Where And How We Die Week 2

In the mid-twentieth century, about the time I was born, most people died at home. There wasn't much to do for heart attacks except 'rest' and nothing on offer for strokes. Most cancers were found too late and took their natural course. Few survived into their late seventies or eighties, never mind reaching the century mark and so dementia and most of the neurodegenerative diseases with which we're become so familiar now, were uncommon. There was little in the way of what would pass these days for home care, palliative care, or hospice and except for surgery for well-localized and less aggressive cancers, and pain control, little to be done. People like my Uncle Bern with Parkinson's disease, died at home looked after by his wife who had little to offer except clean sheets and bedclothes, spoon feedings and love. That was it. In those days there were no drugs or surgery to help. He lasted only a few years and like my wife's aunt Betty who died with what was probably Alzheimer's disease, he too died curled up, unable to move and mostly unaware of himself or others.

Much has changed since. First the good news: The incidence of stroke and heart attack has declined in the face of much better long-term control of hypertension and cholesterol levels. And treatment of acute stroke and heart attack has been revolutionized by a combination of speedy assessments; clot busting drugs, stents and extraction of some clots in the case of strokes affecting large arteries near the base of the brain. However it hasn't all been a success story where vascular disease is concerned. The mortality of rate of heart failure remains high (half die within five years).

My mother-in-law died of heart failure. She had the best of care from London Health Sciences (LHS) but even so spent her last few months shuttling back and forth between the LHS's ER and her small apartment in an assisted living facility, fighting for breathe and dragging her grossly swollen legs about her small apartment. Unfortunately unlike her husband, she died alone on the 'heart floor' of LHS, without family to ease her way.

On the cancer side, combinations of chemotherapy, radiation and bone marrow transplantation have cured or put into long term remission, many bone marrow and lymphatic cancers. The outlook for other cancers has

been no less impressive given current tools for nipping some early breast and colon cancers in the bud using mammography and colonoscopy. These and other greatly improved methods for detecting early cancers and better treatment options have changed the landscape for many cancers, although not without the all too common debilitating adverse side effects and risks associated with radiation and chemotherapy.

The outlook in cancer is about to take a quantum leap forward. We live on the cusp of the gene-driven detection and treatment of many cancers. Not only has sequencing the human genome become much more precise and quicker using nanotechnology pioneered by an Oxford University group but a lot cheaper. It turns out that aberrant mutant genes cause most cancers. These mutants may be hereditary or acquired in life but whatever their source they can now be detected with precise, rapid and relatively cheap sequencing of the whole genome.

What's not surprising, given the very different responses of similar looking and 'named' cancers to standardized 'one size fits all' treatments, is the finding, that at the genomic level, those like-looking cancers are not so alike after all, but caused by different genetic aberrations. Different genes code for different proteins or play different roles regulating the multiplication of errant cells. If those aberrant genes or their downstream effects could be blocked in some fashion, we will have the ultimate treatment at hand - one tailored to a patient's very specific cancer. So one size does not fit all – something we've suspected for a long time. This revolution is underway now as I write. One example reported in the March issue of the Journal *Nature* is the finding of 32 distinct mutated genes in 456 pancreatic ductal adenocarcinomas (that's the bad one if you're wondering). Gene targeted therapies promise to be far more effective than those one-size-fits-all treatments on offer these days that try to kill all cancer cells but cause a lot of collateral damage to other cells in the process and might not be all that effective in any case. So gene-directed treatments and immune targeting of cancer cells is the present and future of Cancer. And as I've reminded my readers in columns past, the genetic revolution is not limited to cancer for within the next few years many genetically transmitted neurological diseases such as Huntington's chorea and many of the muscular dystrophies such as Duchenne dystrophy may be curable by the new gene-

editing techniques coming on stream such as CRISPR-Cas9 and its successors.

However whatever our successes in treating vascular disease and cancer, the end result has been that many more people survive the cancer and vascular disease threats of mid and later life, only to run headlong into the wall posed by neurodegenerative diseases such as Alzheimer's disease, the Fronto-Temporal Degenerations (FTD), Progressive Supranuclear Palsy (PSP), Multiple System Atrophy (MSA), Lewy Body Dementia (LBD), Parkinson's Disease (PD) and others for which we have no effective treatments as yet. As I've pointed out in this column on several occasions, these diseases are associated with misshapen proteins (prions) capable of replicating themselves and in the process destroying much of the brain's Internet of cell processes and neurons. Similar proteins are at the root of the much less common but devastating Creutzfeldt Jacob (CJ) disease and Bovine Encephalopathy (BE) which may be transmitted between humans in the case of CJ and from infected cow tissue to humans in the case of BE.

Medical care has become much more specialized and hospital based. In the process the tertiary care so often needed in Cancer and Vascular Disease has moved out of the community to highly specialized hospitals and outpatient clinics. This move is reflected in where we die. In 1995 close to eighty-percent of deaths took place in hospital. This compares with figures of fifty-percent in 1949, sixty-one-percent in 1958 and by 1977, seventy-percent. The figure has since dropped to about twenty-five-percent of patients but that figure doesn't include deaths in chronic care facilities where many patients with neurodegenerative diseases end up and spend their last few weeks shuttling back and forth between the chronic care facility and the ER. In those last days patients often die alone without family nearby. Of course palliative care and especially hospice, offer more humane care but the fact is that too many patients still spend their last days alone and suffering, physically and emotionally with little control over events and precisely in the position they dreaded in better days and times.

Tragically, in much of the rest of the world dying can be much nastier affair. We need only remind ourselves of the outbreak of Ebola in West Africa recently to see how agonizingly miserable death can be. And throughout

much of the Middle East, Africa and parts of Asia, violent death from road side bombs, artillery and aerial bombing on a horrific scale is the order of the day and so common, that only the worst examples capture headlines anymore. Most victims are innocent but innocent or not, the end is too often the same; bodies broken, burned out of all recognition or vaporized. And for too many, death was but the end of years of dislocation, starvation, and cultural and sectarian violence. So the 'Where' and the 'How of Death varies with where we live and our age. The next section will deal with the role Intensive Care Units and Emergency Rooms at the end of life. Please save each section as it comes along because they will form the basis of a public discussion in the late spring or early fall.

Week 2

How has the landscape of health care changed in your lifetime for you, for your family?

How do you view 'old age' and the changes in your body and mind associated with aging?

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