Germ cell testicular cancer incidence

Testicular cancer is not your normal malignancy. A few cancers occur in children, while most occur in older people. However, hardly any occur specifically in young adults. Testicular cancer is one. Incidence rises rapidly in the teen years to peak sharply in the early twenties. Among men in their twenties, it is the commonest kind of cancer. By the thirties, the risk is low and it is rare thereafter. Its cause is unknown. But there is considerable variation in risk in different countries. And risk is higher in White men than Black men, who have very low risks. These variations suggest that environmental factors are important.

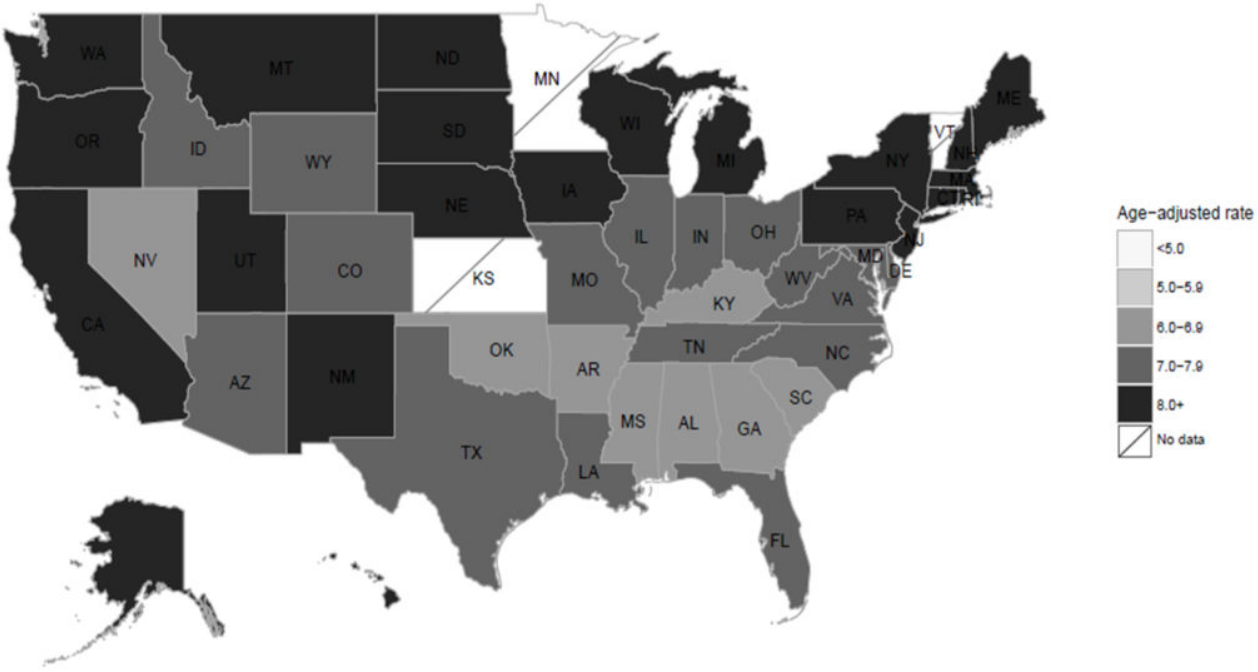

Fig. 1. US testicular cancer incidence in White adult men per 100,000 per year, by state, 2001-2011.

In a recent publication in Photobiology and Photochemistry, scientists from Queensland University of Technology and Queensland Cancer Council in Brisbane, Australia examined the geographic variations in incidence for both Australia and the United States. Using national data through 2010, they examined incidence in local areas covering both countries: 50 US states (68,566 cases) and 61 Australian Districts (5,742 cases).

Both countries showed a consistent pattern: the farther one lived from the equator, the higher the risk of getting the cancer. The increase was small, about 1% per degree latitude, but it was consistent and highly unlikely to be due to chance. Since the latitude variation was about 25

degrees in each country, the risk increase was about 25% from the most equatorial areas to those furthest away.

The central observations were generated among White men. The authors first thought this geographic pattern might arise from protection by vitamin D, since sunlight exposure to skin creates this vitamin. However, when US Black men (2,256 cases) were examined, they appeared to show the same findings, albeit with weaker power given fewer cases. In general, Black men have low vitamin D, especially in areas away from the equator. Despite this, they still have low testicular cancer risk.

The authors propose two alternative explanations. One is simple. Perhaps sunlight entering the eyes affects risk. The pathway could be via the hypothalamus, the part of the brain just behind the eyes that controls hormones. For optimal survival, evolution must time births to occur in warmer months, an effect possibly mediated by visual sunlight. This hormonally-controlled ‘reproductive readiness’ is present in many animals, varying from frogs to lynxes and cows. In fact, even though humans have protection from harsh environments, we still have hormonal swings that shape our ‘readiness’. By this hypothesis, the farther away from the equator, the more extreme the sunlight swings and hence, the more testicular cancer.

An alternative explanation is more complicated. We know that all cancers involve problems with faulty genes. Particular to testicular cancer, one gene stands out, KITLG. Among men with testicular cancer, a variant (‘G variant’) is found three times more frequently. Curiously, this variant is associated with lower production of melanin, the pigment that makes our skin dark. Caucasians have a higher frequency of G variant than Africans. Perhaps the higher frequency makes Whites more likely to get testicular cancer. However, the variant frequency has not been sufficiently explored by distance from the equator.

This observation is what is called ‘ecological’, meaning unfocused. The authors establish that testicular cancer risk increases as men live farther from the equator. However, anything that is associated living away from the equator,e .g., temperature, clothing, food, or occupations, might increase risk. They acknowledge this in the paper. Even so, the strong finding in two countries in different regions, both with well developed medical coverage and strong surveillance for cancer, provides a strong clue to establishing what factors might increased testicular cancer risk.

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