

World Cancer Day 2011 – A World without Cancer One Day?

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World Cancer Day is spearheaded by the global consortium International Union Against Cancer (UICC) and falls on 4th February every year. This year's theme is 'Cancer can be prevented'.

In the past 60 years, deaths from heart disease and stroke have dramatically declined but not for cancer. By 2010, cancer surpassed cardiovascular disease as the leading cause of death in the world.¹ Over 50% of all diagnosed cancers in the world today are cured by surgery, chemotherapy, radiation and other established therapies. Still, cancer remains *The Emperor of all Maladies*,² a title taken from a *Time Magazine* 2010 top ten non-fiction book by medical oncologist Siddhartha Mukherjee who annotates this disease through history and Man's monumental struggles, achievements and failures against it. Cancer-related mortality has been rising for decades and has only recently plateaued, turned the corner and declined by about 5%.¹

Richard Nixon signed into law the National Cancer Act in 1971, heralding the *War on Cancer*, where Nixon vowed that cancer would be defeated by the American bicentennial 1976. By 1976, cancer was not cured, and deaths from cancer continued to rise. In 2003, the former Director of the National Cancer Institute Dr Andrew von Eschenbach promised to eliminate suffering and death from cancer by 2015. In 2009, President Barack Obama vowed that cancer would be cured in this lifetime and pumped billions more to defeat it. As advanced pancreatic cancer has barely improved its survival odds since the 17th century, these promises sound potentially quixotic. The NCI alone has spent \$105 billion dollars in the War against Cancer and hundreds of billions more by others with almost 2 million journal publications to show for it, but only a handful of successful FDA approvals have been granted for new cancer drugs in recent years. It would arguably be easier for a politician to commit to eradicating terrorism in this lifetime.

Cancer and terrorists have uncanny similarities. Mutations and insults occur early, they become dysfunctional and extreme, they migrate to distant sites to cause destruction, they are masters of disguise and conceal differentiating features to evade detection and those that survive attack grow more resistant and resilient. If terrorists cluster in a mountain hideout, a surgical strike might suffice, and some radiating bombardment of the surroundings might be

needed to wipe out some escaped terrorists. But to eradicate disseminated terrorists requires a systemic approach which is much more challenging. Much effort is now being made to look for, measure and track circulating cancer cells,³ and to study self-renewing early cancer cells in the hope that drugs can be designed against them.⁴

Cytotoxic chemotherapies sourced from such diverse roots as mustard gas (carmustine), periwinkle flower (vincristine), the bark of the Pacific yew tree (paclitaxel), the sea sponge (trabectedin), a Chinese ornamental plant (irinotecan) and even a metal famous for awarding modern music achievements (platinum) have contributed immensely towards the War on Cancer, spectacularly against testicular cancer, lymphoma and leukemia. However, its overall significant benefit in many advanced solid cancers remains limited.

Enter the Molecular Era. With the breathtaking conquest of chronic myeloid leukaemia (CML) by the bcr-Abl tyrosine kinase imatinib (Glivec) which switches off the singular CML oncogenic drive, a renewed and hopeful light appeared.⁵ Glivec can also convert advanced gastrointestinal stromal tumour (GIST) into a smoldering, indolent disease, a strategy now being employed against many cancers. Unfortunately, many subsequent molecular targeting drugs are not as successful against a disease as complex, mutation-ridden and heterogenous as cancer, kept alive by a network of signals and circuits.⁶ If one activating signalling pathway is switched off by a molecular targeting drug, like blocking one of the underground train lines, many alternative bypass routes can still circumvent the obstruction. Cell lines and animal models to test anti-cancer drug development often end up lost in translation, with many cancer-bearing mice being cured of cancer but most of such drugs found to be ineffective in cancer patients. A good move forward is to identify cancer patients that have an activating molecular pathway, mutation or gene pattern and enrich this patient group for a targeting drug has exceptional specific response against so as to maximise benefit in this enriched population and move this up the clinical development value chain more rapidly.^{7,8} Global cancer research leaders have urged for better integration of the scientific community with the clinical interface to focus on designing and delivering drug development with more efficiency, discernment and clarity

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to benefit cancer patients more quickly.

Other strategies to combat cancer include shutting down the blood supply that feeds the cancer,⁹ modulating the surrounding terrain of hostile immune cells including regulatory T lymphocytes¹⁰ and myeloid suppressor cells that protect the cancer from assault,¹¹ and targeting the surrounding stroma that cross-talks with the cancer cells to sustain cancer survival.¹² For the first time, a therapeutic cancer vaccine has been approved by the FDA, against hormone refractory prostate cancer.¹³ New drugs that activate the immune system may also add a new dimension against cancer.¹⁴

Cancer prevention can be as simple as lifestyle modification such as stopping smoking, getting more exercise, dietary discretion, and reducing obesity, to abiding by established screening strategies which can be potentially enhanced by a new era of molecular, technological, predictive biomarker and bioimaging discoveries.

Treating the number one global disease with over 40% of everyone in the world affected comes with a hefty price tag. America spends 15 billion of a 12 trillion dollar GDP (or 1/800th of the GDP) on cost of cancer drugs, and United States economic experts say this is too miniscule for such a top priority national health problem. The cost of cancer care in the United States in 2010 is above 124 billion dollars and increasing still, a situation expected to reach 173 billion dollars by 2020 heightened by an ageing population.¹⁵

Every national government and involved agencies would explore ‘the best bang for the buck’ when calculating the cost for cancer care, wholly aware that cancer patients and their families and communities can be bankrupted in their struggles to pay for cancer treatment. One of the key health policy strategies in Singapore for cancer prevention is in establishing practical guidelines for cancer screening to potentially diagnose earlier disease for Singapore’s number one killer. Also importantly, such guidelines emphasise which cancers should not be screened where there are no benefits to the patient and community as a whole, with no evidence for impact on cancer related mortality.¹⁶ Screening compliance is still less than ideal in low income communities in Singapore.¹⁷ Undoubtedly, the overall detection rate is low for even cancers such as breast and colorectal cancer where benefit for screening is generally accepted, as current screening technology are still blunt tools. The future must belong to devising more sensitive and specific technology for cancer detection, but such enabling technologies must not be abused for consumer and profit driven screening.

The War on Cancer should realistically be about further reducing cancer-related mortality. As to envisioning for a world without cancer, this malady is still very much an existential part of life and death for now. A movement

to conceptually define and describe cancer as a series of metabolic processes may further help find new ways to combat this disease.¹⁸ More than ever before, we can detect cancer earlier, cure more cancers, convert other cancers into a less acutely fatal disease, alleviate suffering of more cancer patients and potentially identify at-risk individuals to prevent more cancers from forming. Compelling evidence points towards cancer chemoprevention as a potentially constructive intervention.¹⁹ Hence we can and should confront this disease with hope and not fear.

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