#BIOLOGY

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CANCER, SNAKES AND LADDERS

WHY SOME SMOKERS LIVE TO 100

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CANCER, SNAKES AND LADDERS

We've all heard the stories.

Your friend's Uncle Bob smoked 40 a day and lived to 97 in perfect health. Yet a fitness freak, who ate all the right things and never touched a cigarette, was taken by cancer at 25. There are countless similar anecdotes. Life can have a cruel sense of humour.

Cancer is a lot like a game of Snakes and Ladders: cancer sits at the top of the board and the object of the game is to stay as close to the bottom as possible.

But not everyone is playing with a six-sided dice. Someone born with a high genetic risk of cancer may have a 20-sided dice – and will face moving up the board at lightning speed. But someone with low predisposition may have the equivalent of a four-sided dice – with a much lower risk of having to move too far up the board on each roll. It's the luck of the genetic draw.

How often you roll depends on where you live and how you live. If you rarely roll even with a high-sided dice you could live a cancer-free life. If you have a low-sided dice but smoke, or are exposed to radon gas, you have to roll more often. Of course there's always the possibility you'll be lucky and roll a '1' many times. It's all about chance.

The body you have now is not the one you are born with

Cancer is not like measles or mumps; it comes from within our own cells, not from some invading germ. And because of this, cancer becomes an odd lottery.

Nearly every part of your body is continuously regenerating itself. The cells of the skin and liver, for example, grow continuously: individual cells die and are rapidly replaced. Normally, this cycle of life is carefully controlled in a beautiful, elaborate molecular dance within cells: genes and their products interact, switch on and off, and send messages to make cells grow, develop, or die, depending on what and where they are.

With each new cell division our cells must duplicate their DNA. And every time this happens there's a roll of the dice – a risk that an error (a mutation) will creep in while the DNA is being copied. Being unlucky – getting a mutation – is like landing on a ladder, propelling you towards the end of the board. Many errors may have no noticeable effect, and some may even be beneficial. But with each new division there's a small chance of a cancer-causing mutation creeping in.

Add to this risk the damage to your DNA caused by chemicals from the environment, such as those in tobacco smoke or in burnt food, and you can see how the rolls can begin to add up over a life time.

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Rarely will a single mutation alone be enough to cause cancer. It typically takes many errors, each of which interrupts a different part of the molecular dance. One mutation might make a cell able to grow continuously, deaf to the calls of its neighbours to stop growing. Other mutations may make matters worse, encouraging a blood vessel to grow into the uncontrollably-expanding mass of cells, keeping them fed.

Loading your dice: discovering your risk factors

So if there's usually no single cause for cancer – no single error that will push a cell over the precipice of uncontrolled growth – how can we know which risk factors should really concern us?

Enter 'epidemiology': the study of disease distributions in human populations. By looking at the rates of different cancers in different populations, it is possible to get clues about what causes them. For example, China has high rates of liver cancer, whereas the US has high rates of prostate and breast cancer.

Knowing this lets us ask specific questions. Is it just that being Chinese makes you more likely to get liver cancer, or is it something about living in China? If you look at Chinese immigrants in the US, you see that prostate and breast cancer rates amongst Chinese immigrants go up, while liver cancer rates go down – unless they keep to a more traditional Eastern diet. This gives us the hint that there may be something in the Eastern diet or lifestyle that puts people at risk of liver cancer.

Busting the tobacco industry

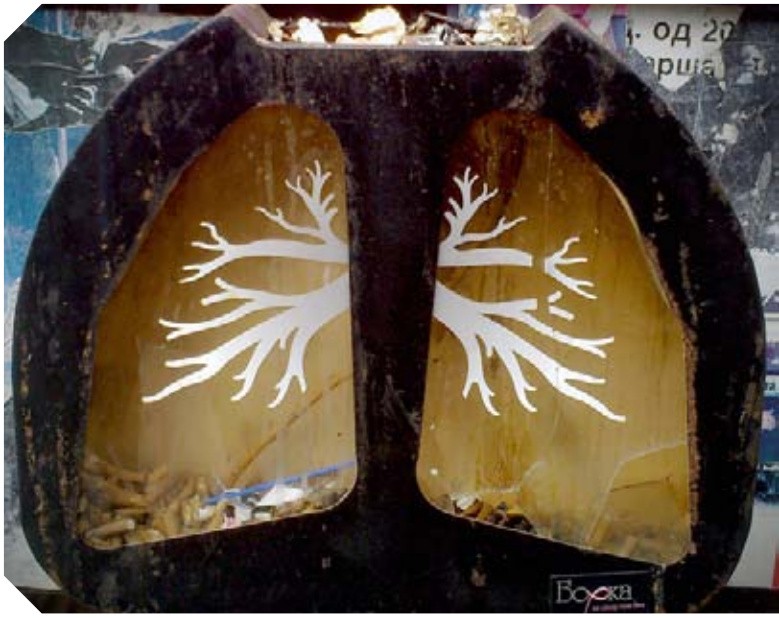
This kind of approach to studying the distribution of disease was more or less pioneered by Sir William Doll and Sir Austin Bradford Hill who showed conclusively in 1950 that smoking causes cancer. Examining in detail the number of patients diagnosed with different types of cancer (including lung cancer) and their smoking habits, they demonstrated that smoking is associated with lung cancer. Despite their denials, this evidence ultimately proved to be the undoing of the tobacco industry.

Identifying causes, or risks, in this way helps us zero in on our personal risk factors for cancer. As soon as the stats allow us to be confident about the specific risks, like smoking, then we know how we can live our lives to roll the dice less often.

The analysis of how breast cancer runs in families was a pivotal step in understanding that having particular types of two genes – the BRCA1 and BRCA2 genes – increases the risk of developing cancer over a woman's lifetime by about 45-65%. But, importantly, it also led to the development of tests for these versions of the genes. We can now be on the look-out for these genes, monitoring those individuals that carry them so that we can catch the cancer – if it develops – as early as possible, minimising the risk to life.

Ultimately, cancer is going to be a game of chance for the foreseeable future: the longer you play, the more likely you are to lose. We can now minimise some of the risks, but each cell that replaces itself is still a role of the dice.

The good news is that we are starting to tip the odds in our favour. Our understanding of how cancer develops, spreads and grows is improving all the time. We're better at detecting, predicting and treating those at risk than we ever have been. It's still going to be a long battle, but we can be thankful that tomorrow's game board will be less tricky to play than today's.



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