IN THE NEWS

Deodorant debate rages on Public concern has once again been raised over the link between underarm deodorants and cancer, after a recent report that frequent underarm shaving combined with deodorant use could increase the risk of breast cancer.

The study, which was carried out by Kris McGrath from Northwestern University, USA, surveyed the underarm-hygiene habits of 437 women with breast cancer. Women who shaved their underarms more than twice a week and applied deodorant more than once a week were almost 15 years younger when they were diagnosed with breast cancer than those who used neither regimen. Consistent with previous studies, McGrath found no link with a younger age of breast cancer diagnosis when either shaving or deodorant was used alone.

This finding was published shortly after a report from Philippa Darbre, Reading University, UK, showed that traces of parabens — preservatives used in cosmetics, food and pharmaceutical products — in breast tumours. Although there is no proof that parabens cause cancer and most deodorants no longer contain these compounds, Darbre said "Their detection in human breast tumours is of concern since parabens have been shown to mimic the action of the female hormone oestrogen, [which] can drive the growth of human breast tumours" (*Reuters*, 12 January 2004).

Darbre is excited by McGrath's work and claims "It is a landmark publication because it provides the first epidemiological evidence for a link between the use of antiperspirants/deodorants and breast cancer development" (*NewScientist.com*, 24 January 2004). It is clear that more studies will be needed to resolve this controversial issue.

Emma Croager

MATHEMATICAL MODELS

Accelerating cancer understanding

So, cancer incidence increases with age…doesn't it? Although this longstanding assumption is mostly true, incidence in many tissues departs from the expected linear log–log plot. In a recent article from *Current Biology*, Steven Frank uses mathematical models to explore how clonal expansion and the number of cell lineages in a tissue might explain the departures from the standard plot that occur in breast and prostate cancer.

The typical log–log curves show the rate of cancer at different ages, and Frank began by plotting the slope of the rate curve at each point. This provides the age-specific acceleration of cancer — acceleration can decline even though the frequency of cases increases, because acceleration measures how fast the frequency of cases rises with age. The acceleration plots show that breast cancer acceleration is highest early in life, acceleration then steadily declines with age. By contrast, the acceleration of prostate cancer rises rapidly to a peak at ~40 years, and then drops just as rapidly through later life (see figure). Frank first developed a general set of equations to model that cancer arises when a certain number of rate-limiting mutations occur within a cell lineage — this standard multistage model was thought to give a constant acceleration throughout life — he then attempted to explain the observed deviations from expected constant acceleration.

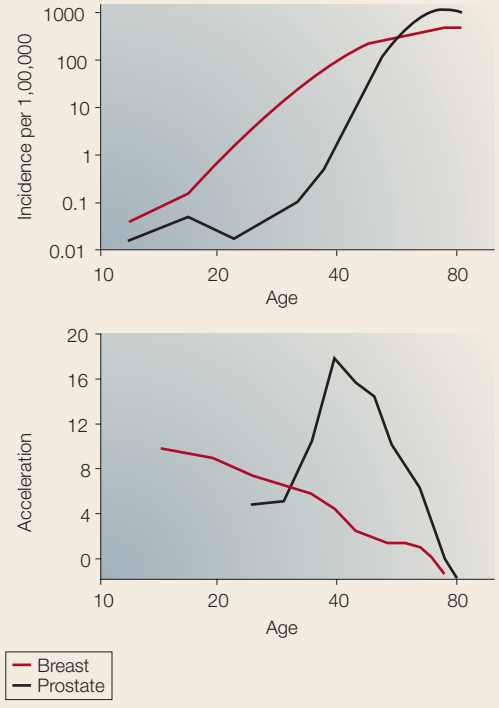

Figure modified, with permission, from Frank, S. © (2004) Cell Press.

He hypothesized that the decline in acceleration at later ages could be caused by the fact that individual cell lineages accumulate mutations, so that they need fewer steps to become tumorigenic. The number of lineages that are present in a tissue would affect this. If there were more lineages, only a few would become transformed, so most would have ~0 mutations; however, if there were fewer lineages, more of these would have to undergo some of the steps towards cancer in order for the total incidence to be the same. The number of mutations in each lineage would therefore be higher, and there would be a corresponding decrease in acceleration. This mimics the situation in breast cancer, which could be explained by the tissue having fewer lineages either because there are fewer stem cells than in other tissues or because precancerous lineages frequently expand at the expense of neighbouring lineages.

The clonal expansion of a cell population could also influence the acceleration of cancer. For example, if the rate of expansion is slow, the rate at which a lineage acquires the next rate-limiting mutation would accelerate slowly over time, causing a peak of acceleration in midlife. The more rapid clonal expansion, the earlier the peak in acceleration. Also, as the size of the clone increases, the peak of acceleration increases, but only to a certain extent. When the number of cells reaches a certain size, the probability that a mutation will occur after a short time is so high that further clonal expansion can not further increase the rate. Finally, the number of rounds of clonal expansion could also affect the acceleration of cancer. When three rounds of clonal expansion occur — because different mutations cause waves of proliferation — the peak acceleration is greatly increased, and this could explain the high acceleration of cancer in midlife that is observed in prostate cancer.

So, Steven Frank goes beyond mere descriptions of known processes here. He investigates the observation that the age-specific acceleration of cancer varies according to the tissue type of origin and provides models to explain these. Although these are not the only possible solutions, he suggests specific experiments that could be used to test these hypotheses and suggests alternatives that could also be considered. This type of instructive use of mathematical models should aid the understanding of other cancer processes.

Emma Greenwood

References and links

ORIGINAL RESEARCH PAPER Frank, S. Age-specific acceleration of cancer. *Curr. Biol.* **14**, 242–246 (2004)
WEB SITE Steven A. Frank's home page: http://stevefrank.org/
FURTHER READING Michor, F., Iwasa, Y. & Nowak, M. A. Dynamics of cancer progression. *Nature Rev. Cancer* **4**, 197–205 (2004).