

Recognising the Many Faces of Cancer

Min Han Tan,¹ *MBBS, MRCP, PhD, FAMS*

World Cancer Day falls annually on February 4th. An initiative by the Union for International Cancer Control, it is an event meant to focus governments and individuals on the need to ease the worldwide burden of cancer.

Cancer is a global disease, inflicting worldwide suffering but with distinctly local impact in terms of different epidemiology. Such a highly variable nature of worldwide cancer survival reflects differing disease patterns, environments and health infrastructure.¹ For example, the locally advanced fungating breast cancers seen in the Third World would be almost unimaginable in the industrialised nations of Northern Europe. Similarly, while worldwide mortality arising from smoking-related lung cancers dwarf that of almost every other cancer, it remains poorly understood why non-smoking East Asian females seem unusually predisposed to lung cancer.²

There have been great advances in cancer prevention in the last few decades, and these have been broader than the more limited gains seen in cancer therapeutics. This is despite the latter receiving far more attention and funding, particularly in the last decade where considerable efforts were made to rationally design targeted cancer therapy. The divergent outcomes are striking: vaccination against the hepatitis B virus, introduced in 1984 in Taiwan and 1986 in Singapore, have already resulted in falls in hepatocellular carcinoma incidence,³ whereas Dr Antonio Fojo, head of the Experimental Therapeutics Section at the National Cancer Institute was recently quoted commenting that “Zero [is] the number of targeted therapies that have prolonged survival by 1 year, when compared to a conventional treatment”.⁴

Cancer therapeutics has enjoyed some prominent successes. Few clinicians today remember the period when childhood leukaemia was associated with 95% mortality. The majority of these revolutionary advances are however decades old, and this promised era of targeted therapy has often failed in its deliverables. It has also been ironic that after narrowing target selection a la promised silver bullets, researchers and clinicians are now seeking to

return to approaches involving broader spectrum agents or combination therapies with more molecular targets and inevitably more toxicities. Indeed, a plateau seems to have been reached, with many classic cytotoxics discovered in the 1960s, including cisplatin and 5-fluorouracil, still forming the cornerstone of many therapeutic regimens.

It has been mooted that perhaps a better understanding of cancer is needed, and that greater and continued investments in genomics are required to realise the promises of personalised medicine. Certainly, cancer is a strange enemy that bears many guises, and in both researching and treating this disease, empathy with the proverbial 6 blind men is inevitable. Medical students are usually taught that it is an implacable foe to be given no quarter, no ground, that the raw power of the medical-industrial complex must be brought to bear onto this entity with inevitable collateral damage inflicted. For the layman, it is a strange and terrifying disease evocative of past losses and personal mortality. The surgeon wields a knife at the affrontery presented by the tumour; while the radiation oncologist and the medical oncologist measure out doses with exquisite care. The laboratory scientist often meets cancer as proliferating tumour cells requiring feeding and cultivation on flat petri dishes in air-conditioned comfort. But perhaps strangest of all is the cancer slowly being discerned by epidemiologists through large screening cohort studies in industrialised countries—a disease widely varying in aggressiveness, with a large proportion of indolent non-life threatening disease that may even spontaneously regress, and which may never need treatment.

The tumultuous debates of the last 10 years over the value of screening mammography and prostate-specific antigen screening in the community are testimony to the increasing and profoundly uncomfortable realisation where both the diagnosis and apparently curative treatment may have been unnecessary in a proportion of patients. While there is overall population benefit,⁵ it has been estimated in the USA that among the 60% of women with breast cancer that

¹Biodevices and Diagnostics, Institute of Bioengineering and Nanotechnology, Singapore

Address for Correspondence: Dr Min Han Tan, Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, The Nanos, #04-01, Singapore 138669.

Email: mhtan@ibn.a-star.edu.sg

was detected by mammography, only a small proportion were directly helped by the test.⁶ This contradicts the commonly held presumption that those who survived after a diagnosis of cancer did so because of early detection. The reason is because community screening results in detection and inevitable treatment of slow-growing and potentially insignificant cancers which may be more common than their aggressive counterparts. While it is true that mammography remains the best available tool for community screening,⁷ absolute benefit and the risk of overdiagnosis are difficult to convey to the lay public. For prostate cancer, a similar enigma is captured eloquently by a prominent urologist Dr. Willet Whitmore, “Is cure necessary in those for whom it is possible, and is cure possible in those for whom it is necessary?”⁸

The threat of cancer overdiagnosis is far less in low-resource countries, where cancer poses a clear and present danger as large, fungating, invasive, and deforming tumours which are sources of tremendous suffering and misery. There are very real opportunities here for reducing the burden of suffering caused by cancer. It has almost become trite to say that smoking remains the single greatest cause of preventable deaths worldwide, with 21% of cancer deaths attributable to smoking.⁹ Smoking prevention through effective taxation and legislation are likely to do more for cancer prevention than almost any current available measure,¹⁰ but this remains difficult to execute in many countries. For cervical cancer, a major threat in developing countries, the immediate availability of human papilloma virus (HPV) vaccines—though still very expensive—may mean a possible future dramatic reduction of cervical cancer. In low-resource countries, visual inspection with acetic acid¹¹ is becoming a preferred alternative relative to the infrastructure-intensive Pap smear requiring cytology and skilled interpretation. HPV DNA technologies look set to supercede the Pap smear, and may eventually have an even wider impact if self-sampling is validated. In recognition of the opportunity afforded by these advances to reduce cervical

cancer in developing countries, the Gates Foundation has chosen to take up this cause.

In summary, World Cancer Day gives an opportunity to reflect on the great advances that have brought us a little closer to the promised day when the former things have passed away; it also reminds us just how far there is to go.

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