

Hereditary Pheochromocytoma

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Familial paraganglioma-pheochromocytoma

- **Multiple endocrine neoplasia type 2(MEN2, 10q)**
- **Von Hippel Lindau (3p)**
- **Neurofibromatosis type 1(von Recklinghausens disease, 17q)**
- **Succinate dehydrogenase subunit B and D(SDHB 1p, SDHD 11q)**
- **Uncommon like Familial pheochromocytoma with unknown genetics, Tuberous sclerosis**



Paraganglioma-pheochromocytoma

Always consider the possibility of familial disease. In “sporadic” cases it may be close to 25%.



Multiple Endocrine Neoplasia type 2(MEN 2)

- **Medullary thyroid carcinoma**
- **Pheochromocytoma, 10-50%**
- **Hyperparathyroidism(2A) or marfanoid habitus and mucosal neurinoma(2B)**
- **Mutations in the RET gene on chromosom 10**
- **Genetic testing mandatory**
- **Prophylactic thyroidectomy early in childhood**

Von Hippel Lindau (VHL)

- **Retinal hemangiomas**
- **Cerebellar hemangioblastoma**
- **Renal cysts or carcinoma**
- **Pancreatic cysts and tumors**
- **Pheochromocytoma, 10-20%**
- **Mutations in tumor suppressor gene on 3p**



Neurofibromatosis type 1 (von Recklinghausens disease, NF1)

- **Café au lait spots,**
- **Neurofibromas**
- **Optic glioma**
- **Pheochromocytoma, 1%?**
- **Mutations on tumor suppressor on 17q**

Succinate dehydrogenase subunit B and D (SDHB 1p, SDHD 11q)

- **Nuclear genes encoding mitochondrial proteins**
- **Frequently found in familial paraganglioma**
- **Screening in healthy first degree relatives detect new paraganglioma**



Succinate dehydrogenase subunit B and D (SDHB 1p, SDHD 11q)

SDHB

- Higher risk for extraadrenal disease
- Higher risk for malignant disease
- Median age for penetrance 47 years

SDHD

- More often multiple tumors
- Head and neck paraganglioma
- Median age for penetrance 31 years

European-American Paraganglioma Study group JAMA 292 943-951 2004

International SDH consortium, Benn et al JCEM 91 827-836, 2006

Suggested genetic testing in paraganglioma/pheochromocytoma

- **Positive family history or below 30**
 - **VHL**
 - **RET**
 - **SDHB**
 - **SDHD**
- **Extraadrenal and/or malignant**
 - **VHL**
 - **SDHB**
 - **SDHD**
- **Bilateral**
 - **RET**
 - **VHL**

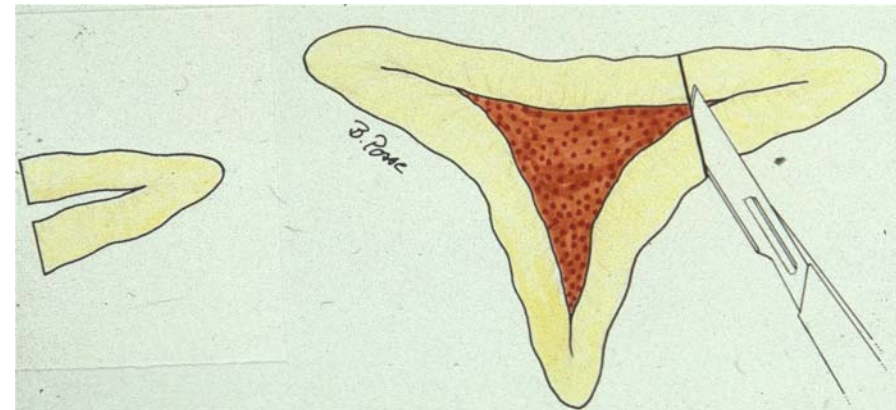
Suggested by a workshop at the First International Symposium on Pheochromocytoma NIH October 2005

Surgical options for adrenal disease in hereditary cases

- **Usually bilateral adrenal medullary hyperplasia with development of tumors slowly and not symmetrically**
- **If unilateral tumor only remove one side and continue following patient**
- **In patients with malignancy or high risk for malignant pheochromocytoma adrenalectomy**
- **If not consider conservative cortex-sparing operation**

Surgical options for adrenal disease in hereditary cases

- If bilateral and low risk for malignancy, conservative treatment with partial resection can be recommended
- This can be done with knife or stapler, open or laparoscopically
- The tumor can recur and may need reoperation



Life long steroid supplementation after total adrenalectomy has a considerable morbidity and some mortality

Conclusions

- **A potentially lethal, curable and usually benign adrenal tumor**
- **More often hereditary than previously thought**
- **Program for genetic testing advisable**
- **Preservation of cortical tissue valuable in bilateral disease**

