Benign

- Papillary Adenoma: discrete nodule that looks just like a low-grade renal cell carcinoma sharing not only histology but also immunochemistry/cytogenetic changes and thus b/c of its striking similarity to renal cell carcinoma this benign cancer is treated as an early cancer and thus is immediately removed
- Angiomyolipoma: harmatoma of fat, smooth muscle, and blood vessels, associated with Tuberous Sclerosis Syndrome

## Malignant

- Mets: lung, GI, breast, MM, lymphoma, sarcoma, etc (10%)
  - Renal Cell Carcinoma (RCC) (90%)
    - Epidemiology 0
      - 39k/yr incidence vs 13k/yr deaths (increased incidence b/c of increased detection but only modest increase in survival)
      - ~60yo, M>F, White
        - There are RFs but no specific cause unlike bladder cancer
          - 95% Sporadic (one mass) acquired mutation of VHL gene in 60% of cases
            - 0 1° tobacco, 2° HTN, obesity, long term dialysis resulting in cyst formation that can turn into RCC, phenacetin induced nephropathy, A-PCKD
            - 5% Familial (several masses) inherited mutations below
              - von-Hippel-Lindau (VHL) Syndrome 0
                - VHL gene is a tumor suppressor gene (normally the VHL protein inhibits hypoxia induced genes like VEGF, PDGF, GLUT-1 which promote vasculature growth therefore when mutated there is increased vasculature which can support a tumor otherwise the tumor would die)
                - (1) RCC, (2) Cerebellar/Retinal Hamangioblastomas, (3) Pheochromocytoma
                - Birt-Hogg-Dube (BHD) Syndrome 0
                  - c-MET gene is an oncogene
                    - (1) RCC, (2) Cutaneous/Uterine Leiomyomas

- Morphology 0
  - (1) Clear Cell (75%) adenocarcinoma of PCT epithelium resulting in a grossly yellow mass b/c of microscopic lipid vacuoles
  - (2) Non-Clear Cell including Chromophilic Papillary (15%)
  - (3) Chromophobic (very rare)
  - (4) Oncocytic (very rare)
  - Metastasis
    - invades renal vein extending through IVC to R heart as a solid column of cells with eventual metastasis primarily to 1° lung and 2° liver, brain, bone (important b/c metastasis occurs before any symptoms manifest!!!)
    - Metastasis to lung, soft tissue, bone, liver, CNS, thyroid
- S/S 0

0

- Early (5-year survival 70%)
  - Classic Triad: (1) hematuria (2) palpable flank mass and (3) CVAT  $\mathsf{PA}$ 
    - however, this triad is only seen in 10% of pts
    - the most common of these symptoms is hematuria
    - constitutional symptoms
    - left varicocele from obstruction of the testicular vein b/c it comes off of left renal vein
    - Stauffer's Syndrome (nonmetastatic hepatic dysfunction) is a very poor prognostic indicator, reversible with removal of affected kidney
- Late aka metastasis (5-year survival 45%)
  - General Constitutional Symptoms
    - Paraneoplastic Syndromes: "The Internist's Tumor" but this term is not appropriate these days as most (30%) tumors are detected incidentally as asymptomatic masses due to the increased use of imaging
  - Erythropoietin = Polycythemia
  - PTH = Hypercalcemia
  - Renin = HTN
  - Gonadotropins = Feminization/Masculinization
  - Cortisol = Cushing Syndrome
  - Hypercoagulable State
  - Hyponatremia
- D7 0
- US differentiate b/t mass vs. cyst and if + mass then CT for diagnosis and staging and MRI best for assessing renal vein and vena cava involvement
- Do you need to Bx if + positive mass or should you just do nephrectomy?

- Check renal/liver fxn/CBC/electrolytes
- Mets: CT-C (lung), Bone Scan (bone), CT-A/P (liver)
- Poor Prognostic Factors: anemia, hypercalcemia, low performance status, high LDH, long period from Dx to time to Tx
- Staging/Tx (refer below)

| Stage | Т                    | Ν                             | М | 2/5/10      | Treatment  |  |  |  |
|-------|----------------------|-------------------------------|---|-------------|--|--|--|--|
| (%)   |                      |                               |   | Year        | Chemotherapy resistant   |  |  |  |
|       |                      |                               |   | Survival    | Radiation resistant  |  |  |  |
|       |                      |                               |   |             | Hormone resistant  |  |  |  |
| 1     | 1 (<7cm)             | 0                             | 0 | 98/95/95    | <ul> <li>Partial Nephrectomy (wedge kidney resection)</li> </ul>   |  |  |  |
| Ш     | 2 (> <b>7cm</b> )    | 0                             | 0 | 95/88/81    | <ul> <li>Radical Nephrectomy (complete kidney + Gerota's Fascia + LN +<br/>adrenal if unner note)</li> </ul>   |  |  |  |
| 111   | 1-2                  | 1 (1 regional LN)             | 0 | 74/59/43    |  |  |  |  |
|       | 3 (a = renal vein, b | 0-1                           | 0 | , , .       | LN / Renal Vein / Adrenal / Vena Cava Resection  |  |  |  |
|       | = adrenal &          |                               |   |             | , , ,  |  |  |  |
|       | perinephric tissue,  |                               |   |             |  |  |  |  |
|       | c = vena cava)       |                               |   |             |  |  |  |  |
| IV    | 4 (beyond Gerota's   | 0-1                           | 0 | 23/20/15    | " " (surgery is really only done for palliation it should not be done with   |  |  |  |
| (50%) | fascia)              |                               |   | (usual      | intention of treating the cancer in cases of metastatic dz)  |  |  |  |
|       | #                    | 2 ( <u>&gt;</u> 1 regional LN | 0 | survival is | <ul> <li>Immunologic Chemotherapy (it has been found that pts w/ metastatic</li> </ul>   |  |  |  |
|       |                      | >5cm)                         |   | ~12mo)      | dz can have prolonged stabilized dz and even rare spontaneous  |  |  |  |
|       | #                    | #                             | 1 |             | regression, there is a distinct cytotoxic T-cell milieu, and the presence  |  |  |  |
|       |                      |                               |   |             | of HLA antigens on tumors cells suggesting that the immune system  |  |  |  |
|       |                      |                               |   |             | might play an important role)  |  |  |  |
|       |                      |                               |   |             | - 1980s: <b>α-IFN</b> (15% response rate)  |  |  |  |
|       |                      |                               |   |             | - 1990s: IL-2 (30% response rate)  |  |  |  |
|       |                      |                               |   |             | <ul> <li>Novel Chemotherapy (based on the VHL model above the focus is now<br/>indication of the section of the</li></ul> |  |  |  |
|       |                      |                               |   |             | on inhibiting certain parts of this pathways from making vEGF, PDGF,   |  |  |  |
|       |                      |                               |   |             | Baf Tyrosine Kinase Inhihitor: sunitinih (Sutent) and  |  |  |  |
|       | Mantas               |                               |   |             | sorafenih (Nevayar) Unique SEs: diarrhea, HTN, hand-foot   |  |  |  |
|       |                      |                               |   |             | syndrome   |  |  |  |
|       |                      |                               |   |             | - Inhibitors of mammalian Target Of Rapacvin (mTOR):   |  |  |  |
|       |                      |                               |   |             | temsirolimus (Torisel) and vorlimus (new) Unique SEs:  |  |  |  |
|       |                      | ACID                          |   |             | asthenia and pulmonary fibrosis  |  |  |  |
|       |                      |                               |   |             | Direct VEGF Inhibitors: bevacizumab (Avastin)  |  |  |  |
|       |                      |                               | - |             |  |  |  |  |

- "Bladder Cancer"
  - Types
    - 1° Transitional Cell Carcinoma (TCC) 85%
      - 2° SCC (rare except in Schistosomiasis, less amenable to Tx)
    - 3° Adenocarcinoma (very rare, less amenable to Tx)
  - Epidemiology
    - M>F, >50yo, 45k/yr w/ 12k deaths/yr
    - RFs
      - Smoking
      - Phenacytin Analgesic
      - Radiation
      - Inflammation Chronic (catheters esp in paraplegics who have indwelling bladder catheters, tubes, stones, etc)

- Unknown Urban Carcinogens (many carcinogens are concentrated in the urine, hence more common in urban than rural pts, esp exposure to agents used in dye/rubber/leather/chemical plants, (truckers, tire/rubber factory workers, industrial cities)
- Cyclophosphamide (initially causes hemorrhagic cystitis 2/2 metabolite acrolein which causes bladder epithelium to slough off forming thin friable mucosa that bleeds and after several sloughs w/ epithelial replacement cancer can form, Tx: MESNA which binds acrolein and converts it to inert thioethen
   Schistosoma haemotibium (most common world-wide)
- Morphology
  - tumor of epithelium that lines from renal pelvis to bladder (primarily in bladder)
- S/S
  - Early (5-year survival is 60%)
    - Really Three Different Presentations:
      - painless gross hematuria (75%)
      - irritable bladder symptoms such as frequency, urgency, dysuria, nocturia (50%)
      - palpable hydronephrosis and flank pain b/c of blockage of urinary outflow (1%)

## suggestive of Stage C or greater Late aka metastasis (5-year survival is 10%)

Stage/Tx (refer below)

.

| UA w/ Cytology                        | then                 | then                 |             | Тх   |
|---------------------------------------|----------------------|----------------------|-------------|--|
| NB important to also evaluate the     | Cystoscopy w/ Bx     | CT-C/A/P & Bone Scan |             | NB remember that bladder cancer is                 |
| upper urinary tract regardless of     |                      |                      |             | considered a field defect type of malignancy       |
| what you find in the bladder b/c of   |                      |                      |             | in that other areas of bladder epithelium          |
| the increased r/o upper tract disease |                      |                      |             | are equally at risk therefore strict and           |
| in pts with bladder cancer therefore  |                      |                      |             | frequent surveillance is necessary even if         |
| do a RP. IVP. CT. etc                 |                      |                      |             | the entire bladder is taken out                    |
|                                       | Т                    | N                    | М           |  |
| Stage 0                               | TIS (Carcinoma In-   |                      |             | <b>Eulguration</b> aka Excisional Biopsy followed  |
| ettage e                              | Situ)                |                      |             | hy intravesical instillation of 1° Bacillus-       |
|                                       | Situy                |                      |             | Calmette-Guerin aka <b>BCG</b> (live               |
|                                       |                      |                      |             | Mycohacterium hovis vaccino which infacts          |
|                                       |                      |                      |             | the typer cells and then stimulates an             |
|                                       |                      |                      |             | immune response against the infected cells         |
|                                       |                      |                      |             | initial e response against the infected cens       |
|                                       |                      |                      |             | causing cell death) or 2° Thiotepa,                |
|                                       |                      | -                    |             | Miltomycin, Doxorubicin                            |
| Stage A                               | 1 (up to lamina      | 0                    | 0           | TransUrethral Resection of Bladder ( <b>TURB</b> ) |
|                                       | propria)             |                      |             |  |
| Stage B                               | 2 (into lamina       | 1                    | 0           | Radical Cystectomy (complete bladder               |
|                                       | propria)             | (homolateral         |             | resection, urethral resection, LN dissection,      |
|                                       |                      | LNs)                 | 4           | removal of prostate / uterus / ovaries /           |
| Stage C                               | 3a (into muscle)     | 2                    | 0           | anterior vaginal wall) w/ Urinary Diversion        |
|                                       | 3b (into perivesical | (contralateral       |             | or Neo Bladder Formation                           |
|                                       | fat)                 | or bilateral         |             |  |
|                                       | 4 (into surrounding  | or multiple          |             |  |
|                                       | organs: prostate,    | LNs)                 |             |  |
|                                       | uterus, vagina, etc) |                      |             |  |
| Stage D                               | #                    | #                    | 1 (Liver.   | ""+  |
|                                       |                      |                      | Adrenal.    | Systemic Chemo: any type of platinum               |
|                                       |                      |                      | Lung, Bone) | based combination with the most common             |
|                                       |                      |                      |             | being MVAC (Methotrexate + Vinblastine +           |
|                                       |                      |                      |             | Adriamycine + Cisplatin)                           |
|                                       |                      |                      |             | Automycine - cispidelity                           |
|                                       |                      |                      |             |  |

## Wilm's Tumor

Epidemiology

- Children (<5yo), 3<sup>rd</sup> most common solid organ tumor in children

- Morphology
  - One gigantic mass that is smooth, lobulated, mobile and NEVER crosses midline
  - Unilateral 95% Bilateral 5%
    - Tumor of metanephric tissue with the main characteristic that the tissue is **variable** having all types of premature kidney tissue + connective, bone, muscle tissue, etc.
- Genetics
  - Gene #1: WT1 Gene (11p13) associated w/ Denys-Dash Syndrome "WAGR"
    - Wilms Tumor
    - Aniridia
    - Genitourinary Malformation (cryptorchidism, hypospadias, genital ambiguity)
    - Mental/Motor Retardation
    - Gene #2: WT2 Gene (11p15) associated w/ Beckwith-Wiedmann "WOMAN"
    - Wilms Tumor
      - Organomegaly / Omphalocele
      - Macroglossis
      - Asymmetry of body due to unilateral muscular hypertrophy / Adrenal Cortical Carcinoma
      - Neonatal Hypoglycemia

• S/S

- Asymptomatic Ab mass (child appears well) but sometimes
  - HTN 2/2 renal artery obstruction or renin production by tumor
  - ab pain
  - hematuria
  - anorexia
- MET: lungs, liver, bone, brain
- Staging/Tx

- Stage I (under capsule) or Stage II (beyond capsule but still easily removable) = surgery + chemo
- Stage III (beyond capsule + LNs) + Stage IV (hematogenous spread) + Stage V (bilateral renal involvement) = " " + XRT

## Neuroblastoma

- Epidemiology
  - Children (<3yo), 2<sup>nd</sup> most common solid organ tumor in children
- Morphology
  - One gigantic mass that ALWAYS crosses midline
  - Unilateral 95% Bilateral 5%
  - Tumor of neural crest cell origin (which normally give rise to sympathetic chain ganglia and the adrenal medulla)
  - Variants:
    - Classic Neuroblastoma (100% malignant) very UNdifferentiated cells, neural crest cells, UNcapsulated thus
      infiltrates surrounding tissues
    - Ganglioneuroblastoma: (50% benign 50% malignant)
    - Ganglioneuroma (100% benign) very differentiated cells, adrenal medulla / sympathetic chain ganglia cells, capsulated thus does NOT infiltrate surrounding tissue
- Genetics
  - Prognosis α # of N-myc oncogene copies
- S/S
  - Symptomatic mass (child appears ill)
    - Ab (70%) half extra adrenal / half adrenal
      - ab pain
      - HTN 2/2 renal artery obstruction
        - watery diarrhea (if tumor secretes vasoactive intestinal peptide)
      - Posterior Mediastinum (20%)
        - Dyspnea
        - incidental finding on CXR
        - Head & Neck (5%)
          - neurologic symptoms 2/2 compression of nerve root
          - Horner's Syndrome
          - Acute Myoclonic Encephalopathy = opsoclonus (multidirectional spontaneous rapid eye
          - movements), myoclonus, truncal ataxia
  - Epidural (5%)
     Most Present w/ Metastasis: classic B symptoms, BM (BM failure), Cortical Bone (bone pain, limp, ecchymoses 2/2 orbital involvement, proptosis 2/2 retrobulbar involvement), Liver (hepatomegaly), Skin (palpable subcutaneous nodules)
- Dx
- Urine (high vanillylmandelic acid and homovanillic acid)
- Serum (high ferritin and lactate dehydrogenase are poor pronostic indicators)
- MIBG Scan (Meta-Iodo-Benzyl-Guanidine) for detecting small primaries and mets
- Staging/Tx (typically unsuccessful)
  - Stage I-II (do not cross midline) = surgery
    - Stage III (crosses midline) IV (hematogenous metastasis) = " " + chemo/XRT/HSCT