat underlying dz (BOO, indwelling catheters) to prevent recurrence. In pts with indwelling catheters may use an irrigation of 0.25–0.5% acetic acid solution 2–3 times/day to help prevent stone recurrence.

Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS)

- **Definition**: The International Continence Society (ICS) advocates the term "painful bladder syndrome," defined as the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and nighttime frequency, in the absence of proven urinary infection or other obvious pathology. The NIADDK research defines IC by the presence of Hunner ulcers or glomerulations on cytoscopic examination, pain associated with bladder or urinary urgency and cystoscopy, and hydrodistention demonstrating glomerulations in $\geq$ 3 quadrants of bladder and $>$ 10 glomerulations per quadrant; bladder distended under anesthesia to 80–100 cm H_2O for 1–2 minutes, 1–2 times for evaluation of glomerulations as well as meeting a variety of exclusion criteria. Most argue that the NIADDK criteria are overly restrictive and may lead to misdiagnosis of patients presenting with early stages of IC/PBS and falsely decrease the prevalence of the disease.
- **Cause**: Exact etiology unknown. Most literature supports a disruption in the the glycosaminoglycan (GAG) layer that normally lines the bladder urothelium. This leads to increased urothelial permeability and the potential for penetration of the underlying urothelium by potentially caustic agents in the urine, thereby affecting nerves and muscles in the bladder wall. Some hypothesize that IC/PBS may have an autoimmune component, as more than 50% of pts with IC/PBS have a history of allergies. Antiproliferative factor (APF) has been identified in the urine of some patients with IC. APF inhibits repair of the GAG layer and normal turnover of the urothelium.
- **Epidem**: Estimates of the prevalence of IC/PBS have increased over time, and it is proposed that between 0.5% and 12.5% of US women may have IC/PBS. Historically, 90% of all patients with IC/PBS were women; however, a more recent study demonstrates women to men ratio of 5:1 rather than the historic 9:1. Prevalence among women $<$ 50 yrs of age has been demonstrated to be higher than women $\geq$ 50 yrs of age. The pt with IC/PBS often has the disease for more than 7 yrs before diagnosis.
- **SSX**: urinary frequency, urinary urgency, nocturia, bladder or pelvic pain that is temporarily relieved by voiding, tender bladder base on pelvic examination, dyspareunia, flares and remissions of symptoms. Women may note exacerbation during

premenstrual week. Flares may be triggered by diet, allergies, stress, and sexual activity. Pain also may occur in lower abdomen, back, urethra, and vaginal area.

- **DX**: Detailed history. Surveys to assess SX are O'Leary Sant indices and PUF scale. O'Leary Sant indices for monitoring progress following treatment; PUF designed for screening.
  - ➢ Lab: UA and culture, urine cytology if hematuria (microscopic or gross) or high risk (i.e., smoker), blood glucose
  - ➢ Further tests to support diagnosis:
    - ° Potassium sensitivity test (PST) – potassium (40 mL of a soln of potassium chloride [0.4 mol/L]) instilled into bladder of a pt with suspected IC/PBS may induce SX. Correlation btn PST results and SX-defined IC/PBS documented in numerous studies.
    - ° Anesthetic bladder challenge in pt with active discomfort is useful to determine if origin of pain is the bladder. Intravesical administration of lidocaine and bicarbonate.
    - ° Cystoscopy/hydrodistention less frequently performed for diagnostic purposes; hydrodistention may have a role in treatment of pts with refractory IC/PBS.
- **RX**:
  - ➢ Nonpharmacologic therapy:
    - ° Educating pt about SX, behavior modification for urinary urgency and frequency, physical therapy for trigger point release, stress reduction, and dietary manipulation.
    - ° Foods thought to act as irritants include: tomatoes, chocolate, citrus fruits and juices, coffee, alcohol, and carbonated beverages.
  - ➢ Pharmacologic therapy: Oral therapy:
    - ° Pentosan polysulfate sodium (PPS) – only oral medication currently approved by FDA for RX of IC/PBS, as it provides the bladder with a compound that is structurally analogous to the GAG layer; 100 mg PO TID for at least 6 mos.
    - ° Hydroxyzine – not FDA approved for IC/PBS – suppresses mast cell degranulation. Dosing starts at 25 mg QHS and may increase to 50–100 mg/day during allergy season.
    - ° Amitriptyline – not FDA approved for IC/PBS – used to regulate pain and urgency in bladder by modulating neuronal dysfunction and also has antihistamine properties. Dosing often starts at 25 mg QHS and may increase in 25-mg increments to 75 mg qhs as needed.
  - ➢ Intravesical therapy:
    - ° Dimethyl sulfoxide (DMSO) only intravesical therapy approved by FDA for IC/PBS. DMSO (50 mL of a 50% soln) placed in bladder via catheter and left in bladder for 15 min. Adminstered at 1–2 wk intervals for 4–8 treatments, with maintenance therapy every 1–2 months as needed. Intravesical heparin has been added to DMSO, but not approved by FDA.
    - ° Intravesical anthestics have been helpful in providing prompt pain relief during flares. Often contain an anesthetic such as 8 mL of 1–2% lidocaine accompanied by 3 mL 8.4% sodium bicarbonate or 1–2% lidocaine diluted in 8.4% sodium bicarbonate; PPS (a 100 to 200 mg capsule) or heparin (40,000 IU) is added to help restore the bladder mucosa overlying the urothelium.
    - ° Sacral nerve room stimulation has been shown to relieve pain, urgency, and frequency.
    - ° Cystectomy and urinary diversion performed only as a last resort.

Bladder Cancer

- **Cause**: Neoplasm. TCC accts for 90% bladder cancers. Other malignancies include: squamous cell carcinoma, adenocarcinoma, urachal carcinoma, and nonurothelial bladder tumors such as carcinosarcoma, spindle cell carcinoma, sarcoma, leiomyosarcoma, rhabdomyosarcoma, neurofibroma, pheochromocytoma, lymphoma, and metastatic disease to bladder.
- **Epidem**: In men 3 × more common than women. In 74% of cases, the bladder cancer is confined to the bladder at diagnosis. The American Cancer Society estimates 70,980 new cases diagnosed and 14,330 deaths in 2009 in the U.S. Despite the increased incidence, the rate of people dying from bladder cancer has decreased over the past 20 years.
  - ➢ Risk factors: cigarette smoking, exposure to aniline dyes, recurrent UTIs, chronic foley catheters, bladder stones, and previous pelvic XRT as treatment for another cancer. Hair coloring and dietary factors may also be risk factors. A review of the Surveillance, Epidemiology, and End Results (SEER) database found that pts with other primary tumors had a tenfold higher risk of bladder cancer compared with the general population; risk was highest in pts previously diagnosed with prostate cancer. Infection of the bladder with the parasite schistosomiasis markedly increases the risk of bladder cancer. Loss of chromosome 9q seen more frequently with superficial bladder cancers; loss of 17q, 5q, and 3p is more commonly associated with invasive bladder cancer.
  - ➢ Squamous cell carcinoma is associated with chronic infection with *Schistosoma hematobium*. Other causes include chronic irritation from calculi, infection, foley catheters, or bladder diverticula.
  - ➢ Adenocarcinoma is the most common type of bladder cancer occurring in exstrophic bladders.
  - ➢ Urachal carcinoma develops outside of the bladder and invades into the bladder wall beneath the normal urothelium.
- **SSX**: hematuria (gross or microscopic), urinary frequency, urgency, dysuria, flank pain if associated ureteral obstruction, weight loss, and lower extremity edema with advanced disease
- **DX**: Lab – UA and culture, serum alkaline phosphatase and chest x-ray if muscle-invasive disease identified
  - ➢ Urine cytology able to detect 40–60% of bladder cancers, but the ability of cytology to detect a tumor varies depending on the grade, stage, and location of the tumor. In low-grade, low-stage tumors, it detects 25–40% of the tumors. It will perform better as the grade and stage of the tumor increase, with the best detection rate (~90%) being for carcinoma in situ.
  - ➢ NMP 22 (Matritech, Newton, MA) is a protein that undergoes changes when a bladder cell becomes cancerous. A test for this protein looks for the altered protein in the urine; 70–80% of patients with bladder cancer will have a pos result, but only 64% of patients with a pos result have cancer.
  - ➢ BTA (Polymedco, Cortlandt Manor, NY) is another protein found in bladder cancer cells but not in normal cells.The test identifies 50–80% of patients with bladder cancer, but the false-pos rate is similar to NMP 22, limiting its use.
  - ➢ ImmunoCyt tests for the presence of 3 different proteins simultaneously. Its ability to detect bladder cancer varies from 40–100%. The false-pos rate is somewhat better than NMP 22 or BTA at approx 20%. ImmunoCyt appears to be somewhat better in detecting low grade tumors.

- ➢ Fluorescent in situ hybridization (FISH; Uro Vysion kit, Visys, Inc./Abbot Laboratories, Downers Grove, IL) test is able to look directly at the DNA of a cell, searching for malignant cells. Under the microscope, malignant cells light up like a neon sign. Can detect more cases than conventional cytology (73% for FISH vs. 63% for cytology) with a false-pos rate of close to 0%. It may detect a tumor up to a year before it can be seen with a cystoscope and is reliable in pts who have had intravesical therapy with BCG or mitomycin C, situations in which cytology and ImmunoCyt do not work well at all.
- ➢ Imaging: A CT scan of the abdomen and pelvis with and without contrast is indicated in patients with newly diagnosed bladder cancer and those with muscle invasive disease.
- ➢ Cystoscopy identifies the lesion and a cystoscopy and transurethral resection of the bladder turmor (TURBT) will help in grading and staging of the tumor. In the case of small superficial tumors, the TURBT is also therapeutic.

• **RX**: depends on the type of bladder cancer, the grade and stage and the pt's overall medical status.
- ➢ Staging of bladder cancer – TNM staging system
  - ° T0 – no evidence of primary tumor
  - ° Ta – noninvasive papillary tumor
  - ° Tis – carcinoma in situ
  - ° T1 – tumor invades subeptihelial connective tissue
  - ° T2 – tumor invades muscle
    - ▪ T2a – superficial muscle
    - ▪ T2b – deep muscle
  - ° T3 – tumor invades perivesicle tissue (fatty tissue surrounding bladder)
    - ▪ T3a – microscopically
    - ▪ T3b – macroscopically
  - ° T4 – tumor invades adjacent organs/pelvic structures
    - ▪ T4a – tumor has spread to the prostate, uterus, and/or vagina
    - ▪ T4b – tumor has spread to the pelvic wall or the abdominal wall
  - ° N0 – no evidence of lymph node metastases
  - ° N1 – bladder cancer is found in one lymph node, $\leq$ 2 cm (0.8 in.) in dimension
  - ° N2 – bladder cancer is found in one or more lymph nodes, none $>$ 5 cm (2 in.) in dimension
  - ° N3 – bladder cancer is found in one or more lymph nodes, $>$ 5 cm (2 in.) in dimension
  - ° M0 – no evidence of metastases
  - ° M1 – metastatic disease

• **RX**:
- ➢ TCC
  - ° CIS – Assoc with increased risk of invasive disease. Most effective RX is intravesical BCG (Bacillus Calmette Guerin, a live attenuated form of *Mycobacterium bovis*); complete response in 70–75% pts. Other intravesical therapies include: mitomycin C, doxorubicin, interferon, valrubisin, and thiotepa. Combination of BCG plus interferon may work in BCG failures. Intravesical gemcitabine and photodynamic therapy remain investigational.
  - ° Ta – low grade disease – cystoscopy, urine cytology q 3 months for the first 2 years, q 6 months for the next 2 years and yearly thereafter as long as no recurrences are noted. If a recurrence is identified, it is treated and the pt returns to

the initial surveillance schedule. In pts with high grade disease, multiple tumors and/or recurrent disease consider intravesical BCG therapy.
    - T1 – consider re-resection if any question of residual tumor. Approx 30% will progress to invasive disease, particularly if high grade. Consider intravesical BCG. Factors that predict risk of progression include depth of invasion, multifocality, and presence of CIS. In high-risk pts radical cystectomy is an alternative to intravesical therapy and surveillance.
    - T2–T4, N0–N2, M0 – best treated with radical cystectomy, bilateral pelvic lymph node dissection (BPLND) (the extent of the dissection is controversial), urinary diversion, or orthotopic neobladder. Role of adjuvant chemotherapy in pts at high risk for recurrence/metastatic disease is not well defined.
    - Metastatic TCC – chemotherapy with MVAC (methotrexate, vinblastine, adriamycin, and cisplatin) is standard chemotherapy regimen. The combination of gemcitibine and cisplatin produces similar response rates and less toxicity, and is preferred RX regimen in pts with good renal function.
  - Other bladder malignancies
    - Squamous cell carcinoma – aggressive surgical management if possible, radical cystectomy, BPLND, and urethrectomy
    - Adenocarcinoma – radical cystectomy and BPLND is best chance for cure; responds poorly to XRT and chemo
    - Urachal carcinoma – radical cystectomy with en bloc excision of the urachus

Bladder Trauma

- **Cause**: Blunt or penetrating trauma to lower abdomen/pelvis
- **Epidemiology**: Blunt trauma (MVA most common) accts for 67–86% of bladder ruptures and penetrating trauma 14–33%; pelvic fractures identified in 89–100% of extraperitoneal bladder ruptures; 10% pts have combined intraperitoneal and extraperitoneal bladder rupture.
- **SSX**: lower abdominal tenderness, suprapubic pain, suprapubic/perineal/pelvic ecchymosis, hematuria, anuria
- **DX**: high index of suspicion – if pelvic fracture need to r/o urethral/bladder injury – if blood at the meatus, pt needs to have a retrograde urethrogram first to rule out urethral trauma.
  - Labs – UA and culture, CBC, electrolytes, BUN, creatinine
  - Imaging – cystogram – bladder should be filled with at least 300 mL of H_2O-soluble iodinated contrast and anterior/posterior, oblique/lateral, and post void/drainage films obtained.
  - CT cystogram – advantage – allows for assessment for other intra-abdominal or pelvic pathology and if properly performed is as sensitive as cystogram for identifying bladder rupture
- **RX**: Intraperitoneal rupture best treated with exploration and repair
  - Extraperitoneal rupture may heal with urethral catheter drainage for 7–10 days – if bony spicules penetrating, bladder will require open repair

Inverted Papilloma

- **Definition**: A benign bladder lesion characterized on histopathology by papillary fronds projecting into the fibrovascular stroma of the bladder with a thin layer of urothelium overlying the lesion.
- **Cause**: May result from chronic inflammation or bladder outlet obstruction

- **Epidem**: Most common in bladder trigone and bladder neck. Men:women ratio of 3–7:1. May contain cystitis cystica or squamous metaplasia. If high immunoreactivity for p53, may be susceptible to malignant transformation.
- **SSX**: flank pain, LUTS, hematuria
- **DX**: Labs – urine cytology to rule out malignant cells
  - ➢ Cystoscopy: lesion appears as small raised nodule
- **RX**: TUR of the lesion

Squamous Metaplasia of Bladder

- **Definition**: Reactive process where there is replacement of urothelial mucosa by squamous epithelium.
- **Cause**: chronic bladder irritation, chronic indwelling foley catheter
- **Epidem**: Women > men; nonkeratinizing squamous metaplasia of the bladder is believed to be benign while keratinizing squamous metaplaplasia is believed to be a premalignant condition.
- **DX**: Labs – UA and culture
  - ➢ Cystoscopy and biopsy if lesion appears suspicious
- **RX**: non-keratinizing squamous metaplasia does not require treatment. Individuals with chronic indwelling foley catheter for > 5 yrs require surveillance for malignant transformation.

Nephrogenic Adenoma

- **Definition**: A benign tumor of the urinary bladder mucosa, composed of glandular structures resembling renal tubules.
- **Cause**: Metaplastic response of the urothelium to local traumatic irritation, e.g., UTI, open or endoscopic procedures, calculi, intravesical chemotherapy/immunotherapy, radiation therapy
- **Epidem**: Men > women; manifests a long time after initial insult. Most cases involve bladder, 11% renal pelvis, and less frequently prostatic urethra and ureter. Size varies from small to > 7 cm. Incidence up to 4.8% in renal transplant recipients.
- **SSX**: dysuria, urinary frequency, urgency, hematuria
- **DX**: Labs – UA, culture, urine cytology to r/o malignant cells
  - ➢ Cytoscopy – may appear similar to muscle invasive TCC or be papillary and exophytic
- **RX**: TUR lesion

Cystitis Glandularis

- **Definition**: A rare proliferative disorder of the mucus-producing glands within the mucosa and submucosa of the bladder epithelium
- **Cause**: Assoc with chronic UTIs, obstruction, stones. Other possible etiologies include: avitaminosis, toxic metabolites, hormonal imbalance, carcinogen-related, humoral immunology alterations.
- **Epidem**: Incidence 0.1–1.9%. Increased incidence in pts with pelvic lipomatosis. Occurs in children. Malignant potential; 10–42% coincidence with adenocarcinoma
- **DX**: Differential
  - ➢ von Brunn's nests – normal epithelium in lamina propria
  - ➢ Cystitis cystica – similar to von Brunn's nests, but urothelium has undergone liquefaction
  - ➢ Cystitis follicularis – submucosal follicles; nonneoplastic response to chronic bacterial infection

- **SSX**: dysuria, urgency, frequency, hematuria, mucus in urine
- **DX**: Lab – UA and culture, urine cytology
  - ➢ Cystoscopy – often multiple lobulated or papillary lesions
- **RX**: TUR to diagnose. Treat inciting disease process. Recommend f/up cysto in 1 yr due to increased incidence of adenocarcinoma.

Cystocele

- **Definition**: Herniation of the bladder through the wall of the vagina.
- **Cause**: Due to either overstretching and attenuation of anterior vaginal wall or detachment or elongation of anterior vaginal supports to pelvic diaphragm.
- **Epidem**: About 70–80% cystoceles caused by damage to lateral support
  - ➢ Cystoscele grading on physical examination
    - ° Grade 1 – minimal bladder descent
    - ° Grade 2 – descent to vaginal introitus with stress maneuver
    - ° Grade 3 – descent to vaginal introitus at rest
    - ° Grade 4 – descent beyond vaginal introitus
- **SSX**: difficulty emptying the bladder during urination, frequent urination, urgency to urinate, painful urination, feeling of a bulge in the vagina and, rarely, stress incontinence, incomplete bladder emptying, UTI, dyspareunia, back pain
- **DX**: Lab – UA and culture
  - ➢ Imaging – bladder scanner or ultrasound postvoid residual determination to evaluate bladder emptying. Renal US indicated in pts with grade 4 cystocele to rule out hydronephrosis
  - ➢ Urodynamics may be helpful in select cases.
- **RX**: Depends on severity of the cystocele and bother. A vaginal pessary may be used in those individuals who do not want or are not candidates for surgery. Surgical approaches include transabdominal, Kelly plication/anterior colporrhaphy and transvaginal procedures – will vary depending on surgeon and extent of disease. Complications of cystocele repair include: de novo urge incontinence (14%), de novo stress incontinence (2%), and recurrent cystocele. Other less common complications include urinary retention, ureteral obstruction, bladder injury, and significant bleeding.

Urodynamic Testing

- **Definition**: A study to assess how the bladder and urethra function both in storing and releasing urine. Urodynamic tests assess bladder, urethral and pelvic floor muscle functioning, and may be indicated for evaluation of urinary incontinence, frequent urination, sudden strong urges to void, difficulty initiating voiding, pain with urination, incomplete bladder emptying, recurrent urinary tract infections, weak stream, and urinary retention.
- **DX**: There are several components to urodynamic testing and which components are used varies with the pt's symptoms.
  - ➢ Uroflow – volume of urine voided per urethra per unit of time (mL/sec), reflects combined activity of detrusor and urethra. Parameters to asses include maximum flow rate (Q max) (normal for men $>$ 60 yrs is $>$ 13 mL/sec and women $>$ 50 yrs $>$ 18 mL/sec), total volume voided (to be considered an adequate study pt should void at least 150 cc), and flow pattern (normal pattern is a bell shaped curve); with outflow obstruction and/or decreased bladder contractility may have a flattened curve or staccato pattern.
  - ➢ CMG and VCUG – Continuous measurement of bladder (CMG) pressure during bladder filling to measure bladder compliance (ability of bladder to store urine at low pressure, measured as change in volume/change in pressure, and to identify

involuntary detrusor contractions which are phasic increases in bladder pressure during filling that may or may not be sensed by the patient). The fluoroscopic visualization of the bladder and urethra during bladder filling and voiding (VCUG) is helpful to assess for vesicoureteral reflux, bladder diverticuli, and bladder outflow obstruction. If fluoroscopy is used, referred to as videourodynamics.

- ➢ Pressure/Flow Study – simultaneous measurement of detrusor pressure and flow rate. Useful to assess bladder outlet obstruction.
- ➢ Bladder leak point pressure (BLPP) – a measurement obtained in pts with neurogenic bladder, the bladder pressure at which urinary leakage per urethra occurs. BLPP $>$ 40 cm H_2O is associated with increased risk of upper tract damage.
- ➢ Valsalva leak point pressure (VLPP) measures pressure that abdominal musculature must generate to overcome resistance of sphincteric mechanism for urethral leakage to occur. A normal sphincteric mechanism will not allow for urethral leakage no matter how high the abdominal pressure. VLPP $>$ 90 cm H_2O is associated with stress urinary incontinence (SUI), VLPP $<$ 60 cm H_2O is associated with intrinsic sphincteric deficiency (type III SUI).
- ➢ Electromyograph (EMG) – simultaneous measurement of sphincteric activity during filling and voiding. Useful in assessing for detrusor sphincter dyssynergia (DSD) in patients with neurogenic bladders and dysfunctional voiding. Normally sphincter activity increased during bladder filling, relaxes just prior to voiding and remains relaxed during voiding and increases when voiding completed.

Urinary Incontinence

- **Definition**: the inability to control the flow of urine
- **Cause**: May be transient (reversible) or established (persistent). Etiologies of transient incontinence include DIAPPERS: delirium, infection, atrophic urethritis/vaginitis, pharmacologic, pyschologic, endocrine, restricted mobility, and stool-fecal impaction. Persistent incontinence may be due to a disorder of the bladder, the bladder outlet, or both, including urgency incontinence, stress incontinence, overflow incontinence, and mixed urinary incontinence.
- **Epidem**: In the community, 5–15% of the elderly suffer from incontinence at least weekly and $>$ 50% in a nursing home setting. SUI has an overall prevalence of 10% to 30% in women btn the ages of 15 and 64 years. Approximately 16% of adult Americans suffer from overactive bladder.

Differential Diagnosis for Urinary Incontinence

	Stress Urinary Incontinence (SUI)	Urgency Urinary Incontinence (UUI)	Mixed Urinary Incontinence	Overflow Urinary Incontinence
Definition/Cause	Complaint of involuntary leakage on effort or exertion, or on sneezing or coughing. May be secondary to abnormal urethral closure function, loss of normal function of supporting structures of the urethra from anatomic, hormonal, or neurologic causes.	A symptom syndrome including urgency (a sudden compelling desire to void that is often difficult to defer with or without urgency urinary incontinence and often associated with urinary frequency and nocturia in the absence of pathologic or metabolic conditions which may cause/mimic the symptoms. Affects approximately 33 million Americans, males and females. Neurogenic, myogenic, and combined theories have been proposed	Combination of SUI and UUI	Involuntary loss of urine due to overdistention of the bladder. May be secondary to decreased bladder contractility and/or bladder outlet obstruction (benign prostatic enlargement, urethral stricture, bladder neck obstruction)
SSX	Leakage of urine on exertion, or on sneezing or coughing	SX of overactive bladder include: urgency, urinary frequency (8 or more micturitions per day) and nocturia (awakening at night one or more times to void). Men tend to be OAB dry and women more likely to be OAB wet	SX of both SUI and UUI	Decreased force of stream, urinary frequency, feeling of incomplete emptying. Lower abdominal distention, incontinence without urgency

Differential Diagnosis for Urinary Incontinence (cont'd)

	Stress Urinary Incontinence (SUI)	Urgency Urinary Incontinence (UUI)	Mixed Urinary Incontinence	Overflow Urinary Incontinence
DX	Two generic types of SUI: urethral hypermobility and intrinsic sphincter deficiency (ISD). Differentiation btn them involves physical examination and a urodynamic study. On physical examination, urethral hypermobility characterized by downward descent of the blader neck and urethra on exam during a valsalva manuever. Urodynamic studies allow for assessment of the abdominal leak point pressure (ALPP) also called valsalva leak point pressure, i.e., the increase in abdominal pressure required for urine leakage. Urethral hypermobility ALLP $>$ 60 cm of H_2O. ISD ALPP $<$ 60 cm of H_2O. Hypermobility and ISD frequently coexist.	Urinalysis and culture, bladder scan PVR if SSX of bladder outflow obstruction. History important – assess fluid intake (volume and type), severity of SX and bother. Physical exam – to rule out neurologic lesion, significant pelvic organ prolapse, prostatic abnls, fecal impaction. Urodynamic study rarely needed in the initial evaluation and management – may be useful in refractory cases.	See DX SUI and UUI	Increased postvoid residual determined by bladder scanner, bladder US, or catheterization. Check BUN and creatinine; if elevated obtain renal US to rule out hydronephrosis.

	Stress Urinary Incontinence (SUI)	Urgency Urinary Incontinence (UUI)	Mixed Urinary Incontinence	Overflow Urinary Incontinence
RX	Pelvic floor muscle exercises, weight reduction Medical therapy – alpha-adrenergic agents, imipramine and, if no contraindications, topical estrogen therapy. Minimally invasive procedures such as transvaginal tape (TVT), transobturator tape (TOT), pubovaginal sling, periurethral collagen injection.	Behavioral and pharmacologic therapy either alone or ideally in combination are first line therapies. Behavioral therapy consists of education, bladder training, pelvic floor muscle exercises (quick flicks), dietary and lifestyle modifications (avoiding caffeine, acidic foods, too much/too little fluid intake, weight loss, smoking cessation). Pharmacologic therapy – antimuscarinic agents are the only FDA approved therapies for treatment of OAB. Common side effects of antimuscarinics include dry mouth and constipation. Other side effects, including tachycardia, blurry vision, and cognitive effects, may vary among agents. Oxybutynin immediate release (Ditropan) – 2.5 to 5.0 mg bid to qid. Oxybutynin extended release (Ditropan XL)– 5 mg to 30 mg qd.	Typically treat most bothersome symptoms first.	If acute, a trial of foley catheter drainage followed by a voiding trial. If SX are chronic, and/or failed voiding trial, best to start clean intermittent catheterization (CIC) three to four times a day to keep PVRs less than 500 cc. Urodynamic studies to assess detrusor contractility. For individuals with BOO secondary to benign prostatic enlargement may try alpha-blocker (terazosin, doxazosin, tamsulosin, afluzosin) to see if improve SX. If urethral stricture may require surgical intervention depending on severity. If atonic, bladder will require long-term CIC.

Differential Diagnosis for Urinary Incontinence (cont'd)

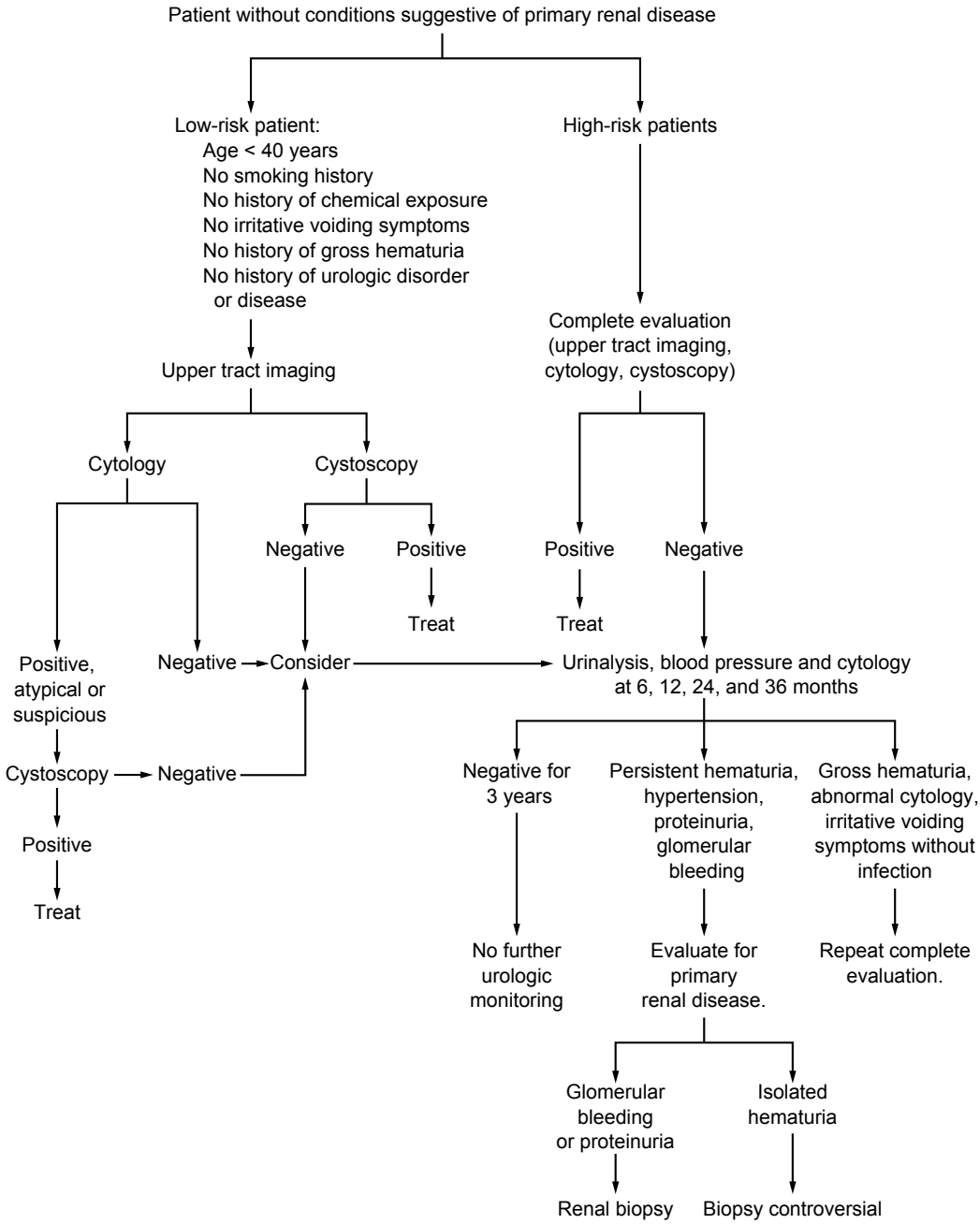
	Stress Urinary Incontinence (SUI)	Urgency Urinary Incontinence (UUI)	Mixed Urinary Incontinence	Overflow Urinary Incontinence
RX		Transdermal oxybutynin patch (Oxytrol) – delivers 3.9 mg of oxybutynin/day, applied twice weekly. Transdermal oxybutynin gel (Gelnique). Apply one sachet per day. Each sachet contains a 1 gram unit dose (1.14 mL) of 100 mg/g oxybutynin chloride gel. Tolterodine immediate release (Detrol) – 1–2 mg PO bid. Tolterodine extended release (Detrol LA) – 2–4 mg PO qd. Solifenacin (Vesicare) – 5 mg to 10 mg PO qd. Trospium chloride immediate release (Sanctura) – 20 mg PO bid. Trospium chloride extended release (Sanctura XR) – 60 mg QD. Darifenacin (Enablex) – 7.5 to 15 mg PO qd. Fesoterodine (Toviaz) – 4 mg to 8 mg PO qd. Neuromodulation may be indicated for refractory patients. Botulinum toxin remains experimental for use in OAB.		

OAB = overactive bladder; BOO = bladder outflow obstruction; PVRs = postvoid residual (volume); CIC = clean intermittent catheterization.

Hematuria

- **Defintion**: Presence of red blood cells in the urine. May be gross or microscopic (3 or more red blood cells per high power microscopic field in urine sediment).
- **Cause**: medical renal disease, stones, infection, tumors
- **Epidem**: Approx 20% of asxic men with microscopic hematuria will have urologic pathology, 5–15% have bladder cancer. Renal vs. urologic disease: casts, significant protein, and dysmorphic red blood cells suggest medical renal disease.
- **DX**:

DecisionT reeforHem aturia



Adapted with permission from Grossfeld GD, Wolf JS, Litwin MS, Hricak H, Shuler CL, Agerter DC, Carroll P. Evaluation of asymptomatic microscopic hemauria in adults: the American Urological Association best practice policy recommendations. Part II: patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation and follow-up. *Urology* 2001;57(4): 631-2.

- Gross hematuria – UA and culture, urine cytology
- CT scan of abdomen and pelvis with and without contrast to rule out stones, tumors, obstruction
- Cystoscopy to rule out bladder lesions and if actively bleeding identify source of bleeding
- May require further evaluation to rule out arteriovenous malformation if recurrent bleeding without identifiable source and cystoscopy identifies bloody efflux from one ureteral orifice, in the absence of underlying medical renal disease.

Genital Ulcers

	Genital Herpes	Syphilis	Chancroid	Lymphogranuloma Venereum	Granuloma Inguinale
Cause	Herpes simplex virus, usually type II but 10–25% cases assoc with type I (*NEJM* 1981;305:315; *J Antimicrob Chemo* 1983;12:79)	Spirochete, *Treponem pallidum* incubation about 3 wk	*Haemophilus ducreyi* gram-negative coccobacilli, "school of fish" appearance on Gram stain	*Chlamydia* trachomatis serotypes L1, L2, and L3	*Calymmatobacterium granulomatis* encapsulated gram (+) bacteria
Si/Sx	1st episode more severe than recurrent, dysuria 44% males, 83% females, weakness, sensory loss, impotence, malaise, anorexia, urinary retention, constipation, fever, tender adenopathy	Primary: painless lesion (chancre) heals in 3–4 wk, adenopathy Papule becomes indurated and punched out. Secondary: skinrash, painless adenopathy, low-grade fever, malaise, pharyngitis, laryngitis, anorexia, weight loss, arthralgias. Tertiary: sx reflect organ, sx affected; classic neurologic sx include tabes dorsalis, Argyll-Roberts pupil	Incubation 1–4 d, nonindurated, ragged, undermined painful ulcer may be assoc with painful adenopathy. Base of ulcer is friable. If untreated, becomes suppurated with periadenitis (bubo formation). Chronic draining sinuses may occur	Incubation 3–30 d. 3 stages: (1) small asx papule or herpetiform lesion; (2) occurs days to wks after 1st, tender, discrete lymphadenopathy with fever, myalgias, possible meningitis; (3) extensive periadenitis that spreads to surrounding tissues yielding inflammatory mass, abscesses within coalesce to form bubo that may rupture and cause fistula (*Arch Pathol* 1939;27:1032)	Incubation 8–80 d. Primary: Small painless papule or indurated nodule; lesion ulcerates, leads to beefy-red, granulomatous ulcer with rolled edges that bleed easily; lesions may coalesce; spontaneous healing with scar formation; may cause lymphedema and elephantiasis of external genitalia from obstruction of lymphatics
Lab	Viral isolation by culture most sensitive but takes 5 d; in situ DNA hybridization (*J Infect Dis* 1983;147:829)	Dark-field exam quicke stand most direct for primary, secondary, tertiary. VDRL most often used to follow pt response to rx. RPR should be nonreactive in primary syphilis 1 yr after successful rx and 2 yr after successful rx of secondary syphilis (*JAMA* 1985;253:1269). Fluorescent antibody absorbed test (FTA abs) once pos remains so, *T. pallidum* hemagglutination assay (TPHA, MHA-TP) (*Sex Transm Dis* 1980;7:111)	Gram stain smear obtained from base of lesion shows gram-negative coccobacilli in chains or clusters (*Derm Clin* 1994;12:1). Definitive dx culture on specific media	Microimmunofluorescent ab test most specific and best. Bx of lesion shows heavy infiltration with neutrophils and plasma cells (*Derm Clin* 1994;12:1; *Genitourin Med* 1992;68:130)	Histologic exam of punch bx specimen taken from edge of active lesion or from scraping edge shows intracellular Donovan bodies on stained smear in direct immunofluorescent test
Rx	Acyclovir drug of choice, inhibits viral polymerase, acts as chain terminator.Primary: oral acyclovir 200 mg 5 ×/d for 7–10 d or 400 mg po tid for 7–10 d. Acyclovir decreases viral shedding, time to crusting, healing of lesions, duration of pain and itching in primary. Recurrent herpes: may decrease duration of viral shedding and time to crusting. If taken in prodromal period, may abort episode in some (*J Am Acad Derm* 1986;15:256). 400 mg po tid × 7–10 d. Prophylactic: 400 mg po bid decreases recurrences; safe, effective up to 5 yr (*Arch Derm* 1993;129:582). Consider for pts with > 6–8 recurrences/yr	Benzathine penicillin G2.4 million units im × 1 for primary. Penicillin allergic: doxycycline 200 mg po bid 15 × d	Ceftriaxone 250 mg im × 1 (*Rev Inf Dis* 1990;12:S580) or azithromycin 1 gm po dose or erythromycin base 500 mg po qid for 7 d or ciprofloxacin 500 mg po bid for 3 d. HIV+ patients don't respond as well	Doxycycline 100 mg po bid for 21 d or erythromycin base 500 mg po qid for 21 d. Local wound care	Rx continued until epithelialization occurs. Doxycycline 100 mg po bid × 3 wk min or erythromycin 500 mg po qid or Tm/S DS 1 tab po bid for min 3 wk. Optimum abx and rx duration not well defined

Gonorrhea (GC)

- **Cause**: Sexually transmitted disease. Organism *Neisseria gonorrhea*
- **SSX**: Men have a urethral discharge, usually profuse and purulent, but up to 2/3 asxic.
  - ➢ Women may present with Bartholin cyst (80% acute Bartholin's gland cyst infections are due to GC); vaginal discharge, dysuria, pelvic inflammatory disease, pain typically with menses or pregnancy, abdominal distention, chandelier sign (severe pain with cervical motion), pus in cervix.
- **DX**: Urine tests for gonorrhea and Chlamydia may be performed via the use of NAAT (nucleic acid amplification tests). 3 NAATs available: polymerase chain reaction (PCR), transcription-mediated amplification, and strand displacement amplification. Pt should not void for 1 hr prior to collecting urine sample. All 3 NAATs have $>$ 95% specificity for both gonorrheal and chlamydial infections in urine, cervical, and urethral samples. Transcription-mediated amplification and strand displacement amplification have sensitivities btn 80 and 93%, PCR of urine, however, detected only 56% of gonococcal infections in women compared with 94% for cervical samples.
- **RX**: Single dose of ceftriaxone 125 mg IM or alternative regimen is single dose spectinomycin 2 g IM. Only oral agent currently recommended by CDC for uncomplicated urogenital GC is single-dose Cefixime 400 mg.

Nongonoccal Urethritis (NGU)

- **Cause**: *Chlamydia trachomatis* accounts for 30–50% of cases, 20–50% men with NGU may have ureaplasma urealyticum. Incidence is 2.5 times that of GC urethritis.
- **SSX**: dysuria, urethral discharge
- **DX**: Direct fluorescent ab (DFA): rapidly detects *C. trachomatis* elementary bodies; enzyme immunoassay (EIA) can produce results in 24 hr; PCR is highly specific for fluorescence of chlamydial nucleic acids but contamination by foreign DNA is a problem.
- **RX**: CDC recommends 7 day course of tetracycline 500 mg qid or doxycycline 100 mg PO bid or erythromycin 500 mg PO qid. Single 1 g dose of azithromycin is equally effective and may improve compliance. If recurrent or persistent SX, r/o other causes of urethritis. If no cause identified, treat for ureaplasma urealyticum with erythromycin 500 mg qid for 14 days.

Urethral Carcinoma in Men

- **Cause**: Rare neoplasm of the urethra, thought to be related to chronic inflammation.
- **Epidem**: Most frequent site is bulbomembranous urethra (60%), followed by penile urethra (30%) and prostatic urethra (10%). Majority (80%) are squamous cell carcinoma, 15% TCCs, 5% adenocarcinomas and undifferentiated tumors.
- **SSX**: urinary frequency, penile pain, dysuria, palpable urethral mass, palpable inguinal nodes (20%), decreased force of stream, urethral bleeding, urethrocutaneous fistula
- **DX**: Labs – UA and culture to r/o UTI
  - ➢ Cystoscopy and biopsy to confirm malignancy
- **RX**: Treatment depends on location and stage of tumor. TNM staging used (for urethral carcinoma in women and men).
  - ➢ T (primary tumor)
    - ° Tx – primary tumor cannot be assessed
    - ° T0 – no evidence of primary tumor
    - ° Ta – noninvasive papillary, polypoid, or verrucous carcinoma
    - ° Tis – carcinoma in situ
    - ° T1 – tumor invades subepithelial connective tissue

- T2 – tumor invades corpus spongiosum, prostate, or periurethral muscle
- T3 – tumor invades corpus cavernosum or beyond prostatic capsule, anterior vagina, or bladder neck
- T4 – tumor invades other adjacent organs

➢ N (regional lymph nodes)
- Nx – regional lymph nodes cannot be assessed
- N0 – no regional lymph node mets
- N1 – mets in single lymph node, $\leq$ 2 cm
- N2 – mets in single lymph node $>$ 2 cm $<$ 5 cm, or multiple nodes, none $>$ 5 cm
- N3 – mets in lymph node $>$ 5 cm

➢ M (distant mets)
- Mx – presence of distant mets cannot be assessed
- M0 – no distant mets
- M1 – distant mets

➢ Distal urethra – if superficial can treat with transurethral resection (TUR) and fulguration. If invasive then partial or total penectomy indicated. Lymph node dissection indicated if palpable adenopathy.

➢ Bulbomembranous urethra – if superficial may treat with TUR and fulguration or segmental excision and reapproximation. If invasive, then radical cystoprostatectomy plus total penectomy and pelvic lymph node dissection.

➢ Prostatic urethra – may be squamous cell, TCC, or adenocarcinoma. If superficial TUR; if invasive radical cystoprostatectomy and urethrectomy.

➢ XRT used as palliative treatment, as an adjunct to surgical treatment or as primary treatment.

➢ Overall survival rate for superficial disease 83% compared to 36% for invasive disease. Pts with stage T3 disease or higher have best outcomes when multimodal therapy (neoadjuvant chemo and radiation therapy with or without surgery) administered.

Urethral Carcinoma in Women

- **Cause**: May be related to chronic irritation, infection.
- **Epidem**: Women $>$ 50 yrs more commonly affected and whites more frequently. Squamous cell most common (60%) followed by TCC (20%), adenocarcinoma (10%), undifferentiated carcinomas and sarcomas (8%), and melanoma (2%). Most are locally advanced at diagnosis and involve proximal 1/3 or entire urethra.
- **SSX**: dysuria, urinary frequency, palpable urethral mass or induration, foul-smelling discharge, palpable lymph nodes in 1/3 pts which represent cancer mets in 90%.
- **DX**: Labs – UA and culture to r/o UTI
  - ➢ Cystoscopy and biopsy for diagnosis
  - ➢ Imaging: chest x-ray to rule out lung mets. CT abdomen/pelvis to assess for mets and lymph node involvement. May need barium enema if bowel SX or bone scan if bone pain.
- RX: Treatment depends on tumor location and extent. Same TNM staging system used as with urethral carcinoma in men.
  - ➢ Proximal urethra – if invasive requires total urethrectomy, radical cystectomy (bladder plus most/all vagina) and lymph node dissection.
  - ➢ Bladder-sparing surgery may be performed in select pts with locally advanced TCC of the urethra.
  - ➢ Brachytherapy appears to have better response rate then external beam as primary therapy. XRT successful for small distal lesions (67% survival vs. 83% for surgery), but minimally effective for proximal tumors (20%).

➢ Other options include combined therapies such as preoperative chemotherapy and XRT followed by radical cystourethrectomy.

Urethral Trauma

- **Cause**: Blunt or penetrating trauma to pelvis, perineum, or penis in men.
- **Epidem**: Men > women. Injury of posterior urethra in 5% men with pelvic fracture. Anterior urethral injury more common than posterior urethral. Anterior urethral injury secondary to straddle injury or blunt trauma to perineum.
- **SSX**: suprapubic pain, inability to void, blood at meatus, gross hematuria, perineal ecchymosis, high-riding prostate on digital rectal exam
- **DX**: Imaging – pelvic films to rule out pelvic fracture. CT scan if intra-abdominal injury suspected. Retrograde urethrography indicated in pts with suspected urethral trauma.
- **RX**: varies with location and type of injury.
  - ➢ Posterior urethral injury
    - ° Type I – stretching and elongation of the posterior urethra without disruption
      - ▪ RX: foley catheter for 3–5 days
    - ° Type II – partial or complete disruption of prostatomembranous urethra
      - ▪ RX: if tear is partial can attempt to place catheter under fluoroscopic visualization or endoscopically, if successful remains in place for 7–14 days with VCUG obtained after removal. If complete disruption, may place open suprapubic tube initially and performed delayed repair > 3 mos postinjury or primary repair.
    - ° Type III – partial or complete disruption of prostatomembranous urethra and rupture of urogenital diaphragm and bulbous urethra
      - ▪ RX: same as with type II complete disruption. Primary repair is indicated for severe prostatomembranous dislocation, major bladder neck laceration and concomitant vascular or rectal injury.
  - ➢ Anterior urethral injury
    - ° If contusion, catheter placement
    - ° If disruption – surgical exploration, debridement, and direct repair. If extensive tissue loss then urinary diversion may be indicated.

Urethral Diverticulum

- **Cause**: May be congenital or acquired (infection, injury). In men, congenital diverticula may occur in the prostatic urethra (a mullerian duct remnant) in intersex disorders or represent an enlarged utricle in men with proximal hypospadias. Acquired may occur as complication of hypospadias repair. In women may result from obstruction of periurethral glands and subsequent decompression into urethral lumen or from birth trauma.
- **SSX**: dysuria, urinary frequency, tenderness to palpation, recurrent UTIs, postvoid dribbling, outflow obstruction, tender urethral mass on vaginal examination in women and/or blood, pus, or urine from meatus with compression of anterior vaginal wall.
- **DX**: Labs – UA and culture
  - ➢ Imaging: VCUG is useful to detect diverticula, particularly in women. US and MRI also may be useful.
  - ➢ Cystoscopy may be able to identify the mouth of the diverticulum.
- **RX**: Congenital urethral diverticuli in men may be asxic and not require treatment. If large and sxic, may be excised transvesically or transacrally. Urethral diverticuli post-hypospadias may be approached through the penis. In women, urethral diverticuli are excised transvaginally. In select cases, the diverticulum may be marsupialized.

DISEASES OF THE TESTES, SCROTUM, AND INTRASCROTAL CONTENTS

Epididymitis/Epididymo-orchitis

- **Cause**: Men < 35 yrs acute epididymitis usually caused by STDs (Chlamydia, gonorrhea, ureaplasma). In older men, gram-negative bacteria more common. Acute epididymitis of < 6 wks duration, chronic is 3 month or longer duration of SX.
- **SSX**: swollen, tender epididymitis (+/− testis), scrotal wall erythema, reactive hydrocele, tender spermatic cord
- **DX**: Lab – UA and culture
  - ➢ Imaging: Scrotal US may be helpful if abscess or torsion suspected.
- **RX**: In men < 35 yrs recommended treatment is ceftriaxone 250 mg IM single dose plus doxycycline 100 mg PO bid for 10 days. For acute epididymitis most likely caused by enteric organisms or with negative test recommended treatment is ofloxacin 300 mg PO bid for 10 days or levofloxacin 500 mg qd for 10 days.

Genital Condyloma

- **Cause**: Usually a sexually transmitted disease. They can be caused by strains 6, 11, 30, 42, 43, 44, 45, 51, 52, and 54 of human papilloma virus (HPV). Types 6 and 11 are responsible for 90% cases of genital warts.
- **Epidem**: Risk factors in men include younger age, cigarette smoking, alcohol consumption, and greater number of lifetime partners. In women, risk factors include younger age, never having been married, unemployed, cigarette smoking, and alcohol consumption. Need to differentiate from penile cancer and molluscum contagiosum.
- **SSX**: One- to 6-month incubation period, may cause pain. Three types of lesions: cauliflower-like condyloma accuminata usually involve moist surfaces, keratotic and small papular warts are usually on dry surfaces, and subclinical flat warts are found on any mucosal or cutaneous surfaces. In women, the warts occur on the outside and inside of the vagina, the cervix, or around the anus. In men, genital warts are less common. If present, they are usually on the tip of the penis, but may be found on the shaft of the penis, on the scrotum, or around the anus. Rarely, genital warts also can develop in the mouth or throat of a person who has had oral sex with an infected person.
- **DX**: Physical examination. May be able to identify some otherwise invisible warts in the genital tissue by applying vinegar (acetic acid) to areas of suspected infection. This solution causes infected areas to whiten, which makes them more visible.
- **RX**: CDC recommendations for treatment of genital warts (adapted from CDC Web site, www.cdc.gov)
  - ➢ Patient-applied:
    - ° Podofilox 0.5% solution or gel. Pts should apply podofilox solution with a cotton swab, or podofilox gel with a finger, to visible genital warts tid for 3 days, followed by 4 days of no therapy. This cycle may be repeated, as necessary, for up to 4 cycles. The total wart area treated should not exceed 10 cm^2, and the total volume of podofilox should be limited to 0.5 mL/day. If possible, the healthcare provider should apply the initial treatment to demonstrate the proper application technique and identify which warts should be treated. The safety of podofilox during pregnancy has not been established.
      OR
    - ° Imiquimod 5% cream. Pts should apply qd at bedtime, 3 × a week for up to 16 weeks. The treatment area should be washed with soap and water 6–10 hours after the application. The safety of imiquimod during pregnancy has not been established.

- ➢ Provider-administered
  - ° Cryotherapy with liquid nitrogen or cryoprobe. Repeat applications every 1–2 weeks.
    OR
  - ° Podophyllin resin 10–25% in a compound tincture of benzoin. A small amount should be applied to each wart and allowed to air dry. Treatment can be repeated weekly, if necessary. To avoid the possibility of complications associated with systemic absorption and toxicity, follow two important guidelines: (1) application should be limited to < 0.5 mL of podophyllin or an area of < 10 cm^2 of warts per session, and (2) no open lesions or wounds should exist in the area to which treatment is administered. Some specialists suggest that the preparation should be thoroughly washed off 1–4 hours after application to reduce local irritation. The safety of podophyllin during pregnancy has not been established.
    OR
  - ° Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80–90%. A small amount should be applied only to the warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate (i.e., baking soda), or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.
    OR
  - ° Surgical removal either by tangential scissor excision, tangential shave excision, curettage, or electrosurgery
- ➢ Alternative regimens
  - ° Intralesional interferon
    OR
  - ° Laser surgery
  - ° Podofilox 0.5% solution or gel, an antimitotic drug that destroys warts, is relatively inexpensive, easy to use, safe, and self-applied by pts. Most pts experience mild-to-moderate pain or local irritation after treatment. Imiquimod is a topically active immune enhancer that stimulates production of interferon and other cytokines. Local inflammatory reactions are common with the use of imiquimod; these reactions include redness and irritation and are usually mild to moderate. Traditionally, follow-up visits are not required for pts using self-administered therapy; however, follow-up might be useful several weeks into therapy to determine the appropriateness of medication use and the response to treatment.
  - ° Cryotherapy destroys warts by thermal-induced cytolysis. Healthcare providers must be trained on the proper use of this therapy because over- and under-treatment might result in complications or low efficacy. Pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, is common. Local anesthesia (topical or injected) might facilitate therapy if warts are present in many areas or if the area of warts is large.
  - ° Podophyllin resin, which contains several compounds, including antimitotic podophyllin lignans, is another treatment option. The resin is most frequently compounded at 10–25% in a tincture of benzoin. However, podophyllin resin preparations differ in the concentration of active components and contaminants. The shelf life and stability of podophyllin preparations are unknown.

A thin layer of podophyllin resin must be applied to the warts and allowed to air dry before the treated area comes into contact with clothing; overapplication or failure to air dry can result in local irritation caused by spread of the compound to adjacent areas.

- ° Both TCA and BCA are caustic agents that destroy warts by chemical coagulation of proteins. Although these preparations are widely used, they have not been investigated thoroughly. TCA solutions have a low viscosity comparable with that of H_2O and can spread rapidly if applied excessively; therefore, they can damage adjacent tissues. Both TCA and BCA should be applied sparingly and allowed to dry before the pt sits or stands. If pain is intense, the acid can be neutralized with soap or sodium bicarbonate.
- ° Surgical therapy has the advantage of usually eliminating warts at a single visit. However, such therapy requires substantial clinical training, additional equipment, and a longer office visit. After local anesthesia is applied, the visible genital warts can be physically destroyed by electrocautery, in which case no additional hemostasis is required. Care must be taken to control the depth of electrocautery to prevent scarring. Alternatively, the warts can be removed either by tangential excision with a pair of fine scissors or a scalpel or by curettage. Because the majority of warts are exophytic, this procedure can be accomplished with a resulting wound that only extends into the upper dermis. Hemostasis can be achieved with an electrocautery unit or a chemical styptic (e.g., an aluminum chloride solution). Suturing is neither required nor indicated in the majority of cases if surgical removal is performed properly. Surgical therapy is most beneficial for pts who have a large number or area of genital warts. Carbon dioxide laser and surgery might be useful in the management of extensive warts or intraurethral warts, particularly for those pts who have not responded to other treatments.
- ° Interferons, both natural and recombinant, have been used for the treatment of genital warts. They have been administered systemically (i.e., subcutaneously at a distant site or IM) and intralesionally (i.e., injected into the warts). Systemic interferon is not effective. The efficacy and recurrence rates of intralesional interferon are comparable to other treatment modalities. Administration of intralesional interferon is associated with stinging, burning, and pain at the injection site. Interferon is probably effective because of its antiviral and/or immunostimulating effects. Interferon therapy is not recommended as a primary modality because of inconvenient routes of administration, frequent office visits, and the association between its use and a high frequency of systemic adverse effects.
- ° Because of the shortcomings associated with all available treatments, some clinics employ combination therapy (i.e., the simultaneous use of two or more modalities on the same wart at the same time). No data support the use of more than one therapy at a time to improve efficacy of treatment, and some specialists believe that combining modalities might increase complications.

➢ Recommended regimens for cervical warts

- ° For women who have exophytic cervical warts, high-grade squamous intraepithelial lesion (SIL) must be excluded before treatment is initiated; management should include consultation with a specialist.

➢ Recommended regimens for vaginal warts

- Cryotherapy with liquid nitrogen. The use of a cryo-probe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation.
  OR
- TCA or BCA 80–90% applied to warts. A small amount should be applied only to warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate, or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

➢ Recommended regimens for urethral meatus warts
- Cryotherapy with liquid nitrogen
  OR
- Podophyllin 10–25% in compound tincture of benzoin. The treatment area must be dry before contact with normal mucosa. Treatment can be repeated weekly, if necessary. The safety of podophyllin during pregnancy has not been established.
- Although data evaluating the use of podofilox and imiquimod for the treatment of distal meatal warts are limited, some specialists recommend their use in some pts.

Male Genital Tuberculosis (TB)

- **Cause**: *Mycobacterium tuberculosis* (TB of testis, epididymis, and prostate). Most (80%) male genital TB assoc with coexistent renal disease. Epididymal disease usually occurs in young, sexually active men, up to 70% have prior h/o TB. Testicular involvement is almost always secondary to epididymal TB. Genital TB also may involve penis, seminal vesicle, and prostate.
- **SSX**: painful/tender testis/epididymis, draining scrotal sinus, scrotal swelling, nodular prostate, tender prostate, decreased ejaculate
- **DX**: Lab – UA and culture, culture for TB, culture of draining sinus for TB
  ➢ Imaging: KUB may show calcification of epididymis, prostate
- **RX**: Medical therapy as for renal TB. Epididymectomy if gross destruction/abscess formation of epididymis

Genital Filariasis

- **Cause**: *Wuchereria bancrofti* accts for 90% cases, *Brugia malayi* and *B. timori* in 10%. *Onchocerca volvulus* can infect humans. Transmitted by mosquitoes – may take up to a year for onset of symptoms and a large percentage of infected pts may remain asymptomatic permanently.
- **SSX**: Local swelling and redness of skin where microfilaria enter; fever. Pts with filarial fever sustain episodic fevers, lymphangitis, lymphadenitis, funiculoepididymitis, transient edema, small acute hydroceles. Pts with chronic disease have chronic hydroceles, fixed edema, elephantiasis, chyluria, scrotal lymphedema.
- **DX**: Lab – Presence of microfilaria in peripheral night blood samples is diagnostic.
  ➢ Can also use chylous urine or hydrocele fluid.
  ➢ Imaging: Adult worms within the scrotum can be demonstrated by ultrasound with a 7.5 MHz transducer. Demonstrating microfilaria becomes more difficult in late stage disease.
- **RX**: Diethylcarbamazine (DEC) in three divided doses of 6 mg/kg/day for 12 days kills adults and microfilariae. The death of worms can provote intense systemic and

local reactions but usually doesn't require withdrawal of treatment. DEC treatment alone does not produce regression of hydroceles. Ivernectin is effective only against microfilariae.

➢ Surgery for scrotal elephantiasis produces much more satisfactory results than surgery for elephantiasis of the legs. Aspiration followed by sclerotherapy with tetracycline offers a useful alternative method for dealing with thin-walled hydroceles. Good skin care and prompt treatment of bacterial skin infections is important to stop the disease progressing.

Fournier's Gangrene

- **Cause**: (Also, necrotizing fasciitis.) Infection most commonly arising from the skin, urethra or rectal regions. Involves multiple organisms including aerobes (*E. coli*, *Klebsiella*, enterococci) and anaerobes (*Bacteroides*, *Fusobacterium*, *Clostridium*). Bacteria probably pass through Buck's fascia of the penis and spread along the dartos fascia of the scrotum and penis, Colles fascia of the perineum and Scarpa fascia of the anterior abdominal wall. Onset is usually abrupt and rapidly fulminating.
- **Epidem**: Risk factors include DM, local trauma, paraphimosis, periurethral extravasation of urine, perirectal or perianal infections, and surgery such as circumcision or herniorrhaphy. Higher mortality in those with DM, alcoholics, and those with colorectal sources.
- **SSX**: pain, malaise, fever, tachycardia, hypotension, crepitus, gangrene, swelling, erythema of affected tissues
- **DX**: Lab – CBC, electrolytes, BUN, creatinine
  ➢ Imaging: plain film of area or US of affected area may show subcutaneous air
- **RX**: Fluid resuscitation, intravenous antibiotics (double or triple therapy). Once resuscitated, emergent surgical debridement. Often need subsequent debridement in next 24–48 hours. Extensive tissue coverage is often needed when the infection is eradicated.

Benign Lesions of the Epididymis and Testis

Differential Diagnosis of Benign Lesions of the Epididymis and Testis

	Cystadenoma of Epididymis	Adenomatoid Tumor	Epidermoid Cyst
Cause	Benign lesion originating from efferent ducts	Benign neoplasm of adnexal structures. Poss etiologies: reaction to injury/ inflammation, mesothelial or endothelial origin	Benign neoplasm of the testis. May represent a benign monolayer teratoma
Epidemiology	May be seen in von Hippel-Lindau disease, bilateral lesions in 1/3 cases	Most common paratesticular tumor. Majority in head or tail of epididymis. Males in 20s–30s age	Accts for 1–2% of all testis tumors. Half occur in age 20s, remainder between teens and 30s. Right side > left

	Cystadenoma of Epididymis	Adenomatoid Tumor	Epidermoid Cyst
SSX	Minimal or no discomfort, enlarged epididymis	Extratesticular solid mass, does not transilluminate	Usually painless, painless nodule/cyst
DX	Scrotal US: epididymal mass that is partially cystic	Scrotal US: solid mass, does not transilluminate	Labs: serum markers (AFP, beta-HCG, and LDH if diagnosis is uncertain) Scrotal US: well-circumscribed intratesticular cyst with hypoechoic center and circumferential echogenic whorls that do not shadow
RX	Epididymectomy	Surgical excision	If confident of preoperative diagnosis – local excision and biopsy of adjacent testicular tissue to assess for testicular intraepithelial neoplasia to r/o mature teratoma. If diagnosis is unclear, radical orchiectomy

AFP = alpha fetoprotein; beta-hCG = beta subunit human chorionic gonadotropin; LDH = lactate dehydrogenase.

Testicular Cancer—Germ Cell Tumors

- **Cause**: Abnls of chromosome 12 identified in patients with testis cancer as well as mutations in tumor suppressor genes *p53* and *p16*. Significant birth cohort effect on testicular germ cell tumor incidence, suggesting risk is determined in utero. Also, higher levels of several polychlorinated biphenyl (PCB) congeners in blood of case compared to control mothers suggests role for toxin exposure in utero. Testicular carcinoma in situ considered a precursor lesion for testicular germ cell tumor.
- **Epidem**: Most common malignancy in men age 15–35 yrs. Estimated 8400 new cases and 380 deaths from testicular cancer in the U.S. in 2009. About 7–10% of pts with testicular cancer have h/o of undescended testes. Two to 3% of testicular tumors are bilateral. Controversial as to whether or not testicular microlithiasis is a risk factor. Germ cell tumors account for 90–95% of all testicular cancers. Seminoma most common germ cell tumor in adults, yolk sac most common germ cell tumor in children.
  - ➢ Adults: Primary tumors of testis: seminoma (40%); embryonal carcinoma (20–25%); teratocarcinoma (25–30%); teratoma (5–10%); choriocarcinoma (1%).
  - ➢ Patients may present with mixed germ cell tumors.
- **SSX**: palpable firm testicular mass, reactive hydrocele, if extensive adenopathy may have lower extremity edema, may have pain if mets
- **DX**: Labs – serum markers including AFP, beta-hCG, and LDH
  - ➢ Beta-hCG – elevated in pts with choriocarcinoma and may be increased in pts with embryonal carcinoma and seminoma. Elevated beta-hCG may be seen with other malignancies including those of liver, pancreas, stomach, breast, kidney, and bladder, and may be increased in those who smoke marijuana. Beta-hCG produced by syncytiotrophoblast cells. Serum half-life 24–36 hrs.

- ➢ AFP may be elevated in pts with pure embryonal carcinoma, teratocarcinoma, yolk sac tumor, and mixed tumors. Not produced by pure seminoma or pure choriocarcinoma. AFP may be elevated in pts with lung, gastric, pancreatic, and hepatocellular cancers as well as liver disease. Half-life is 5–7 days.
- ➢ LDH may be elevated in pts with testicular tumors, but sensitivity and specificity are limited. Elevated levels may indicate extensive or bulky disease, and post-treatment increases indicate relapse.
- ➢ Imaging: Scrotal US may help confirm presence of an intratesticular mass.
  - ° CT chest, abdomen, and pelvis to evaluate for metastatic disease
  - ° Fluoro-deoxy-D-glucose positron emission tomography (FDG PET) is more sensitive and specific for residual tumor post-chemotherapy in pts with seminoma, 100% sensitivity and 80% specificity for FDG PET compared to 74% and 70%, respectively, for CT scan.

• **RX**: Radical inguinal orchiectomy. Subsequent RX based on clinical stage, tumor histology, and status of tumor markers.

- ➢ TNM staging system for testicular cancer
  - ° TX – tumor cannot be assessed
  - ° T0 – no evidence of primary tumor
  - ° Tis – carcinoma in situ
  - ° T1 – tumor confined to testis
  - ° T2 – tumor has spread to blood or lymph vessels near the tumor, or the tunica vaginalis
  - ° T3 – tumor invades the spermatic cord
  - ° T4 – tumor invades the scrotum
  - ° Nx – regional lymph nodes cannot be assessed
  - ° N0 – no spread to regional nodes
  - ° N1 – Spread to at least one lymph node, but no node $>$ 2 cm
  - ° N2 – Spread to at least one lymph node that is $>$ 2 cm but $\leq$ 5 cm
  - ° N3 – Spread to at least one lymph node that is $>$ 5 cm
  - ° Mx – distant metastasis cannot be assessed
  - ° M0 – No distant metastasis
  - ° M1 – distant metastasis present
    - ▪ M1a – tumor has metastasized to distant lymph nodes or to the lung
    - ▪ M1b – tumor has metastasized to other organs, such as liver, brain, or bone

SerumMarkers

	LDH (U/L)	**hCG (mIU/mL)**	**AFP (ng/mL)**
Sx	Marker studies not available or not performed	Marker studies not available or not performed	Marker studies not available or not performed
S0	Normal	Normal	Normal
S1*	$<$ 1.5 $\times$ normal	$<$ 5000	$<$ 1000
S2†	1.5 10 $\times$ normal	5000 50,000	1000 10,000
S3†	$>$ 10 $\times$ normal	$>$ 50,000	$>$ 10,000

AFP = alpha fetoprotein; beta-hCG = beta subunit human chorionic gonadotropin;
LDH = lactate dehydrogenase.
* All markers must be in the stated range to be S1.
† Only one marker needs to be in stated range to be S2 or S3.
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StageGrouping

Stage	T	N	M	S
Stage 0	Tis	N0	M0	S0
Stage 1	T1–4	N0	M0	SX
Stage 1A	T1	N0	M0	S0
Stage 1B	T2–4	N0	M0	S0
Stage 1S	Any T	N0	M0	S1–S3
Stage II	Any T	N1–N3	M0	SX
Stage IIA	Any T	N1	M0	S0–S1
Stage IIB	Any T	N2	M0	S0–S1
Stage IIC	Any T	N3	M0	S0–S1
Stage III	Any T	Any N	M1	SX
Stage IIIA	Any T	Any N	M1a	S0–S1
Stage IIIB	Any T	N1–N3	M0	S2
	Any T	Any N	M1a	S2
Stage IIIC	Any T	N1–N3	M0	S3
	Any T	Any N	M1a	S3
	Any T	Any N	M1b	Any S

- ➢ Treatment varies with Stage and type of testicular cancer (seminoma vs. nonseminoma)
- ➢ Stage I testicular cancer
  - ° Seminoma – treatment may include the following
    - ▪ Radical orchiectomy with or without XRT to nodes in the abdomen
    - ▪ Radical orchiectomy followed by chemotherapy
  - ° Nonseminoma – treatment may include the following
    - ▪ Radical orchiectomy, retroperitoneal lymph node dissection
    - ▪ Radical orchiectomy and surveillance
    - ▪ Radical orchiectomy followed by chemotherapy for pts at high risk for recurrence
- ➢ Stage II testicular cancer
  - ° Seminoma – treatment may include the following
    - ▪ Radical orchiectomy, if tumor is $\leq$ 5 cm, radiation therapy to nodes in the abdomen and pelvis
    - ▪ Radical orchiectomy, if tumor is $>$ 5 cm, combination chemotherapy or radiation therapy to nodes in abdomen and pelvis.
  - ° Nonseminoma – treatment may include the following
    - ▪ Radical orchiectomy and retroperitoneal lymph node dissection (RPLND) with surveillance
    - ▪ Radical orchiectomy and RPLND followed by combination chemotherapy
    - ▪ Radical orchiectomy, followed by combination chemotherapy and RPLND if adenopathy persists
    - ▪ Combination chemotherapy prior to removal of the testis, for cancer that has spread and is thought to be life-threatening
    - ▪ Radical orchiectomy and clinical trial of combination chemotherapy instead of RPLND

- ➢ Stage III testicular cancer
  - ° Seminoma – treatment may include the following
    - Radical orchiectomy followed by chemotherapy and surveillance
    - A clinical trial of a new therapy
    - A clinical trial of a high-dose chemotherapy with bone marrow transplant
  - ° Nonseminoma – treatment may include the following
    - Radical orchiectomy followed by combination chemotherapy
    - Combination chemotherapy followed by surgery to remove any residual tumor. If viable cancer cells detected at surgery then additional chemotherapy
    - Combination chemotherapy combined with radiation therapy to brain if brain mets
    - Combination chemotherapy prior to orchiectomy, for cancer that has spread and is thought to be life-threatening
    - A clinical trial of a new therapy
    - A clinical trial of high-dose chemotherapy plus bone marrow transplant

Leydig Cell Tumors

- **Cause**: Unknown. Does not appear to be associated with undescended testis
- **Epidem**: Accounts for 1–3% of testis tumors. Affects men 20–60 yrs, 25% occurring before puberty; 97% are unilateral, 10% malignant, usually in those $>$ 6th decade of life.
- **SSX**: Pain in 20%. May have impotence, decreased libido and gynecomastia. In prepubertal boys may see isosexual precocity, prominent external genitalia, masculine voice, hair growth, testicular enlargement. Most adults have no endocrine manifestations; 20–25% have feminizing effects.
- **DX**: Labs – In prepubertal cases – increased testosterone, +/− increased 17-ketosteroids. Adults may see increase in urinary and plasma estrogens, and low gonadotropin and testosterone levels.
  - ➢ Imaging: scrotal US – intratesticular lesion, may be bilateral. MRI may be useful for detecting small, nonpalpable lesions not detected on US.
- **RX**: radical orchiectomy. If question of malignancy then CT of abdomen/pelvis. Virilizing and feminizing effects are to some extent irreversible.

Sertoli Cell Tumors

- **Cause**: Unknown. Majority occur in normal testes, but some occur in undescended testes
- **Epidem**: Accounts for $<$ 1% of all testicular tumors, 10% malignant, 1/3 in pts age $\geq$ 12 yrs. Large cell calcifying assoc with Carney complex (myxoma, adrenocortical hyperplasia, pituitary tumor, skin pigmentation) and Peutz-Jeghers syndrome
- **SSX**: may be painful or painless, testicular mass, +/− gynecomastia
- **DX**: Labs – increased testosterone in pts with virilization
  - ➢ Imaging: scrotal US: intratesticular mass. If ? of mets, CT of abdomen/pelvis, chest x-ray, bone scan
- **RX**: Radical orchiectomy. If malignant and adenopathy, then RPLND

Carcinoid of Testis

- **Cause**: malignant neoplasm
- **Epidem**: Testis is infrequent site. May be site of metastasis.
- **SSX**: slow-growing intratesticular mass, painless

- **DX**: Labs – serum AFP and beta-HCG are normal. 24-hr urine for 5-hydroxyindoleacetic acid (5-HIAA)
- **RX**: Radical orchiectomy

Gonadoblastoma

- **Definition**: tumor of dysgenetic gonads
- **Cause**: occurs mostly in pts with gonadal dysgenesis
- **Epidem**: Accts for 0.5% of testicular neoplasms. Affects all age groups, but majority are men < 30 yrs. Y chromosome present in almost all pts, 46XY and 45X/XY most common. Most (4/5) pts with gonadoblastoma are phenotypic women. Histopathology: presence of Call-Exner bodies. Three elements present: sertoli cells, interstitial cells, germ cells in varying proportions. Most common tumor is invasive germinoma (seminoma), but other germ cell tumors also develop.
- **SSX**: In phenotypic women – small breasts, hypoplastic internal genitalia, +/− clitoral enlargement and streak gonads. In phenotypic men – gynecomastia, hypospadias, some internal female genitalia, dysgenetic testis
- **RX**: radical orchiectomy. Due to the high incidence of bilateral disease (50%), contralateral gonadectomy is recommended. If seminoma or other germ cell tumor is identified, full staging evaluation is indicated and further management based on the tumor type and stage.

Lymphoma of the Testis

- **Cause**: May be manifestation of primary extranodal disease, initial manifestation of clinically occult nodal disease, or later manifestation of disseminated nodal lymphoma.
- **Epidem**: Accts for about 2% of malignant testis tumors in men < 50 yrs and 25% of testicular tumors in older men. Median age 60 yr. Bilateral in 50%, simultaneous in 10%, metachronously in remainder. Primary lymphoma of testis may occur in children. Usually intermediate to high-grade B cell.
- **SSX**: enlarged painless testis, about ¼ pts have generalized constitutional SX including weight loss, anorexia, and weakness.
- **DX**: Labs – CBC with peripheral smears, bone marrow studies
  - ➢ Imaging: scrotal US – diffuse infiltration of testis by tumor, chest x-ray, bone scan, CT, possibly liver/spleen scan
- **RX**: radical orchiectomy and referral to oncologist

Leukemia of the Testis

- **Cause**: Testis is prime site of relapse in boys with acute lymphocytic leukemia (ALL).
- **Epidemiology**: incidence 8% in boys with ALL
- **SSX**: enlarged, often painless testis; may be bilateral, scrotal discoloration
- **DX**: bx of testis
- **RX**: testicular irradiation – 2000 cGy with reinstitution of adjunctive chemo or reinduction therapy for children who relapse in testis while on chemo

Metastatic Disease to Testes

- **Cause**: Most common primary sources include prostate, lung, GI tract, melanoma, and renal cell carcinoma.
- **SSX**: testicular mass that may be multiple plus SX related to primary disease and other sites of metastasis
- **DX**: Labs – serum AFP, beta hCG, LDH to rule out primary testis malignancy
  - ➢ Remainder of labs as dictated by primary lesion
- **RX**: testis biopsy if suspect metastatic lesion, treat as per primary lesion

Leiomyosarcoma of the Spermatic Cord

- **Cause**: Malignant neoplasm that orginates from the smooth muscle of the spermatic cord vessels
- **Epidem**: rare, accounts for 10% spermatic cord sarcomas in adults. Three patterns of spread – high risk of local recurrence and extension, hematogenous spread to lung, and lymph mets such as para-aortic nodes
- **SSX**: painless firm intrascrotal mass that does not involve testis or epididymis, gradually enlarging
- **DX**: Lab – AFP and beta-hCG to rule out testicular neoplasm
  - ➢ Imaging: scrotal US – paratesticular solid mass. MRI has specificity of 88% for intrascrotal lesions. CT abdomen/pelvis to rule out retroperitoneal adenopathy. Chest x-ray or CT to rule out lung mets
- **RX**: radical orchiectomy. Retroperitoneal lymph node dissection (RPLND) indicated if enlarged nodes on CT scan. Adjuvant chemo and XRT advantageous in high-grade sarcomas. Adjuvant XRT helps reduce local recurrence.

Testicular Torsion

- **Cause**: Intravaginal torsion in children and adults. Gubernaculum is fixed to scrotal wall and torsion occurs due to a narrow mesenteric attachment from the cord onto the testis and epididymis, the bell-clapper abnormality. Extravaginal in infants
- **Epidem**: Can occur at any age, but most common during adolescence. Increased risk of contralateral torsion
- **SSX**: Testicular pain, nausea/vomiting, scrotal swelling, absent cremasteric reflexes, reactive hydrocele, abnormal testicular lie
- **DX**: Hx and physical examination. UA and culture to rule out epididymo-orchitis
  - ➢ Imaging: scrotal US with Doppler study – decreased or absent flow to affected testis; may have hyperemia around testis, abnormal testicular echogenicity
- **RX**: Emergent scrotal exploration. If affected testis appears viable after detorsion, then bilateral scrotal orchidopexy. If testis is ischemic/necrotic after detorsion, then orchiectomy and contralateral scrotal orchidopexy.

Testicular Rupture

- **Cause**: Blunt or penetrating trauma to the scrotum
- **Epidem**: May be accidental or self-induced
- **SSX**: painful scrotal swelling, scrotal ecchymosis/hematoma, inability to fully palpate the testis
- **DX**: scrotal US: lack of integrity of the tunica albuginea, overall accuracy for detecting traumatic rupture; specif 75%; sens 64%; pos predictive value, 77.8%, neg predictive value 60%.
- **RX**: Immediate exploration if rupture suspected. Debridement of necrotic, extruded tissue and closure of the tunica albuginea, drain, abx.

Varicocele

- **Cause**: Dilatation of the pampiniform plexus of veins around the testis, may be secondary to anatomic considerations (left testicular vein drains into left renal vein), incompetent venous valves, "nutcracker phenomenon" (compression of left renal vein btn superior mesenteric artery and aorta) or obstruction of the vena cava. Deleterious effects may be related to increases in intrascrotal temperature as a result of pooling of warm venous blood. Other theories include reflux of adrenal metabolites from renal vein, decreased blood flow, and hypoxia.

- **Epidem**: Rare prior to puberty. Left side more commonly affected (90%), may be bilateral. Approx 10% adolescents have a varicocele. Approx 15% of all men have a varicocele. Approx 40% men seen for infertility have a varicocele and up to 70% have improvement in semen analysis after varicocelectomy.
- **SSX**: "bag of worms" in ipsilateral scrotum, decreased ipsilateral testicular size, scrotal discomfort
- **DX**: physical examination in supine and standing position
  - ➢ Lab – semen analysis – decreased motility most common, 65% with decreased sperm concentration ($<$ 20 million/cc), stress pattern – increased numbers of amorphous cells and immature germ cells. Normal testosterone level, occasionally increased follicle stimulating hormone (FSH level)
  - ➢ Scrotal US – appears to be most accurate way to assess testicular size. If right sided varicocele, need renal ultrasound to rule out retroperitoneal pathology and vena caval obstruction
- **RX**: Adolescent varicocele – surgical treatment is indicated for clinically detectable varicocele associated with ipsilateral decreased testicular size.
  - ➢ Adult varicocele – if male is infertile with abnormal semen analysis. Motility is most common factor improved with varicocelectomy, followed by density and morphology.
  - ➢ Goal of RX is ligation or occlusion of the dilated veins and may be accomplished via inguinal or subinguinal approach, retroperitoneal or laparoscopic approach, or radiologic occlusive technique. Risks of surgery include: recurrence, hydrocele, and injury to testicular artery. Conception rates average 40–50% in previously infertile men.

Male Infertility

- **Cause**: Structural, chromosomal, infectious (genital tract and pospubertal mumps orchitis), medication/drug-induced, immunologic, chemotherapy and XRT-induced, and obstructive causes. May also be secondary to incorrect coital habits, abnl sperm count (oligospermia, azoospermia), abnormal sperm motility (asthenospermia), abnl sperm morphology, and ejaculatory dysfunction.
- **Epidem**: Approximately 20% cases of infertility are due to male factor and additional 30% involve both male and female factors
- **DX**: H&P exam
  - ➢ Evaluate coital habits, use of lubricants that may affect sperm motility (e.g., lubafax, K-Y jelly, Keri lotion, Surgilube, and saliva)
  - ➢ recent febrile illness (may impair fertility for 1–3 mos), medications, surgical hx, and hx of trauma
  - ➢ Assess secondary sex characteristics, testis size and position, presence of vas, palpate epididymis, r/o hypospadias, assess for varicocele, DRE to r/o seminal vesicle enlargement
  - ➢ Lab: semen analysis: 2 days of abstinence, brought to lab within 2 hrs of collection
    - ° Normal semen parameters
      - volume, 1.5–5.0 mL
      - total sperm count $>$ 50 million ($\geq$ 20 million/cc)
      - motility $>$ 50%
      - forward progression $>$ 2
      - morphology $>$ 50% nL sperm morphology by standard criteria or $>$ 14% normal forms by strict criteria

- If hx or physical exam supportive or sperm density $<$ 5–10 million/mL, then check LH, FSH, and testosterone.
- Absent or low-volume ejaculate – may be secondary to retrograde ejaculation, ejaculatory duct obstruction, germ cell failure, or hypogonadotropic hypogonadism
- Retrograde ejaculation – $>$ 5–10 sperm/hpf found in post-intercourse urine, also if low volume ejaculate and urine shows more sperm than in ejaculate suggests retrograde ejaculation
- Ejaculatory duct obstruction – if absent or low-volume ejaculate and no sperm present in urine – need TRUS of seminal vesicles and ejaculatory ducts to r/o congenital anomaly or obstruction
- Germ cell failure – if absent or low volume ejaculate and no sperm in urine and TRUS is normal, then perform testis bx to assess for spermatogenesis. If testis bx shows no sperm, check LH, FSH, and testosterone. If FSH $>$ 2–3 $\times$ nl, with normal LH and testosterone, and testes small suggests germ cell failure. If FSH and LH elevated and testosterone normal or low, suggests testicular failure.
- Hypogonadotropic hypogonadism – If both FSH and LH low, further endocrine evaluation to r/o hypogonadotropic hypogonadism.

➢ Oligospermia: Rarely seen as an isolated finding on semen analysis. In severe cases, check LH, FSH, and testosterone – if abnl needs full endocrine evaluation. If lab nl, pt is candidate for assisted reproduction or trial of empiric medical therapy with clomiphene citrate.

➢ Asthenospermia (loss or reduction of sperm motility): May be secondary to prolonged abstinence periods, genital tract infection, antisperm antibodies, partial ductal obstruction or idiopathic causes. If antisperm antibody assay is pos, may proceed with immunosuppression or assisted reproduction; if negative, r/o pyospermia, if no pyospermia then r/o obstruction, varicocele, heat, systemic illness, and consider viability assay. Antisperm abs present in 60% men who underwent vasectomy, also may be present if prior testicular torsion or trauma.

➢ Genetic anomalies and syndromes associated with hypogonadism and infertility: A variety of syndromes (Kallman's syndrome, fertile eunich, isolated FSH deficiency, and Prader-Willi syndrome) are associated with deficiencies of GnRH, LH, and FSH. Rx consists of correcting the deficiencies. Genetic anomalies associated with infertility include Klinefelter's syndrome (XXYmale), XX male, androgen abnormalities (deficiencies in androgen synthesis, conversion of testosterone to dihydrotestosterone, and androgen receptor abnormalities), and Noonan's syndrome (46 XY).

➢ Undescended testes may be associated with decreased sperm concentrations. Half of pts with bilateral undescended testes and 25–30% of pts with unilateral undescended testis will have sperm concentrations $<$ 15–20 million/mL. The more proximal the undescended testis, the more severe the testicular dysfunction.

➢ Varicocele is the most common surgically treatable cause of infertility (see varicocele)

➢ Anejaculation may occur in individuals with prior retroperitoneal surgery, spinal cord injury, multiple sclerosis, transverse myelitis, and diabetes mellitus. May be treated with vibratory stimulator or electroejaculation.

➢ Congenital hypoplasia or absence of the vas deferens is manifested as low-volume azoospermia in the presence of a testis biopsy showing spermatogenesis. Rx with epididymal sperm aspiration and intracytoplasmic sperm injection (ICSI).

DISEASES OF THE PROSTATE

Prostatitis

- **Cause**: Bacterial and nonbacterial etiologies. NIH classification and definitions of prostatitis:
  - I. Acute bacterial prostatitis
  - II. Chronic bacterial prostatitis
  - III. Chronic abacterial prostatitis/chronic pelvic pain syndrome: no demonstrable infection
    - IIIA. Inflammatory chronic pelvic pain syndrome: WBC present in semen/expressed prostatic secretions (VB3)
    - IIIB. Noninflammatory chronic pelvic pain syndrome: no WBC noted in semen/expressed prostatic secretions or VB3
  - IV. Asymptomatic inflammatory prostatitis: detected by prostate biopsy or presence of WBCs in prostatic secretions during evaluation for other disorders
- **Epidem**: Prostatitis affects up to 50% of men at some point in their lives. Only about 8% of men with prostatitis will have bacterial prostatitis. *E. coli* accts for 80% of bacterial prostatitis; other gram-negative organisms (*Pseudomonas*, *Serratia*, *Klebsiella*, and *proteus*) acct for 10–15% of infections and enterococcus in 5–10%.
- **SSX**: urinary frequency and urgency, dysuria, decreased flow rate, nocturia, malaise; pain in perineum, groin, back, testes, suprapubic region; if acute bacterial infection may have fever/chills; tender, boggy, or firm prostate on DRE.
- **DX**: Lab – Meares-Stamey test is gold standard for dx of bacterial prostatitis.
  - ➢ First voided 10 mL – VB1
  - ➢ Midstream 5–10 mL – VB2
  - ➢ Prostatic massage performed and collect expressed prostatic secretions and examine under microscope
  - ➢ First 10 mL of urine after prostatic massage – VB3
  - ➢ Modified Nickel's technique has 91% sens and specif compared to Meares-Stamey test – collect midstream urine and perform prostatic massage; then collect post-massage urine and perform urinalysis and culture on both.
  - ➢ Imaging: bladder scan PVR to ensure adequate bladder emptying
  - ➢ Other: Uroflow may be helpful in pts with voiding complaints; videourodynamics may be helpful in patients with nonbacterial prostatitis to delineate bladder and bladder neck function.
- **RX**: acute bacterial prostatitis: abx for at least 4 weeks, typically a fluoroquinolone
  - ➢ Chronic bacterial prostatits: antibiotic therapy for extended period
  - ➢ Pts with chronic nonbacterial prostatitis may be treated as follows:
    - ° Category IIIA – trial of broad-spectrum abx, alpha-blocker therapy, anti-imflammatory agents, 5 alpha-reductase inhibitor if prostate is enlarged, prostatic massage 2–3 times per week, and supportive therapy (counseling)
    - ° Category IIIB – alpha-blocker therapy, muscle relaxant, analgesics, biofeedback, relaxation exercises, supportive therapy (counseling)
  - ➢ Other therapies: sitz baths, avoidance of spices, caffeine, and alcohol; biofeedback

Prostatic Abscess

- **Cause**: bacterial infection, most commonly with *E. coli* (70%)
- **Epidem**: Most cases occur in men in their 50s to 60s. Incidence has decreased. Increased risk in men with DM, chronic renal failure on dialysis, immunocompromised men, recent urethral instrumentation and those with chronic indwelling catheters.
- **SSX**: dysuria, frequency, perineal pain, low back pain, urinary retention, fever/chills, hematuria, urethral discharge; prostate may be tender, fluctuant, and/or enlarged.
- **DX**: Lab – UA, culture, CBC
  - ➢ Imaging: CT scan or transrectal US helps to DX and serves as guide for percutaneous aspiration for culture, drainage, and to evaluate response to therapy.
- **RX**: drainage – percutaneously or via transurethral incision/resection and antibiotics

Benign Prostatic Enlargement (BPE)

- **Cause**: Benign neoplasm of the prostate – when pathologic evaluation confirms refer to as benign prostatic hyperplasia (BPH). Development requires a combination of androgens and aging.
- **Epidem**: Most common neoplastic condition affecting men. Up to 50% of men will have SX requiring medical or surgical therapy. Hyperplastic tissue is located centrally in the periurethral portion of the prostate. All glandular and stromal elements are involved to a variable degree. SX do not necessarily correlate with prostate size.
- **SSX**: LUTS include storage (OAB) and voiding (BOO) symptoms – storage symptoms include urinary frequency, urgency, urgency incontinence, and nocturia; voiding symptoms include decreased force of stream, hesitancy, straining to void, sensation of incomplete emptying, intermittent stream, and postvoid dribbling.
  - ➢ AUA SX score not specific to BPE but allows for assessment of severity of SX

AUA Symptoms Score

SX	Always 5	> 1/2 the time 4	1/2 the time 3	> 1/2 the time 2	1/5 the time 1	Never	Score
Incomplete emptying							
Frequency > Q 2 hr							
Stop/start voiding							
Urgency							
Decreased force of stream							
Strain to void							
Nocturia 0–5+							

Mild SX = score of 0–7; moderate SC = score of 8–18; severe SX score of 19–35.

- **SSX**: enlarged prostate on DRE, distended bladder, hematuria, incontinence, UTI, urinary retention, SX noted in AUA SX score, bladder stone
- **DX**: Lab – UA and culture to r/o infection; urine cytology if microhematuria and/or predominance of storage SX and a h/o smoking
  - ➢ PSA should be offered to those with at least a 10-yr life expectancy and in whom the presence of prostate cancer would alter their manangement. AUA recommends prostate cancer screening be considered in men ≥ age 40 yrs.

- ➢ Other: uroflow – peak urine flow rate (voided volume must be at least 150 cc to be reliable) – normal flow rate is > 20 mL/sec, moderate flow rate is 10–15 mL/sec, very low flow rate is < 10 mL/sec
- ➢ Pressure/flow study – more definitive for obstruction – is more invasive – increased bladder pressure associated with low flow rate indicative of BOO.

- **RX**: Avoid caffeine and alcohol. Fluid restriction in the evening in pts with bothersome nocturia.
  - ➢ Alpha-blockers – titratable include terazosin and doxasozin. Terazosin start at 1 mg and increase sequentially to max of 5–10 mg qhs. Improves flow within 2 wks. Doxazosin start with 2 mg PO qhs and titrate to max of 8 mg qhs as tolerated. Both terazosin and doxazosin can cause postural hypotension, so BP should be checked with each incremental dose. Tamsulosin is a single dose therapy (0.4 mg), should take ½ hr after same meal each day. Alfuzosin is also a single dose therapy, 10 mg, to be taken immediately after same meal each day. Rapaflo is an 8 mg once daily alpha-blocker that should be taken with a meal. All alpha-blockers have potential side effects of dizziness, nasal stuffiness, and ejaculatory dysfunction. Should not be combined with PDE-5 inhibitors until stable dose of alpha-blocker reached. Alpha-blockers have been associated with floppy iris syndrome during cataract surgery.
  - ➢ 5 alpha-reductase inhibitors – decrease plasma and intra-prostatic diydrotestosterone levels. Two agents currently available, finasteride (5 mg qd) and dutasteride (0.5 mg). Both decrease PSA by approx 50%. Dutasteride appears to have similar treatment responses as finasteride but a more rapid biochemical action. Side effects of 5 alpha-reductase inhibitors include decreased libido, erectile dysfunction, and ejaculatory dysfunction.
  - ➢ The Medical Therapy of Prostatic Symptoms (MTOPS) trial demonstrated that combination therapy of 5 alpha reductase inhibitor plus alpha-blocker was superior to either drug alone for preventing disease progression.
  - ➢ Surgical therapy: TURP is still considered the gold standard. Suprapubic/retropubic prostatectomy useful in large prostate glands or when there is coexistent large bladder calculus (calculi). A variety of minimally invasive treatment options have been used to treat BPE with BOO, including transurethral electrovaporization of the prostate, laser vaporization of the prostate, laser resection of the prostate, laser incision of the prostate, interstitial laser coagulation, transurethral microwave thermotherapy, water-induced thermotherapy, and transurethral needle ablation in pts who are poor surgical candidates can consider UroLume stent.

Prostatic Calculi

- **Cause**: Deposition of calcareous material on corpora amlyacea, develop in the tissues or acini of the gland. May occur secondary to infections and may be associated with ochronosis.
- **Epidem**: Frequently identified in men > 50 yrs. Often noted incidentally on routine x-rays. Composed of calcium phosphate trihydrate and carbonate
- **SSX**: usually asymptomatic, calcification noted on plain film of abdomen and pelvis; may have hematuria
- **DX**: Lab – UA and culture
  - ➢ Imaging: often seen on plain film of pelvis or on transrectal US of the prostate
- **RX**: If asxic, no treatment necessary. If pt has SX, treatment includes TURP or supraprubic prostatectomy. In setting of multiple symptomatic prostatic calculi and

intractable infections, total prostatectomy and bilateral seminal vesiculectomy usually curative.

Prostate Cancer

- **Cause**: Neoplasm of the prostate. Estimated that 9% of all prostate cancers and > 40% of cases of early onset disease are attributable to an autosomal dominant gene. Abnormalities of chromosome 1 and x chromosome are associated with an increased risk.
- **Epidem**: In U.S. men (excluding skin cancer), prostate cancer is the most common cancer; accts for about 33% of all cancer cases. More than 75% of the cases of prostate cancer are diagnosed in men > 65 yrs. Estimated as the cause of death in 9% of men (27,350 prostate cancer-related deaths in 2009). U.S. deaths from prostate cancer have decreased significantly by 4.1%/yr from 1994–2004. In April 2009, the AUA issued new guidelines lowering the age for beginning PSA and DRE screening to 40 yrs for relatively healthy, well-informed men who want to be treated.
- **SSX**: obstructive voiding symptoms (hesitancy, decreased flow rate, intermittency, and postvoid dribbling), SX from bone metastases (bone pain), DRE revealing a firm, hard, nontender mass
- **DX**: Lab – PSA, in the range of 4.0–10.0, PSA lacks specif; about 75% of men with PSA in this range will not have prostate cancer. PSA velocity is the change in PSA/change in time. Some suggest that a rise of > 0.75 ng/mL in a year is cause for concern. PSA density is the PSA/prostate volume. PSA density > 0.15 is proposed as the threshold for performing bx in men with PSA 4.0–10.0 and negative DRE. Free/total PSA: the PSA exists in blood in 2 states, a free state and bound to plasma proteins. Pts with prostate cancer tend to have lower free/total PSA ratios. Ratios of 14–28% have been proposed as cut-offs

Age-AdjustedPSA

Age (year)	White	Black
40–49	0–2.5	0–2.0
50–59	0–3.5	0–4.0
60–69	0–3.5	0–4.5
70–79	0–3.5	0–5.5

- ➢ Imaging: Transrectal US cannot exclude the presence of prostate cancer, but is helpful in guiding prostate biopsies. Bone scan, CT scan, and MRI are used in the staging and follow-up of patients with prostate cancer, but are not indicated in all patients. In newly diagnosed prostate cancer, CT or MRI generally not necessary if PSA < 20.0 ng/mL and bone scan not necessary with PSA < 10.0 ng/mL.
- ➢ Biopsy: biopsy of the prostate provides DX. Typically performed transrectally, but may be performed transperineally in individuals who do not have a rectum. Gleason grade is based on glandular pattern of tumor and ranges from 1–5. Gleason sum (score) is the addition of the primary and secondary patterns present on microscopic examination and ranges from 2–10. Gleason scores ≥ 7 are considered biologically aggressive tumors. High-grade prostatic intraepithelial neoplasia (PIN) is often found in assn with prostate cancer. In 35–45% of men who undergo a repeat biopsy for high grade PIN, prostate cancer cells are identified in the repeat biopsy. Depending on the number of biopsies obtained initially, rebiopsy or delayed rebiopsy may be indicated with high grade PIN. Repeat biopsy is indicated for a pathology report of "atypical gland suspicious for cancer."

- **RX**: depends on patient age at diagnosis, gleason score, tumor stage, and PSA
  - ➢ TNM staging system for prostate cancer
    - ° T1 – clinically unapparent tumor, not palpable or visible by imaging
      - ▪ T1a – tumor found incidentally at TUR, < 5% of tissue is cancerous
      - ▪ T1b – tumor found incidentally at TUR > 5% of tissue is cancerous
      - ▪ T1c – tumor identified by prostate needle biopsy because of elevated PSA
    - ° T2 – Palpable tumor confined within the prostate
      - ▪ T2a – tumor involves half a lobe or less
      - ▪ T2b – tumor involves > half of one lobe, but not both lobes
      - ▪ T2c – tumor involves both lobes
    - ° T3 – palpable tumor through prostate capsule and/or involving seminal vesicles
      - ▪ T3a – unilateral extracapsular extension
      - ▪ T3b – bilateral extracapsular extension
      - ▪ T3c – tumor invades seminal vesicles
    - ° T4 – tumor is fixed or invades adjacent structures other than seminal vesicles
      - ▪ T4a – tumor invades bladder neck and/or external sphincter and/or rectum
      - ▪ T4b – tumor invades levator muscles and/or is fixed to pelvic wall
    - ° NX – Regional lymph nodes cannot be assessed
    - ° N0 – No regional lymph node metastasis
    - ° N1 – Metastasis in a single lymph node, ≤ 2 cm
    - ° N2 – Metastasis in a single lymph node, > 2 cm ≤ 5 cm in greatest dimension, or multiple lymph nodes, none > 5 cm in greatest dimension
    - ° N3 – Metastasis in a lymph node > 5 cm in greatest dimension
    - ° MX – Presence of distant metastasis cannot be assessed
    - ° M0 – No distant metastasis
    - ° M1 – Distant metastasis
      - ▪ M1a – Non-regional lymph nodes
      - ▪ M1b – Bone
      - ▪ M1c – Other sites

Organ-Confined Disease

- **RX**: Three main options
  - ➢ Surgical options: for pts with high-likelihood of organ-confined disease. Includes: open radical retropubic prostatectomy, laparoscopic radical prostatectomy, and robotic-assisted radical prostatectomy. Need for bilateral pelvic lymph node dissection depends on PSA and gleason score.
  - ➢ Nonsurgical options for locally confined disease include conformal external beam radiation therapy and interstitial seed therapy (brachytherapy).
  - ➢ For select pts with organ confined disease, cryotherapy is also an option, although it is more commonly used in those with recurrent prostate cancer after radiation therapy.

Metastatic Disease

- **RX**: Bilateral orchiectomy is an option. Side effects include loss of libido, erectile dysfunction, hot flashes, osteoporosis, fatigue, loss of muscle mass, anemia, and weight gain.

Hormonal Therapy

- **RX**: Options
  - ➢ LHRH analogs and antagonists: After initial phase of stimulation (2–3 wks) lead to suppression of LH and of testosterone production to castrate levels. Include: Lupron, Eligard, Trelstar Depot LA, Vantas, Viadur, Zoladex. Degarelix is an LHRH antagonist and not assoc with initial ↑ in testosterone.
  - ➢ Antiandrogens: Interfere with androgen action by binding to androgen receptor. Pure antiandrogens include Eulexin (flutamide), Nilandron (nilutamide) and Casodex (bicalutamide). Pure antiandrogens do not affect libido and potency. None are approved for use as monotherapy. Side effects of pure antiandrogens include gynecomastia, abnormal liver function tests, diarrhea, and gastrointestinal complaints.
  - ➢ Bone mets: Frequently used regimen is 300 cGy of XRT in 10 divided doses. In pts with significant bony mets and pain, stontrium 89 or samarium 153 may be helpful.

Hormone Refractory Metastatic Disease

- **RX**: In pts who fail complete androgen blockade, antiandrogen plus LHRH analog or antagonist, the initial management is withdrawal of the antiandrogen. When this fails may consider addition of ketoconazole.
  - ➢ Mitoxantrone is FDA approved for palliation of symptomatic metastatic, androgen-independent prostate cancer. Docetaxel (Taxotere) is approved as front-line therapy for metastatic hormone refractory prostate cancer.

Recurrent Prostate Cancer

- **RX**: Salvage radiation therapy
  - ➢ Salvage radiotherapy after radical prostatectomy can provide long-term disease control if the disease is localized within the field of radiation and a sufficient dose of radiation administered.
  - ➢ Salvage radical prostatectomy can be performed for radiation therapy failures in the setting of localized disease in carefully selected individuals. The risk of complications such as urinary incontinence is much higher with salvage radical prostatectomy as compared to radical prostatectomy as first line therapy.
  - ➢ Salvage cryotherapy can be performed for radiotherapy failures.

DISEASES OF THE PENIS

Balanitis and Balanoposthitis

- **Cause**: Inflammation of the glans penis (balanitis) and prepuce (balanoposthitis). May be bacterial, intertrigo, irritant dermatitis, maceration injury, or candidal in etiology.
- **Epidemiol**: More common in uncircumcised men and men with poorly retractile foreskin
- **SSX**: redness, edema, discharge, pain, and may be associated with voiding difficulties
- **DX**: Lab – KOH prep, Tzanck prep, fungal, bacterial, or viral cultures as dictated by clinical examination.
- **RX**: Eliminate irritants, improve personal hygiene, topical antifungals if fungal related, short course of low-potency steroids, retraction of foreskin to allow glans and prepuce to dry after cleansing, circumcision if recurrent

Lichen Sclerosis

- **Cause**: Exact cause uncertain, but genetic predisposition, infections, and autoimmune factors have been implicated. May be related to abnormal regulation of interleukin-1.

- **Epidem**: Occurs commonly on the genital skin. Women > men. In men referred to as balanitis xerotica obliterans (BXO). In both sexes, older individuals more frequently affected; 5% risk of developing squamous cell carcinoma of the vulva in women with vulvar lichen sclerosis. Men may develop urethral stenosis.
- **SSX**: well circumscribed white macules or plaques, atrophic epidermis that is prone to ulceration; in men may have pain with urination and erection, itching and burning
- **DX**: Often made on physical examination. Bx may be helpful if diagnosis in question.
- **RX**: In men – circumcision, high potency topical steroids, if urethral involvement and stenosis, meatotomy or urethral dilation may be needed
  - ➢ In women – high potency topical steroids, e.g., clobetasol 0.05%, are effective.
  - ➢ Because of the risk of developing squamous cell carcinoma, regular follow-up is needed.

Zoon's Balanitis

- **Cause**: Etiology is unknown but may be related to chronic infection with *mycobacterium smegmatis*. Plasma-cell mediated.
- **Epidem**: Occurs only in uncircumcised men. Lesions found on glans or prepuce. Histopathology – band of plasma cells in dermis
- **SSX**: Usually asymptomatic, but may have pain, irritation, and discharge. Lesion is solitary with orange-red distinct borders, may be erosive, up to 2 cm in size
- **DX**: bx of lesion helpful to confirm diagnosis
- **RX**: Often chronic and poorly responsive to topical therapy, but can resolve completely with circumcision.

Sclerosing Lymphangitis

- **Cause**: Local trauma leading to thrombosed lymphatic vessels
- **Epidemiol**: Affects men 20–40 yrs. Associated with vigorous sexual activity
- **SSX**: usually painless, translucent, flesh/red-colored lesion on shaft/glans of penis. Swelling proximal and parallel to corona
- **DX**: clinical
- **RX**: Ususally resolves in 4–6 wks. Avoidance of vigorous sexual activity until resolves. If persists, excise.

Molluscum Contagiosum

- **Cause**: Virus belonging to the DNA pox family. Transmitted primarily through direct skin contact, but fomites have been suggested.
- **Epidem**: Worldwide incidence of 2–8%. Genitalia commonly involved but can involve other areas of body, confined to skin and mucous membranes. Higher incidence in children, sexually active adults, and those who are immunodeficient. Incubation period btn 2 and 7 weeks, but up to 6 months
- **SSX**: Small, firm, umbilicated skin papules, discrete, smooth, and dome-shaped. Skin opalescent
- **DX**: clinical
- **RX**: Usually a self-limiting, benign skin lesion. Can excise, freeze, burn, or laser lesions. Topical therapies include: 0.05 mL of 5% podofilox in lactate-buffered ethanol bid for 3 days, cantharidin (0.9% solution of collodian and acetone) applied to area for at least 4 hr, repeated every week until lesions clear, can cause blistering; iodine solution and salicylic acid plaster, tretinoin 0.05–0.1% cream, aqueous solution 5–10% KOH, imiquod 5% cream, cidofovir 3% cream.

Pearly Penile Papules

- **Cause**: possibly viral in origin or phylogenetic residua
- **Epidem**: affects 30% men – more frequently in uncircumcised
- **SSX**: painless, 1–2 mm pink/white/yellow or transparent papules that encircle corona – more prominent on dorsal surface
- **DX**: clinical
- **RX**: Lesions may resolve with age. Treatment not necessary but if bothersome can excise or treat with CO_2 laser

Nonsquamous Cell Penile Cancers

	Melanoma	Basal Cell Carcinoma	Extramammary Paget Disease of the Genitalia	Kaposi Sarcoma
Cause	Cutaneous malignancy	Malignant neoplasm	Malignant intraepidermal process	Human herpes-8-virus (HHV-8) coinfection
Epidemiology	Uncommon – may occur on shaft of penis, scrotum or glans	Rarely involves male genitalia but can affect penis	Women > men; up to 80% of those with extramammary Paget's have subjacent or visceral malignancy; penile disease may occur in men with bladder CA treated with XRT	Most common malignancy in AIDS pts. 3% of men with AIDS and Kaposi sarcoma may present with genital lesion
SSX	Macule or papule with irregular border; may be pigmented (red, blue, black, or brown) or not	Papular lesion, pearly colored with telangectasia; often ulcerate	Pruritic erythematous plaque with well-demarcated borders, may be excoriated and crusted	Subcutaneous, nontender, nonpuritic nodules. Lesions may be red or blue, may become exophytic and bleed. Lymphedema may occur. May have fever, weight loss, night sweats
DX	Biopsy of lesion	Excisional biopsy	Biopsy to confirm diagnosis	Biopsy may confirm diagnosis if physical exam not definitive
RX	Determined by depth of lesion. In general, poor prognosis with penile lesions	Local excision	Remove plaque and treat underlying malignancy. XRT and 5-FU have been used to treat plaque. For extensive disease of penis and scrotum may use Nd: YAG laser	Treatment of these lesions depends upon whether part of AIDS or isolated lesions in HIV-negative cases. In HIV-pos pts, may regress using highly active antiretroviral therapy (HAART) alone, but aggressive palliation can be offered with combined HAART and XRT conservative surgical excision offers excellent palliation. Photoablation using CO_2 or Nd: YAG laser also has been effective in genital lesions. If extensive lesions of the penis RX with suprapubic cystostomy.

Nd: YAG laser = neodymium doped yttrium aluminum garnet.

Squamous Cell Carcinoma of the Penis

- **Cause**: Presence of foreskin combined with phimosis (present in > 50% men with penile cancer) and poor personal hygiene are the most common predisposing factors. Human papilloma virus (HPV)-16, HPV-18 and HPV-33 also associated with penile cancer
- **Epidem**: Rare in the U.S.; more common in South America, India, and Africa. Accts for 95% of penile cancers
- **SSX**: Often asxic unless infected. Area of induration, erythema, warty growth, nodule, or superficial elevation on the penis. About 70% are found on the glans or prepuce. May bleed if ulcerated. Palpable inguinal adenopathy present in 40–50% on presentation
- **DX**: Bx if diagnosis not definitive
  - ➢ Imaging: CT scan helpful in assessing inguinal nodes in obese patients and those with prior inguinal surgery. May identifiy pelvic adenopathy
  - ➢ TNM Staging of penile cancer
    - ° Tx – primary tumor cannot be assessed
    - ° T0 – no evidence of primary tumor
    - ° Tis – carcinoma in situ
    - ° Ta – noninvasive verrucous carcinoma
    - ° T1 – tumor invades subepithelial connective tissue
    - ° T2 – tumor invades spongiosum or cavernosum
    - ° T3 – tumor invades urethra or prostate
    - ° T4 – tumor invades adjacent structure
    - ° Nx – regional lymph nodes cannot be assessed
    - ° N0 – no regional lymph node mets
    - ° N1 – mets in a single superficial inguinal node
    - ° N2 – mets in multiple or bilateral superficial inguinal nodes
    - ° N3 – mets in deep inguinal or pelvic lymph node(s), unilateral or bilateral
    - ° Mx – presence of distant mets cannot be assessed
    - ° M0 – no distant mets
    - ° M1 – distant mets
- **RX**: Varies with location and size of tumor
  - ➢ Verrucous carcinoma – slow-growing, fungating variant – treated with local excision or XRT
  - ➢ Squamous cell carcinoma in situ – localized to epidermis – treatment options include 5-fluorouracil (5-FU), cryotherapy, laser therapy, or surgical excision. Circumcision is recommended and follow-up is necessary.
  - ➢ Noninvasive small tumors of the prepuce may be treated with circumcision with a recurrence rate of 30%.
  - ➢ Distal penile lesions < 2–3 cm involving proximal prepuce, superficial glans, or coronal sulcus are candidates for Moh's micrographic surgery; excellent cure rate for lesion < 1 cm and 50% for lesion > 3 cm.
  - ➢ Lesions near coronal sulcus, or those involving distal glans or shaft, are best-treated with partial penectomy if a tumor-free margin of 2 cm can be achieved with a remaining penile length of ≥ 3 cm.
  - ➢ Lesions involving proximal penile shaft or bulky lesions and those where tumor-free margins of 2 cm cannot be achieved or a short penile stump will remain are best treated with total penectomy and perineal urethrostomy.

➢ If palpable inguinal adenopathy present 3–6 wks after treatment of primary penile lesion and antibiotic therapy, then inguinal node dissection should be performed. Use of prophylactic inguinal node dissection in the setting of nonpalpable inguinal nodes is controversial. Modified inguinal lymph node dissection decreases morbidity.

PenileT rauma

	Penile Fracture	Penile Amputation	Penile Strangulation
Cause	Buckling injury to erect penis	Accidental, self-inflicted or result of an attack	May be self-induced during self-mutilation or masturbation or accidental from hair tourniquet or condom catheter applied too tightly
Epidemiology	Usually occurs during intercourse		May occur in infants, children, and adults
SSX	Penile pain and ecchymosis, ED, penile curvature, palpable penile scar, blood at the meatus	If significant bleeding apply tourniquet – amputated segment should be placed in sterile bag with sterile saline placed on ice for transport	Penile pain, edema distal to lesion, voiding troubles
DX	Physical examination Urethrography if urethral injury suspected	Physical examination	Physical examination
RX	Immediate surgical exploration and closure of defect in tunica albuginea	Microsurgical repair of dorsal penile arteries, veins, nerves; approximation of corpora cavernosa, debridement of devitalized and contaminated penile shaft skin and skin grafting for skin loss	Apply soap and water to penis to help remove object or apply a string starting at meatus and wrapping around glans circumferentially to compress distal penile edema and facilitate removal of object

Priapism

- **Cause**: Persistent erection ($>$ 4 hr) arising from dysfunction from the mechanisms that regulate penile detumescence and flaccidity or alteration in the regulation of arterial inflow; 30% idiopathic, 21% alcohol (ETOH) abuse or drug/medication, 12% related to perineal trauma, and 11% related to sickle cell disease. Other causes include: neurogenic factors, infections, toxins, local stimuli, inflammatory disease, malignancy, total parenteral nutrition (TPN), and hematologic abnormalities.
- **Epidem**: peak incidence ages 5–10 yrs and 20–50 yrs
- **SSX**: penile pain, penile swelling, fever, sepsis, dysuria, urinary retention
- **DX**: CBC with differential, platelet count, hemoglobin analysis, sickledex, or peripheral smear to rule out sickle cell disease or trait, urine toxicology.

- ➢ Penile blood gas, monitoring of intracavernosal pressure. With ischemic, low-flow priapism the blood gas will demonstrate a $pO_2 < 30$, $pCO_2 > 60$, $pH < 7.25$ and intracavernous pressure > 40 mmHg. In high-flow priapism, penile blood gas is normal.
- ➢ Imaging: color flow Doppler sonography if high-flow is suspected

- **RX**: Varies with cause and duration of priapism. During RX helpful to monitor intracavernouse pressure; if remains < 40 mmHg for 10 min, priapism is resolved.
  - ➢ Low-flow priapism: corporal aspiration with or without irrigation is the first line of treatment. If unsuccessful, then intracavernous injection of alpha-adrenergic agent, which is successful most of the time if duration of priapism < 14 hrs. If alpha-adrenergic therapy unsuccessful, then creation of Winter, Ebbehoj, or Al-Ghorab shunt is indicated.
  - ➢ Alpha-adrenergic therapy for priapism – intermittent injection of 100 to 500 mcg of phenylephrine every 3 to 5 min until detumescence or a duration of 1 hr is reached. Phenylephrine is supplied as 10 mg/mL (1%) in a 1 mL vial and must be diluted with 0.9% NaCl to achieve appropriate concentration.
  - ➢ Sickle-cell related: hydrate, alkalinize, control pain, hypertransfuse or exchange transfuse to decrease Hgb S to 30–40% while treating the ischemic (low-flow) priapism
  - ➢ Stuttering priapism: A trial of gonadotropin releasing agonists (GnRH agonists) or antiandrogens may be useful in adult men with stuttering priapism. Intracavernosal self-injection of phenylephrine should be considered in those who fail or refuse systemic therapy for stuttering priapism.
  - ➢ High-flow priapism: Initial management is observation as often it will resolve without need for treatment. For those pts who request treatment, selective arterial embolization with autologous clot or absorbable gel recommended

Erectile Dysfunction (ED)

- **Definiton**: The consistent inability to achieve and/or maintain an erection satisfactorily for completion of sexual performance.
- **Cause**: Causes include psychogenic, neurogenic (spinal cord injury, Parkinson disease, CVA, brain tumor, Alzheimer disease, trauma, spinal cord abnormality such as myelomeningocele, multiple sclerosis, disc herniation), postsurgical nerve injury (radical prostatectomy, low anterior resection, abdominal perineal resection, radical cystectomy), vitamin deficiency, alcoholism, recreational drug abuse, endocrinologic, vascular and CV, medication induced (antidepressants, antihypertensive, hormonal agents for prostate cancer), Peyronie disease, and metabolic disorders (diabetes mellitus, hemochromatosis, SS disease, hepatic/renal failure, scleroderma, thyroid disease, adrenal disease). Smoking and hyperlipidemia are also risk factors.
- **Epidem**: Affects 50% of men age 40 to 70 yrs. Higher probability of ED directly related to CV disease, HTN, and DM.
- **SSX**: Inadequate penile rigidity for penetration and/or decreased duration of rigidity. SSX of underlying causative disease process include: angina, claudication, palpable penile plaque, penile curvature with erection, decreased peripheral pulses, neurologic deficits, and gynecomastia.
- **DX**: Clinical diagnosis. Evaluation directed at identifying underlying medical condition(s). Serum chemistries, renal function tests, CBC, urinalysis, testosterone, and prolactin. May also check lipid profile, fasting blood sugar, thyroid function tests, and liver function tests if indicated.

- ➢ Imaging: Color Doppler US with intracavernous injection (typically prostaglandin E1, alprostadil) 10 mcg is a useful test to evaluate arterial insufficiency and veno-occlusive disease. Peak systolic velocity $<$ 25 mL/sec indicates arterial disease. Persistent elevated diastolic flow $>$ 5–10 mL/sec in setting of normal arterial inflow is suggestive of veno-occlusive disease. Gold standard for DX and localization of arterial disease is pudendal arteriography with pharmacologic therapy (alprostadil injection). Gold standard for evaluation of veno-occlusive disease is pharmacologic cavernosometry and cavernosography.

- **RX**: Various treatment options are available.

Treatment Options for Erectile Dysfunction (ED)

Treatment	Administration	Dosing	Contraindicatons	Side Effects
Sildenafil (Viagra) PDE-5 inhibitor	Oral; taken on demand 0.5–1.5 hr prior to intercourse; requires stimulation. High fat meal delays absorption and decreases Cmax.	25 mg, 50 mg, and 100 mg; use lower dose if age > 65 yrs, pt on newer protease inhibitors, erythromycin, ketoconazole, or renal failure. Use only once in 24-hr period.	Concomitant nitrate use, retinitis pigmentosa. When concomitant alpha-blocker use, must be on stable dose of alpha-blocker before use of PDE-5 inhibitor. Follow Princeton guidelines regarding use in pts with CV disease.	Headache (16%), flushing (10%), dyspepsia (7%), abnl vision (3%). Priapism uncommon. NAION (nonarteritic anterior ischemic optic neuropathy) has been reported in pts taking oral PDE-5 inhibitors. A causal relationship has not been established. Sudden loss of hearing has been reported in pts on oral PDE-5 inhibitors, a causal relationship has not been established.
Tadalafil (Cialis) PDE-5 inhibitor with long half-life	Oral; taken on demand 2 hrs prior to intercourse, requires stimulation	5 mg, 10 mg, 20 mg. No more frequently than once every 24 hrs. Recommnded starting dose is 10 mg in most patients. Start at 5 mg if moderate renal insufficiency and CYP3A4 inhibitor use. A 2.5 mg dose is approved for daily use.	Same contraindications as with sildenafil.	Headache (11–15%), dyspepsia (4–10%), myalgia (1–3%), back pain (3–6%), flushing (2–3%). NAION and hearing loss also reported with Cialis, no causal relationship established.

Treatment Options for Erectile Dysfunction (ED) (cont'd)

Treatment	Administration	Dosing	Contraindicatons	Side Effects
Vardenafil (Levitra) PDE-5 inhibitor	Oral – take on demand 25 min to 1 hr prior to intercourse; requires stimulation.	2.5 mg, 5 mg, 10 mg, and 20 mg. Recommended starting dose in most pts is 10 mg. Start with 5 mg in pts > 65 yrs of age, concomitant use of CYP3A4 inhibitors.	Same contraindications as sildenafil. May increase QT interval and thus avoid use in pts with congenitally prolonged QT interval or class IA or class III antiarrhythmics	Headache (15%), flushing (11%), dyspepsia (4%). NAION and hearing loss have been reported with vardenafil, a causal relationship has not been established
Intraurethral Prostaglandin E-1, Alprostadil (MUSE)	Intraurethral suppository – used on demand.	125, 250, 500, and 1000 mcg suppository. Use only once every 24 hr.	Hypersensitivity to PGE-1, pregnant partner, predisposition to priapism.	Pain (penile, urethral, testicular, perineal) in 33%, lowers BP in 3%, vaginal irritation in 10% partners.
Intracavernous Injection of Prostaglandin E-1 (Caverject, Edex)	Direct injection into lateral aspect of corpora cavernosa, alternating sides with each injection.	5–40 mcg per injection, no more frequently than every 48 to 72 hrs	Hypersensitivity to PGE-1; predisposition to priapism. Care with use in pts with peyronie disease and those on blood thinners.	Prolonged erection (1.1–1.3%), corporal fibrosis (2.7%), painful erection (15–30%), hematopsermia, ecchymosis (1.5%).
Vacuum Constriction Device	Plastic cylinder with hand or battery-operated pump and constricting bands.	Remove band 30 min after application.	Use with caution in pts taking aspirin or anticoagulants; pts with severe penile curvature.	Painful ejaculation (3–16%), inability to ejaculate (12–30%), petechiae of penis (25–39%), numbness during erection (5%).
Penile Prosthesis	Surgically placed, models range from semirigid to inflatable.	N/A	Requires preoperative patient counseling.	Decreases penile length by 1 cm. Infection < 10%, mechanical malfunction < 5%, erosion.

Peyronie's Disease

- **Cause**: Exact etiology is unknown. An aquired condition characterized by formation of fibrous plaques within the tunica albuginea of the corpora cavernosa of the penis. Thought to be related to blunt trauma during intercourse with tearing of fibers in the tunica albuginea and extravasation of blood and resultant inflammatory response.
- **Epidem**: Up to 3.2% prevalence in men age 30–80 yrs; highest incidence in 45–60 yr age group. Sixteen to 20% have associated Dupuytren's contractures. Prevalence higher in men with plantar and fascial contracture, tympanosclerosis, diabetes, gout, and Paget disease
- **SSX**: painful erection, penile curvature, ED, palpable plaque
- **DX**: clinical
  - ➢ Imaging: may identify calcification within the plaque on US or plain film
  - ➢ In pts undergoing surgical correction of Peyronie's disease a pharmacologic color duplex US is useful to establish patient's erectile function and degree of curvature preoperatively.
- **RX**: Initial treatment is reassurance. Peyronie's disease is an evolving process; in some patients it can improve significantly or resolve such that no surgical treatment is necessary.
  - ➢ Conservative therapies include: oral, local (shock wave therapy, iontophoresis), and intralesional therapies. Oral therapies include: vitamin E 200–300 mg PO QD – associated with decreased pain and plaque size in short-term study. Colchicine 0.6 mg increased up to 2.4 mg/day associated with reduction in pain, curvature, and plaque size in a small short-term study, potassium aminobenzoate (POTABA) in doses of 12 g/day over 3-mo period associated with decreased pain, curvature, and plaque size in study with 8–24 mo f/u. Tamoxifen 20 mg PO bid for 3 mo associated with improvement in pain, curvature, and plaque size. May lower sperm count and have GI side effects.
  - ➢ Intralesional therapies: Intralesional injection of verapamil – multiple 10-mg doses injected every 2–4 weeks, 12 ×, noted to improve penile curvature and sexual performance. Intra-lesional injection of interferon-alpha being evaluated.
  - ➢ Surgical options vary from techniques based on either shortening the tunica albuginea on the side opposite of the curvature or lengthening the shorter side of the penis by incision or excision of the fibrotic area and grafting the area. Those pts with Peyronie's disease and ED who are refractory to topical and oral therapies may benefit from a penile prosthesis, which will straighten the penis and provide rigidity.

Hemospermia

- **Cause**: Blood in the ejaculate may be associated with pathology of the prostate, seminal vesicles or urethra, infection, secondary to trauma, or related to systemic diseases.
- **Epidem**: prevalence unknown, although believed to be common
- **SSX**: blood in ejaculate, may have SX related to underlying disease process
- **DX**: Lab – UA and culture, PSA, urine for GC and Chlamydia, semen analysis, clotting studies if bleeding disorder suspected
  - ➢ Imaging: transrectal US indicated for chronic hemospermia. MRI may be helpful to visualize seminal vesicle pathology.
  - ➢ Cystoscopy indicated for chronic hemospermia
- **RX**: Reassurance; condition related to benign disease in most cases. If infectious, treat with appropriate antibiotics. Urethral or prostatic varices can be fulgurated. Aspiration of seminal vesicle cyst if present, RX of bleeding disorder if present.

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