What Causes a Wilms Tumor? Why Does It Affect Children and Not Adults?

by Giulio J. D'Angio, MD

First, there are no known causes of Wilms tumor (WT). Some cancers in adults are associated with specific environmental factors or with life-style habits; for example, smoking and lung cancer. There are no such direct causative links in the case of a child with WT. Nothing the parent or the child did led to the appearance of a WT. Also, the vast majority of WTs are not inherited. There are very rare families in which WT occurs in more than one member of the family. This is usually a close relative such as a grand-parent, aunt or uncle, parent or sibling.

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Then, why does a WT appear in an otherwise healthy little girl or boy? It may be helpful at this point to liken a rose bush in the spring to one of the known pathways to WT. The rose bush may have many buds some of which will remain as such and never progress beyond the bud stage. Other buds may wither and die, but the much greater number will develop into lovely flowers. Only a rare bud without obvious cause will produce a misshapen, malformed blossom.

The developing kidney in the embryo can be envisioned in that way. The "buds" are the building blocks of the kidney called nephrons. Some of them, like the rose buds, remain dormant without maturing further. These are called "nephrogenic rests" abbreviated as NRs. Others wither away and die, but most develop normally to form the kidney. Rarely, one or more of the NRs for reasons that are largely unknown grows into a misshapen, malformed "blossom;" in this case, a Wilms tumor.

Microscopic NRs are fairly frequent in babies. Dr. Bruce Beckwith found them in the kidneys of approximately one percent of 1000 children under 3 months of age that he examined. So, if NRs always gave rise to Wilms tumors—which is not the case—then one would expect to find 1000 WTs among 100,000 children. The actual incidence of WTs in the pediatric age group is about ten per 100,000. This means that the NRs either faded away or remained dormant in at least 99% of those children who had kidneys that were so affected as infants. Most Wilms tumors do not arise from NRs.

This story of the rose bush may help to picture how seldom the embryonic kidney units become confused along the normal developmental pathways, and how very rarely the confusion results in a WT. Also, WTs tend to occur in rare children with certain body abnormalities that follow a pattern. These abnormal patterns are called syndromes that appear to be linked to specific gene defects. The two most common of these patterns are the Beckwith-Wiedemann Syndrome, and the WAGR Syndrome. The former most notably is associated with overgrowth of body parts; for example, one leg is larger than the other, but there are other important elements to the syndrome as well. The letters WAGR stand for the abnormalities found in these patients; Wilms tumor, Aniridia (absence of the iris of the eye), Genito urinary (pathology affecting the sex and urinary tract organs), and mental Retardation. Patients with signs of either of the two syndromes (and some others that are rarer still) need careful frequent examination to check for the presence of a developing WT.

Above it was said that the reasons for transformation of a benign, non-malignant NR into a malignant WT are unknown. Even more puzzling is the fact that most WTs do not grow from NRs or in patients with the known alerting syndromes. Thus, in most children with WT, there is even less understanding as to why the cancer appeared. It is believed that there are other, as-yet-to-be-identified in-born errors in normal kidney formation that lead to the growth of WTs.

One thing seems clear, however, and that is that the abnormalities that can eventually produce a WT develop during embryonic life. This is because WTs have occasionally been found in newborns, although most are clustered in the one to four year old age group, suggesting a similar "lag time" for the majority. Exceptions are the rare adults who develop typical WTs. These tumors are identical to those found in children both microscopically and in their clinical behavior. The same in-born triggering mechanism of childhood therefore is likely to be responsible in the case of adults. Why there is such a long delay in the malignant transformation in these older individuals remains to be explained.