

# Why Will Cancer Incidence Go On Increasing Around the World?

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As a diagnostic histopathologist working at a major referral centre in Pakistan for over three decades, diagnosing and classifying various cancers is one of the major responsibilities undertaken by the author and colleagues. Every day switching from one case to another for which a biopsy is submitted, the percentage of biopsies with cancer diagnoses of one type or the other has increased substantially over time. This includes a significant number of cases where it is entirely unexpected in an otherwise healthy and in many cases young individuals with no known risk factors.<sup>1</sup> This so-called 'Biological Bad Luck' changes the life of the affected and his/her family overnight upside down and a natural question is asked, why me? I have been living a very healthy and a disciplined life with no consumption of tobacco and alcohol, a balanced diet, and optimum weight ensured by a vigilant exercise schedule. Am I punished by the heavens for any of my sins? What is going to happen to my family? And what are the chances that I will survive and afford terrible expenses that may be inevitable? Overwhelmed with this harsh reality of life, another question is asked, dear doctor when is cancer cure coming? The question is relevant but still naive as unfortunately, cancer is not one disease. There are several hundred types of cancer, each with its unique biology as well as treatment options depending upon its location, grade, and stage among other confounding factors.

To answer these questions, one must go to basics to try to explain this 'Biological Bad Luck' of cancer. Strictly speaking, cancer is due to damage or alteration in the regulation of DNA, the code of life. Cancer is a disorder of growth. All life, including humans, grows from an embryo resulting from the fusion of male and female germ cells. Vertical growth is visible in the early years of life; however, once it apparently ceases, the death of old cells and their replacement by newly formed cells continue to happen at all times and age.

An adult human body has trillions of cells<sup>2</sup> and a percentage of that is recycled round the clock following the so-called cycle of birth-division-differentiation and death replaced by new cells generated by stem cells, present in all organs. Just before a cell divides, it doubles its DNA *via* a photocopying-like process so that both resulting cells have identical content of DNA, so-called diploid DNA content. However, it is not difficult to imagine that during this process, a photocopying error may happen resulting in an abnormal DNA content, so-called aneuploidy, sowing seed for this to progress, and eventually resulting in carcinogenesis.

This is also well researched that though generally speaking DNA (genetic fingerprint) is a so-called immortal molecule and passes on from generation to generation, as we all perish, genes are passed on to the next generation. This is a vivid testimony to the fact that if we are alive today, our link from the beginning of life about 4 billion years ago remains unbroken, otherwise, we simply were not being here. However, during this process, minor alterations in DNA over the span of time may lead to the creation of new species. The same process of wear and tear during a lifetime may lead to growth-related morbidity and mortality.<sup>3</sup> This is well-known that cigarette smoke contains over 100 potent carcinogenic chemicals that cause serious DNA damage (mutation) and is the single most common cause of carcinogenesis in humanity. However, spontaneous damage of DNA is entirely a process that is random and highly complex.<sup>4</sup> Single-stranded DNA breaks are extremely frequent spontaneously. However, as complementary sequences of DNA are in place, these are quickly repaired. In contrast, double-stranded DNA breaks, such as those happening in chromosomal translocations, are difficult to repair as complementary sequences are not simply there and this kind of DNA damage requires DNA repair genes such as BRCA1 and BRCA2.<sup>5</sup> This process may also lead to the loss of many crucial genes. This is precisely for this reason that mutations in these two genes, mostly representing germline mutations, predispose in particular women to develop many common cancers in their lifetime, particularly breast and ovarian cancers.<sup>6</sup>

DNA repair genes and other robust physiological processes such as apoptosis regulating and tumour suppressor genes are of prime importance to take care of hundreds of thousands of environmental and spontaneously induced mutations in dividing cells. However, as we age, this process gets weaker and weaker leading to more and more chances that a mutation will

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go unchecked and will lead to the formation of cancer. It is hypothesised that if we humans, for the sake of assumption, do not die of any other disease such as heart diseases and infections, eventually, all of us will die of cancer as with age, these processes get weaker and weaker and eventually entirely ineffective. This is also an explanation for the fact that with age, we are more likely to develop cancer.

In addition to many uncommon cancers, there are some common cancer types that come out of the blue and have no known risk factors. These include cancers of the pancreas, prostate, ovary, and brain among others. Even cancers of the breast and colon are largely non-preventable.<sup>7</sup> Having said this, all is not doom and gloom and must not lead to the impression that nothing may be done about this. A healthy lifestyle may still be of immense importance for the reason that cancer is a multi-step and multi-hit process and requires multiple mutations for a cell to become and behave as an independent, immortal cancer cell. It is postulated that if for the sake of assumption, a cancer development requires two mutations, one of which is spontaneous and beyond control but the second one may come from environmental factors such as tobacco, hence refraining from tobacco consumption may halt a carcinogenic process just short of developing full-fledged cancer cell and thus preventing from it.<sup>8,9</sup>

Finally, this fact further emphasises the need for early screening to detect and manage non-preventable cancers at an early stage. These screening tests are widely available and include mammograms, prostate-specific antigen (PSA), and occult stool blood for breast, prostate, and colon cancer, respectively. In addition, many other tumour markers in blood and so-called liquid biopsy<sup>10</sup> along with radiologic tests have opened huge new possibilities to screen and detect cancer at a very early stage when it is perfectly curable or controllable.

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