**Prostate**

**Prostate Cancer**

1. Appropriately identify patients requiring prostate cancer screening.

* Initiation
  + CMA
    - Offer screening to all men age 50 or older who have a life expectancy greater than 10 years (CMA 2011)
    - Offer at age 40-45 for those at higher risk (1st degree with Pca, BRCA1or African American ancestry) (CMA and US Task Force)
    - Some trials demonstrated a benefit of establishing a baseline PSA for all men 40-49 yrs but this is not widespread practice yet (CMA 2011)
  + Canadian Task Force
    - The PSA test should be excluded from the periodic health examination for asymptomatic men over 50yrs of age (Grade D recommendation: fair evidence against screening, Level 3-4 evidence)
    - If screening is requested, the patient should be fully informed of the potential risks and benefits (see below)
* Frequency
  + CMA: Annual screening is standard but two trials demonstrate 2-4 year intervals is OK too
  + CTF: You guessed it. Never screen asymptomatic men.

2. In a patient suitable for prostate cancer screening, use and interpret tests (e.g., prostate-specific antigen testing, digital rectal examination [DRE], ultrasonography) in an individualized/sequential manner to identify potential cases.

* History is the simplest screening tool
  + Usually asymptomatic
  + Locally advanced disease
    - Obstructive and irritative LUTS- hesitancy, increased frequency, dribbling, difficulty with stream,dysuria, hematuria… (uncommon w/o spread)
  + Metastatic disease
    - Bony metastasis to axial skeleton is very common (osteoblastic)
    - Also liver, lung and adrenal metastases
    - Sx: B symptoms, Leg pain and edema with nodal metastasis, obstructing lymphatic and venous drainage
* DRE and PSA
  + This is super controversial and I break it down a bit below

**PSA Screening**

* PSA is specific to the prostate, but is NOT specific for prostate cancer
* *PSA alone in screening asymptomatic men for cancer has not been shown to decrease mortality*
  + PSA, DRE and TRUS must be used in conjunction for screening and investigation
  + DRE cannot reach anterior aspect of prostate (miss ~ 40% of ca)

PSA may also be increased with:

* BPH
* Prostatitis
* Prostatic ischemia/infarction
* Acute urinary retention
* Manipulation of lower urinary tract (cystoscopy, bx, foley)
* Ejaculation (minor transient increase) wait for 2 days
* *DRE does not increase PSA*
* PSA is not an ideal tumour marker:
  + Combining PSA with DRE improves screening effectiveness

|  |  |  |  |
| --- | --- | --- | --- |
|  | Abnormal PSA | Abnormal DRE | Combined (PSA/DRE) |
| Sensitivity | 35% | 27% | 38% |
| Specificity | 75% | 33% | 92% |
| PPV | 28% | 18% | 56% |

* Strategies to increase specificity of PSA test:

**Age-Related Norms** have been suggested

Normal PSA Value by Age Group

|  |  |
| --- | --- |
| Age Range (yrs) | Serum PSA Concentration (g/L) |
| 40-49 50-59 60-69 70-79 | <2.5 <3.5 <4.5 <6.5 |

**Free-to-Total PSA Ratio**

* + Complexed PSA increases in prostate cancer, decreasing the percentage of the free fraction
  + Think “free and easy”: increased free/total ratio suggests benign cause of PSA elevation
  + <10% free PSA suggestive of cancer
  + >20% free PSA suggests benign cause

**PSA velocity**

* + Change of >0.75ng/mL (20%) per yr assoc with ↑ risk of cancer

**PSA density**

* + PSA divided by prostate volume as found on TRUS
  + >0.15ng/ml/g assoc w/ incr risk of cancer

***Explaining Sensitivity and Specificity of PSA to pt***

* Out of 100 men who have a PSA test done
  + 90 will have a negative result- of the 90
    - 1 patient will have undiagnosed prostate cancer
  + 10 men with have a positive result – of those 10
    - 7 will NOT have prostate cancer
    - 3 will have prostate cancer

**Digital Rectal Examination**

* Findings increasing the risk of malignancy
  + hard irregular nodule or diffuse dense induration involving one or both lobes
* Canadian Task Force
  + Poor evidence exists to include or exclude digital rectal examination from the PHE of men > 50 years of age [[**C**](http://www.ctfphc.org/Abstracts_printable/Ch67abs.htm#table_1)].
  + Insufficient evidence exists to have physicians who presently do the procedure change their behavior. (Digital rectal examination can be done for other reasons other than to detect prostate cancer.)

**Investigations to Rule Out Suspected Prostate Cancer**

* Family Physician
  + TRUS (transrectal ultrasound) - assesses size and local staging (ask for prostate volume, views of kidneys and bladder with post-void residual before referring to urology)
* Specialist
  + TRUS-guided needle biopsy
  + Bone scan -may be omitted in untreated prostatic ca with PSA <10
  + Lymphangiogram and abdo/pelvic CT scanning to assess metastases

***Gleason Tumour Grading***

|  |
| --- |
| 1-4 = well differentiated  5-7 = moderately differentiated  8-10 = poorly differentiated |

3. In patients with prostate cancer, actively search out the psychological impact of the diagnosis and treatment modality

* FIFE away, young Jedi.

4. In patients with prostate cancer, considering a specific treatment option (e.g., surgery, radiotherapy, chemotherapy, hormonal treatment, no treatment):

a) Advise about the risks and benefits of treatment.

***Management:***  
Depends on:

* Overall health status
* Life expectancy
* Quality of life
* Patient preference

**Staging**

|  |
| --- |
| **T1** (not palpable, not seen on imaging, found by ↑PSA or TURP)   * + If young consider radical prostatectomy, brachytherapy or radiation   + Follow in older population (cancer death rate up to 10%)   **T2** (palpable, confined to prostate)   * + Radical prostatectomy or radiation (70-85% survival at 10yrs) or brachytherapy   **T3** (tumour extends through prostate capsule),  **T4** (tumour invades adjacent structures, besides seminal vesicles)   * + Staging lymphadenectomy and radiation or hormonal treatment   **N>0** (spread to regional lymph nodes) or **M>0** (distant metastasis)   * + Requires hormonal therapy/palliative radiotherapy to metastases   + Bilateral orchiectomy – removes 90% of testosterone   + LHRH agonists (ex. leuprolide (Lupron), goserelin (Zoladex))   + Estrogens (ex. diethylstilbestrol (DES))   + Antiandrogens     - Greater androgen blockage can be achieved by combining an antiandrogen with LHRH agonist or orchiectomy     - Local irradiation of painful secondaries or half-body irradiation   + Chemotherapy regimen that incl docetaxel may improve survival in advanced disease no longer responsive to hormone therapy |

***Risk Stratification***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Yellow-low risk Green- Int. risk Red – high risk | T1-T2 |  |  | T3-T4 |
|  | PSA <= 10 | PSA 10.1 – 20.0 | PSA>=20.1 |  |
| Gleason <=6 | <T2a |  |  |  |
| Gleason = 7 |  |  |  |  |
| Gleason >=8 |  |  |  |  |

Low risk/intermediate risk

* Radical prostatectomy, EBRT, or brachy
* Watchful waiting

High risk

* Curative –
  + Neoadjuvant, concurrent and ongoing Androgen deprivation therapy
  + Radical Prostatectomy, EBRT
* Palliative
  + ADT and or radiation

***Risks/Benefits of Treatment Options***

* Watchful waiting – well differentiated (low Gleason 2-5), do well few die of prostate ca even after f/u 10-15yrs, most differentiated (Gleason 8-10) die of prostate ca, therefore appropriate with low-risk cancer and w/ shorter life expectancies
* Surgery (Radical prostatectomy)
  + Risks: erectile dysfunction, urinary incontinence, urethral stricture, bowel damage, and complications arising from anesthesia and major surgery, including death.
  + Benefits: decreased metastasis, decreased mortality
* Radiotherapy
  + External beam radiation therapy and brachytherapy
  + Risks: genitourinary sx, GI sx (diarrhea, tenesmus), erectile dysfunction, dry ejaculate, incontinence, urethral stricture, bowel damage
* Hormonal (ie. androgen ablation)
  + Used for T3 and T4 stages
  + LH-RH agonists ex. leuprolide (Lupron) or

Antiandrogens ex. cyproterone acetate

* + Risks: loss of libido, erectile dysfunction, hot flashes, gynecomastia, fatigue à after many yrs: loss of muscle mass, osteoporosis, adverse lipid profiles, glucose intolerance
  + Benefit: 80% respond, median disease-free survival is 2-3yrs
* Chemo – ineffective at prolonging life with hormone-refractory ca

***Prognosis***

* Stage T1-T2: excellent, comparable with normal life expectancy
* Stage T3-T4: 40-70% survival at 10yrs
* Stage N+ and/or M+: 40% survival at 5yrs
* Prognostic factors: tumour stage, tumour grade, PSA value

b) Monitor patients for complications following treatment.

After Radical Prostatectomy (side effects)

* + Pelvic pain is common, esp. among younger men after RP
    - For 14 days post op men require catheter that may cause
      * Swelling
      * Pain
      * Urine leak past
      * Bladder spasms
      * Rectal pain
  + Incontinence will occur in the post op period
    - Occurs days- years post op  b/c of strictures and nerve damage
  + Erectile functioning might return slowly over years
    - Depends on age, erectile function before symptoms, size of the gland, and surgical technique
    - Improvement seen up to 5 years
  + PDE5 inhibitors help only 50% of the time
    - Both Nerve bundles spared
      * age< 55 – 80% chance of response
      * age 56-65- 45% chance of response
      * age 66 + - 33% chance of response
    - One nerve bundle spared
      * Age <55 -44%
    - No nerve bundles spared
      * No response regardless of age
  + Penile Shortening or fibrosis can occur
    - 70% of men
  + PSA velocity is more reliable indicator of recurrence than PSA alone
    - Cut point  -0.2-0.4
    - Velocity (doubling/tripling time) – should be assessed

After Radiation Therapy

* + Bladder irritation is common
    - Frequency/dysuria are main symptoms
    - Treat with alpha blockers
  + Bowel Complications might occur in long term
    - Proctitis (rectal pain/irritation)-45% (EBRT)
    - Diarrhea
    - Rectal bleeding (brachytherapy)
    - Rectal Ca (EBRT)
  + Later onset of erectile dysfunction
    - Later onset compared with surgery
    - Brachy better than EBRT for sexual outcomes
    - Use of PDE5 inhibitors soon after tx preserve erectile function

5. In patients with prostate cancer, actively ask about symptoms of local recurrence or distant spread

***Monitoring for Cancer Recurrence***

* Recurrence depends on: Tumor size, Grade, Stage, LN involvement
* F/U at 6 wks à 3, 6, 9, 12 months semi-annually 2nd to 5th year, then annually x 5-10yr
* At each visit
  + Ask about local symptoms  (i.e.; LUTS obst/irritative ) and ask about –potential mets symptoms, (GI sx, and bone pain)
  + Test PSA.
    - An increasing PSA level after curative therapy is termed a biochemical recurrence (BCR). Occurs in 30-50% of pts during the course of their follow-up, regardless of modality of treatment
    - The significance of a BCR is in itself unclear.  In one study, fewer than 1/3 of pts with BCR after RP developed systemic recurrence. In those patients who progress, BCR usually predates metastatic disease progression by an avg. of 7 yrs and prostate-cancer mortality by 15 yrs
    - Recent studies have shown that the speed at which PSA rises, or the PSA doubling time (PSADT), is one of the strongest predictors of clinical progression and cancer mortality.  If PSA doubles slowly (> 12 m), then recurrence is likely local. When PSA doubling time is shorter than 6 m, it is more consistent with disseminated disease.

Factors that suggest BCR – local vs. distant

|  |  |  |
| --- | --- | --- |
| Factor | Local | Distant Recurrence |
| Initial pathology | Gleanson <7, positive surgical margins, no nodes | Gleason>7, extra-prostatic involvement, nodal involvement |
| Time to BCR after tx | >1-2 yr | <1 yr |
| Pre treatment PSA | <10 | >10 |
| PSA doubling time | >12 mo | <6 -12mo |

* Annually
  + DRE (not necessary)- nodules may be confused with scar tissue
* If on anti androgen therapy
  + BMD q2-3 years

**Following Patients with Prostate Cancer**  
  
PSA (usually check q3 months)

* If  EBRT/Brachy used – PSA >0.4 or Nadir +2 = BCR- Refer for treatment and Bone Scan if >20 or pt symptomatic
* If Radical Prostatectomy – PSA >0.4 = BCR – Refer for treatment and bone scan if >20 or symptomatic
* If watchful waiting – PSA >10 or PSADT< 6 mo or symptomatic
  + If currently using watchful waiting only – than begin ADT
  + If currently using ADT – than hormone refractory disease – referral for chemo, palliative radiation, or consider secondary hormonal therapy

Visit q 6 mo

* Assess treatment, clinical assessment, PSA
* DRE optional
* Bone scan if PSA >20 or symptomatic

**Benign Prostatic Hypertrophy**

6. Given a suspicion of benign prostatic hypertrophy, diagnose it using appropriate history, physical examination, and investigations.

***Hx:***

* prior and current illnesses, prior surgery and trauma
* current meds include OTC
* Symptoms of BPH

|  |  |  |
| --- | --- | --- |
| Obstructive symptoms | Irritative symptoms | Late complications |
| * + Hesitancy (difficulty starting urine flow)   + Straining   + Diminution in size and force or urinary stream   + Stream interruption (double voiding)   + Urinary retention (sensation of  incomplete voiding)   + Post-void dribbling   + Overflow incontinence |  Urgency   Frequency   Nocturia   Hematuria   Urge incontinence |  Hydronephrosis   Loss of renal concentrating ability   Systemic acidosis   Renal failure       -fatigue, anorexia,                  nausea, malaise |

* + Assess the severity of symptoms – according to AUA

***P/E:***

* Palpate abdomen, groin LNs, CVA tenderness, testes, scrotum
* DRE for prostate size, symmetry, nodularity, tenderness and texture

-BPH: smooth, rubbery, nontender, symmetrically enlarged prostate

***Diagnostic Tests***

* PSA: normal <4 ng/mL
  + Uncertain how to deal with values between 4-10
  + If >10 can dx prostate pathology
  + Do not test PSA immediately after DRE as level may be falsely elevated
* Cr, BUN
* Urinalysis for hematuria to r/o UTI
* Post-void residual volume by U/S
* Urodynamics – pressure/flow studies
* Not routinely recommended
  + Cystourethroscopy
  + IVP
  + U/S

**Referral** to urologist if symptoms other than mild

Prostatitis

In patients presenting with specific or non-specific urinary symptoms:

1. Identify the possibility of prostatitis.

* Most common urologic dx in men <50yrs
* Very uncommon in men to develop UTI (unless abnormality in structure), therefore most LUTS are due to prostatitis as opposed to Lower UTI

***Clinical features***

* Irritative LUTS- dysuria, hematuria, increased frequency, urgency
* Rectal, low back and perineal pain
* Systemic symptoms: fever, malaise, myalgia, arthralgia
* Hematuria

b) Interpret investigations (e.g., urinalysis, urine culture-and-sensitivity testing, Digital Rectal Exam, swab testing, reverse transcription-polymerase chain reaction assay) appropriately.

***Investigations***

* Rectal exam
  + Enlarged, tender, warm prostate
  + Prostatic massage is not recommended d/t extreme tenderness and risk of inducing sepsis, abscess or epididymo-orchitis
* Urine R&M, C&S – can do Initial void culture (urethritis) and mid stream culture (cystitis)
* Blood CBC, C&S

***Diagnosis***

* Based on a combination of clinical symptoms and tender prostate on exam – culture to dictate what organisms involved