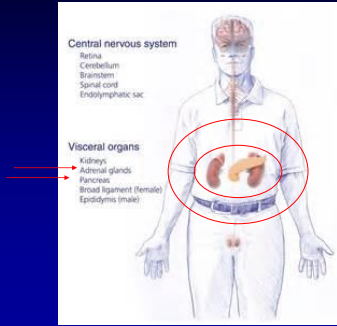
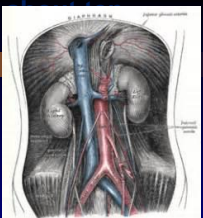
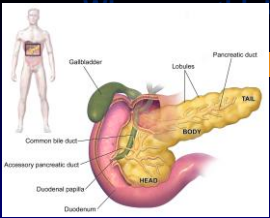


# VHL The Moffitt Cancer Center Experience

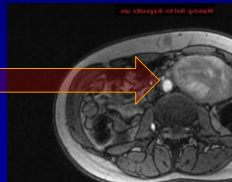
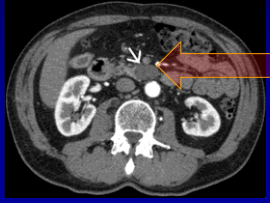
John B. Tourtelot MD  
Associate Member  
Moffitt Cancer Center



...k of VHL you must think  
...ossible locations



- Brain / Spinal Hemangioblastoma
- Retina Hemangioblastoma
- Endolymphatic Sac Tumor
- Benign, Asymptomatic Lung Lesion
- Pancreatic Cysts / Tumor / Cancer
- Pheochromocytoma, Paraganglioma
- Benign, Asymptomatic Liver Lesion
- Kidney Cysts, Renal Cell Carcinoma
- Cystadenomas (for both M and F)




## Endocrine Manifestations of VHL


- Neuroendocrine tumors
- Pheochromocytoma
- Paraganglioma

### VHL Endocrine Tumors

- Pancreatic neuroendocrine lesions
  - Ductuloinsular complexes
  - Islet dysplasia
  - Microadenomas
  - Neuroendocrine tumors
- Pheochromocytomas and Extra-Adrenal paragangliomas
  - Characteristic of VHL although not specific



well-demarcated, variegated, and red-brown to yellow tan masses, most commonly in the background of cystic disease

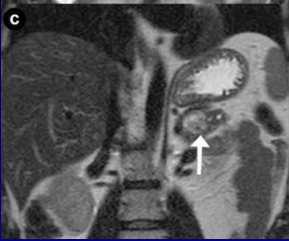


a thick vascular tumor capsule is a distinctive feature of VHL-related pheos and paragangliomas

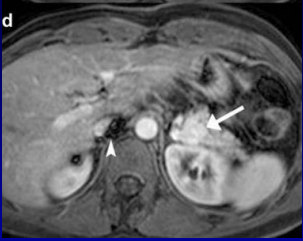
### VHL Endocrine Tumors

37-year-old man with VHL disease

- Pancreatic neuroendocrine tumor



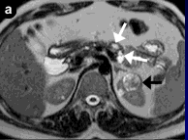
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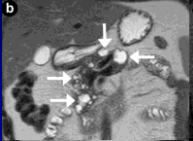
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### Pancreatic cysts

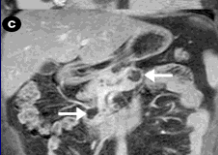
35-year-old man with VHL disease



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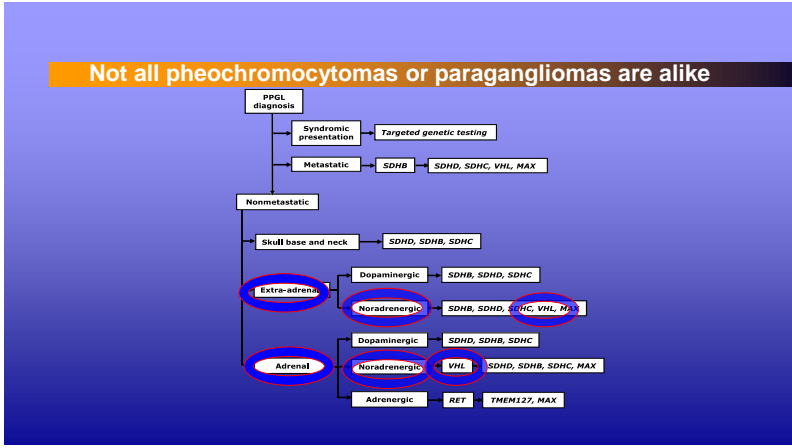


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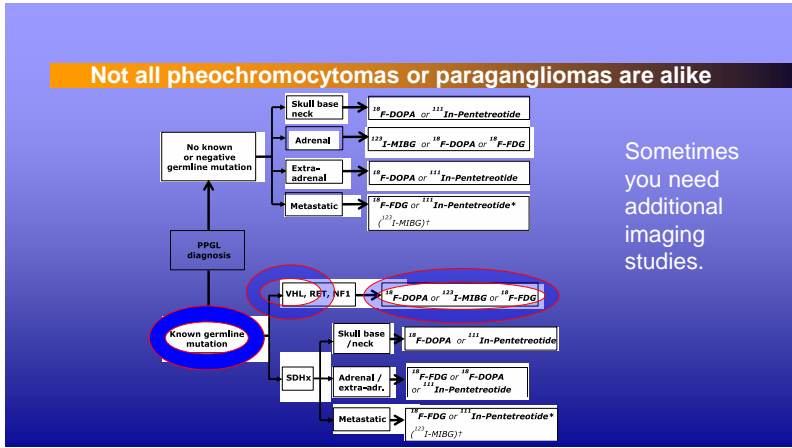
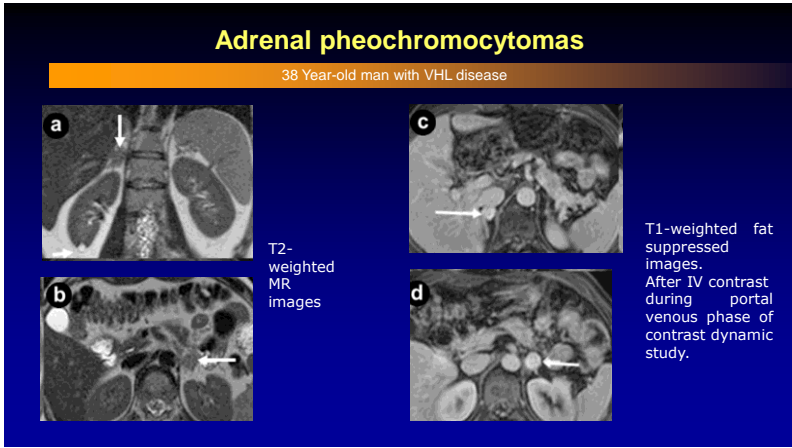


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- A *Pheochromocytoma* is a tumor arising from adrenal medullary chromaffin cells that commonly produces one or more catecholamines:
  - Epinephrine
  - Norepinephrine
  - Dopamine
  - Rarely, these tumors are biochemically silent
- A *paraganglioma* is a tumor derived from extra adrenal chromaffin cells of the sympathetic paravertebral ganglia of
  - Thorax
  - Abdomen
  - Pelvis
- 80 to 85% of chromaffin-cell tumors are pheochromocytomas, whereas 15 to 20% are paragangliomas
- Evidence demonstrates that hereditary pheochromocytomas/paragangliomas (PPGLs) are characterized by
  - distinct clinical presentations
  - Differences in biological behavior
  - Mode of transmission that reflects underlying mutations



- ### Biochemical and radiologic Evaluation for a Pheochromocytoma/Paraganglioma
- We recommend that initial biochemical testing for PPGLs should include measurements of plasma free metanephrines or urinary fractionated metanephrines.
  - We also recommend an MRI of the abdomen/pelvis for screening



### VHL Pheochromocytomas

- Frequently bilateral
- Paragangliomas are common
  - Mediastinum
  - Abdominal
  - Pelvic
- Type II VHL only
- Genotype-Phenotype correlations are documented and specific mutations are associated with particular patterns of tumor formation
- 98 percent of cases: the pheochromocytoma is associated with missense mutations in the VHL gene (rather than truncating or null mutations)

### Phenotype of MEN2 versus VHL syndrome: Pheochromocytoma characteristics

- MEN-2 are more symptomatic than VHL patients
- MEN-2 have a higher incidence of hypertension (primarily paroxysmal)
- MEN-2 have higher concentrations of metanephrine (epinephrine metabolite)
- VHL have elevated serum normetanephrine (norepinephrine metabolite)
- VHL have lower total tissue contents of catecholamines and expression of tyrosine hydroxylase (the rate-limiting enzyme in catecholamine synthesis)
- VHL has a much lower expression of phenylethanolamine N-methyltransferase (PNMT) which converts norepinephrine to epinephrine. Results in lower epinephrine tissue stores.

### Preparation for surgery

- All patients with a hormonally functional PPGL should undergo preoperative blockade to prevent perioperative cardiovascular complications.
- Adrenergic receptor blockers are the first choice.
- high-sodium diet reverses blood volume contraction, prevents orthostatic hypotension before surgery, and reduces the risk of significant hypotension after surgery
- Preoperative co-administration of adrenergic receptor blockers should be considered.
  - To control tachycardia
  - Only after adrenergic receptor blockers have been adequately adjusted

### VHL Endocrine Tumors

#### Type 2 VHL

- Pheochromocytomas only occur in Type II VHL
- Associated with missense mutations

#### Type 1 VHL

- Type I VHL is usually caused by whole or partial gene deletion or a nonsense mutation

## VHL Program at the Moffitt Cancer Center

### In Summary

- At the first visit our VHL patients are evaluated with laboratory studies to include a Plasma and 24 hour urine fractionated metanephrine levels
- MRI for the initial evaluation and then screening exams
- Prompt evaluation with further radiologic studies are considered
- Surgical consultation when a tumor is detected
- Pre-surgical preparation with alpha blockade and close hemodynamic monitoring
- And most importantly:

Total care of our VHL patients in a supportive well coordinated manner

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