If you consistently read the Genetics Corner article in your monthly ONS newsletter, then you may remember reading about von Hippel-Lindau (VHL) syndrome, a condition which predisposes carriers to renal tumors as well as renal cysts. This month we’re going to further explore the world of inherited kidney cancer syndromes.

As you know, kidney cancer affects more than 150,000 people annually worldwide, resulting in 78,000 deaths each year. Risk factors for kidney cancer include:

- Smoking: the increased risk seems to be related to the amount a person smokes.
- Obesity: some doctors think obesity is a factor in about 2 out of 10 people who get kidney cancer. Obesity may cause changes in certain hormones that can lead to RCC.
- Workplace exposure: asbestos, cadmium, some herbicides, benzene, and organic solvents, particularly trichloroethylene
- Genetics and Hereditary Risk Factors: discussed below
- Family history of kidney cancer: People with a strong family history of RCC (without one of the known inherited conditions listed below) also have a higher chance of developing this cancer. This risk is even higher in siblings of those affected.
- High blood pressure
- Certain medicines: phenacetin
- Advanced kidney disease
- Gender: RCC is twice as common in men as in women
- Race: Blacks have a slightly higher rate of RCC than whites.

Genetics and Kidney Cancer

Patients with a family history of kidney cancer comprise about 4% of all cases of RCC. Kidney cancer can be classified according to histology into distinct tumor types: clear cell, papillary type 1, papillary type 2, and chromophobe/oncocytoma. During the past 2 decades, four inherited renal cancer syndromes, which predispose to distinct histologic types of kidney cancer, have been characterized. Knowing a patient’s kidney cancer histology can help a clinician identify and refer a patient at risk for an inherited kidney cancer syndrome.

1. von Hippel-Linda (VHL) syndrome – VHL is characterized by hemangioblastoma of the brain, spinal cord, and retina; **renal cysts and clear cell renal cell carcinoma**; pheochromocytoma; and endolymphatic sac tumors. Nearly 100% of VHL carriers will present with the disease by the age of 60. When to refer: patients with a personal and family history of clear cell RCC or patients with a personal history of VHL characteristics even with a negative family history.
2. Hereditary Papillary Renal Carcinoma (HPRC) syndrome – HPRC is characterized by an autosomal dominant pattern of **multifocal, bilateral renal tumors** with a distinctive papillary type 1 architecture. Approximately 70% of HPRC carriers will present with the disease by the age of 60. **When to refer:** patients with a personal and/or family history of papillary type 1 RCC.

3. Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) syndrome – HLRCC is characterized by cutaneous leiomyomata, uterine leiomyomata, and **renal tumors** of papillary type 2 histology. Nearly all HLRCC carriers develop the characteristic skin lesions and approximately 15% of carriers will develop renal tumors, which tend to be highly aggressive and often result in death within 5 years of diagnosis from metastatic disease. **When to refer:** patients with a personal and/or family history of papillary type 2 RCC and leiomyomata.

4. Birt-Hogg-Dube (BHD) syndrome – BHD is characterized by fibrofolliculomas, trichodiscomas/angiofibromas, perifollicular fibromas, acrochordons; pulmonary cysts/history of pneumothorax; **renal tumors**, most frequently of chromophobe and hybrid oncocytic histology. The median age of onset for BHD carriers to develop renal tumors is approximately 50 years of age. **When to refer:** patients with a personal and/or family history of chromophobe/oncocytic renal tumors and pneumothorax.

**Together, we can identify at-risk patients and their family members to establish an appropriate surveillance plan for early detection! For more information about kidney cancer syndromes or to discuss a possible referral, just call your friendly neighborhood genetic counselor at 817-838-4871.**