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Point of View

Cancer prevention in the year 2025: an anticipation☆

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It is said that only fools make predictions, so let us call my ramblings 'anticipations'.

In the year 2025 the last of the traditional inpatient hospitals closed.

Could such an event come to pass? What assumptions need we make? What could possibly happen that would make this event, not just possible, but inevitable?

One way to explore the anticipation for 2025 is to look at the reality of 1975.

In 1975 there were no microwave ovens or automatic coffee makers.

In 1975 there were no fax machines, Xerox copiers, video conferencing, personal computers, the internet or e-mail.

In 1975 there were no automated telling machines (ATMs), personal global positioning devices, pagers, laser pointers, liquid crystal display (LCD) projectors, mobile phones, compact discs, digital watches or cameras, or Palm Pilots.

In 1975 there were no pipettemens, Northern or Western blots, phosphorimagers, ESTs, polymerase chain reaction (PCR) or gene blasts; no automated DNA sequencing and no kits (of any kind).

In 1975 oncogenes were just surfacing. There were no tumour suppressor genes (at least we didn't think of them that way), no gene cloning and no Dolly.

In 1975 there was no filgrastim (Neupogen) or epoetin alpha (Epogen) or serotonin inhibitors. No interferon or paclitaxel (Taxol) trastuzumab (Herceptin) and so on.

In 1975, computer tomography (CT) scans were primitive. There were no magnetic resonance imagers (MRIs) or positron emission tomography (PETs).

In 1975 fibreoptic endoscopy had not been developed and prostate specific antigen (PSA) was undiscovered. We also still debated whether screening mammography gave you more or fewer breast cancers.

Since 1975 all levels of modern society have been transformed: easier, faster, better, and ... unexpected. In the year 2025 who really knows what the world will be like. In the words of one colleague in commenting about 1975, "It's hard to think of things that are still in use." I agree, and with the accelerated pace of discovery in all the sciences, predictions are hard to make, but I think anticipations, however fanciful sounding today, are reasonable.

The major advances of society and civilisation as a whole in the 20th century were driven by discoveries in physics and chemistry and the selection of Einstein by Time as the Man of the Century reflects that reality. In the 21st century, civilisation and society will be transformed by advances in the biomedical sciences brokered by the power of technological advances in computers and information analysis and implementation.

So what are some of the 'big' assumptions that we need to make to anticipate the reality of 2025?

First, the world must remain at peace. Hopefully, the issue of the economic dichotomy of the rich (and richer) and the poor (and poorer) will be addressed, perhaps using the power of technology to narrow the gap. If not, there will be widespread civil wars or more prisons everywhere.

Second, the public will insist, more than ever as our population ages, that resources be put into keeping John Q. Citizen healthy, rather than in treating his or her disease. The public really is not interested in getting sick and having their diseases treated. This seems obvious, but there is a basic conflict between what many in the medical profession see as important (e.g. more intensive care units (ICUs)) and what the public sees as valuable (more alternative medicine).

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Third, in shorthand parlance, technology meets managed care, or technology meets universal medicines, or limited resources or whatever. In the long-run the issue of how much a society is willing to spend for its healthcare will need to be addressed. The USA currently spends 16% of its gross national product (GNP) on healthcare, Europe about 10%, and Japan about 7%. And the Japanese live an average of 5 years more than people from either of the other two continents. It would seem that we're missing something big here.

And what we are missing, of course, is the broad public health approach to health, and the more considered use of technology near the end of life. After all, 40% of the healthcare dollar is spent in the last year of a person's life. Is this reasonable? Is this reasonable for us as a society? But of course, no more technology is for the other guy. The decision is so intimately personal when it's you or your wife or your father or mother, brother or sister, or other loved one. The cost of high technology for treatment is immense and the process by which it is allocated is coming under intense scrutiny everywhere. Alternatively, we need to develop low-cost high technology for the screening and early detection of disease and the maintenance of health.

And finally, the nature of computing in 2025. Current computer processing speed is basically limited by the intrinsic electronic components and the platform from which it operates; consequently a plateau for computing power using current technology will be reached. But the world changed in January 2000 when scientists at IBM were able to show that a quantum computer was not just an idea, but technically feasible [1]. What does that mean? What that means in general terms is that solid state electronic computers with an unlimited capacity for information transfer, storage and retrieval will happen. We think now of computing advances in terms of doubling, or perhaps, factors of ten. With quantum computers, a Palm Pilot will have the computing power of today's Cray supercomputers, and today's personal computers will be viewed as the equivalent of abacuses, an interesting historical artifact.

What does this mean for biomedical science? It means hand-held CTs, MRIs and PETs, or perhaps these technologies will be totally outdated. It means totally new imaging technology, currently undiscovered.

But what does all this mean for cancer prevention in 2025?

Well, let's spend a day or two in the life of Mrs John A. Smith, or Zosyn (Zosy to her friends), named by her physicist father and her physician mother, after a third-generation antibiotic, popular at the time of her birth, 1 January 2000. (He worked in CERN in Europe and she in Washington, DC. She was French and he American. But no matter, they lived a complicated, but satisfying life.)

Zosy accelerated on to the Community Exit Port, which led to the public transport lanes or PTLs. (The term 'freeway' had gone by the wayside in 2015 when the maintenance of freeways had been transferred to the Federal government and each city or borough controlled access to and from their community. But enough about these social changes.) Zosy's upgraded personal transport vehicle (or PTV), a Maglev 5, engaged the electronic highway and she set the designation and course. She relaxed, turned on the heads up display of her satellite-downloaded e-mail and began to read.

Someone was spamming the airways again, and there was a lot of junk. No matter how diligent Vchips and Pchips and ... whatever. Teenage girls would defeat them every time. She knew; she had been through that phase too, a well described life-transition disease, 'quantum hackerism.' Combined with the newest aroma product ('sniffed not drunk') of the underground pleasuredome company, 'Titusnero,' well... The product was known as 'Clinton de Gallo' and produced strange behaviour in otherwise rational people. And when teenagers began using it, ...

The next e-mail: 'Mandatory Birthdate plus 25, Genomic Scan.'

Zosy had been one of the unlucky ones, born between 1 January 2000 and 31 December 2019. Beginning 1 January 2020 all newborns had a complete genomic scan and whole body light scan performed within 1 week of birth. All information was recorded on the personal identity card or PIC. These tests would be repeated every 10 years throughout life and early changes dealt with by one's geneticist or internist. (At one point it looked like radiologists were going to win the battle for speciality retention, but the widespread introduction of natural radioisotopes assured their demise.)

But Zosy's situation was different. After a long political/medical/scientific battle, it was decided that the 2000–2020 group, known as first generation 21st Century or GST 21 for short, would be tested for the first time at age 25 years. The problem was a simple, but complex one. Individuals who were tested at birth could be followed and new single nucleotide aberrations detected, and subsequent testing at the ages of 10 and 20 years made the process highly accurate. But when to do screening after birth and before serious age-related changes set in for the GST 21ers? Age 25 years was chosen as the equipoise position.

Today was the day for Zosy and tomorrow she would receive her adult genomic analysis (or GA), predisposition assessment (or PA), and whole body light scan (or LS). Taken together they were known as the G-A-P-A-L-S or GAPALS.

Her Maglev 5 deaccelerated, changed lanes and moved into the Health Access Port for the Regional Health Centre (or RHC). The laser-activated transponder beeped, the electronic force beam lowered, and she

glided through. In front of her was the RHC. She had been brought there once at age 15 years after a Maglev access failure led to a 2000 PTV crack-up. She had also seen it many times on her Personal Monitor Viewer (formerly called a TV). It was awe-inspiring, all platinum tempered steel and glass, covering over 500 acres and servicing the entire Southern California basin, now over 35 million people who spoke over 96 languages. There were three major centres: The Bionano-engineering Unit (or B-I-N-U) staffed mainly by surgeons and engineers and a large technical support staff; the Predisposition Center (PC) staffed by physicians and scientists specially trained in molecular biology and chemistry and the Diagnostic Center (DC) staffed by physicians and scientists trained in internal medicine and imaging physics. Both the predispositionists and diagnosticians were commonly supported by a centralised unit of quantum computerists, molecular biophysicists and combinatorial chemists.

Zosy entered the PTV space lot and was dismayed to find no units available. Two hours later: "All this quantum stuff and you still can't get a parking place! Ah, a place, zip in!" She entered the PC lobby and inserted her PIC into the entry scanner: her medical history was reviewed, family history checked, information on the PICs of her parents and sibs accessed and their DNA sequencing information downloaded onto her PIC. For GST 21ers comparison with familial DNA sequences was critical and very useful. (The appearance of mutations in certain polymorphisms was known to be an early sign that intervention was needed.)

Zosy was a little anxious about what was to come, but the Central Authority for the Maintenance of Health had done all it could to smooth the way. After a major political battle in 2015 between the Universal Employer Bargaining Unit and the Union Collective, employee contract language mandated that all GST 21ers be given 3 days off for their GAPALS and fully paid for by their employer.

She proceeded to her room which was patterned after a four seasons suite. Ultrasonic stimulated skin sweat with shed cutaneous cells were absorbed by the robot sleeve monitor and sent for DNA sequence analysis. (Routine blood drawing had been outlawed in 2015 and only in the BINU Reassembly Suite were intravenous (i.v.) drips permitted.) Although the DNA sequence would be determined in less than 10 s, comparison of the sequences with that of her parents and sibs would take until morning.

At precisely 1800 h her self-delivery tray popped out of the wall. On it was a vial and written instructions, given as well by audio if desired in one of 96 languages, as specified on the PIC. Under robot video monitor she was observed as she opened the vial (labelled Predisposition Diagnostic or PD-9A, the 9th generation of PD probes) and inhaled its contents. At precisely 2100 hours this procedure was repeated with a second vial (labelled PD-9B). (In 2025 medications were almost all given transnasally or transdermally.)

The first vial contained a paramagnetic compound that linked in a non-hydrogen bonded manner to thymidine or cytosine nucleotides in every cellular genome in every tissue or organ in the body. The chemistry was such that a stable redox centre was established that would later be activated and signals recorded and abnormalities noted. The second vial contained a paramagnetic compound that linked to melanin in a specific manner, dependent on its degree of oxidation. Until 2005 scientists had always considered melanin a terminal product that had a useful function only as a cutaneous ultraviolet (UV) protectant or was somehow involved in Parkinsonism and some other brain diseases. (It turned out that fine loops of melanocytes and hence melanin were everywhere in the body and served as a structural-electronic network linking all organs to the brain. And it seemed the basis for the success of acupuncture, now widely used. The neural crest origin of melanocytes was no longer — not since 2005 — just an interesting curiosity. In fact . . . , but that would take us too far afield.)

Let's return to Zosy. She has been joined by her male consort (politically correct terminology, 2025) who had popped over on the Stratospheric Shuttle from Europe Nation No. 6 and would be spending the night with her. They were under strict orders, and observed by the robot monitor video to make sure they did so, to remain platonic, as even slight changes in blood gases could interfere with the binding properties of the PD probes and give erroneous results. (Approximately 3 years ago, a clever paramour turned off the robot monitor and the next morning her boyfriend turned to a sticky DNA soup 5 minutes after activation. Reported widely in the cosmos wide.net, there hadn't been another incident yet, but just in case, a second rest platform came out of the wall when Affi entered the room. He was 5 years older than Zosy and named by his quirky parents after the original functional genomics company, Affimetrix. He would be escorted there by the robot monitor at 2300 h and an electronic separation wall established.)

At sun-up the shades on the window opened, activated by the first UV-B rays of the sun, and Zosy awoke naturally. It was critical that circadian rhythms be synchronised with the testing as changes in steroids had been found to affect every molecular parameter in profound ways.

For the next 2 h she would be accompanied by her male consort and a female nurse, as it has been found that humans could not tolerate the 'activation' without human contact. In fact, there had been hundreds of suicides and psychotics produced until the effect of total sensory withdrawal and whole body nucleotide

activation on the human brain and nervous system was realised and appreciated.

Zosy entered the Evaluation Room. What it was in reality was a room-sized Electronic Paramagnetic Resonance Chamber that measured bias voltage differentials at the cellular level. She inhaled the contents of a third vial 5 min later and was scanned in less than 5 s. A rest period ensued; she tried to suppress her trembling. An additional rest period was ordered. A fourth vial was inhaled and she was scanned again.

She awoke 2 h later with 3 human faces observing her with the utmost concern. She would be fine, but would have to stay for an extra day of sensory relaxation and recuperation.

And what did GAPALS show in Zosy?

She had good genes, the GA showed that almost all her polymorphisms were the best known, but there was concern about her adenomatous polyposis coli (*APC*) sequences. Not surprisingly her PA showed several mutations in her colon and the LS scan confirmed a hot point in the same area.

After much discussion, she was offered a clinical trial comparing the now standard virtual colonoscopy with holographic laser capture removal to synthetic endosymbionic progenitor correction (a variant of the artificial genome construct first described in December 1999 [2]). She and Affi debated the pros and cons and she was also conference telelinked to her parents for further discussion. The first alternative was not a permanent solution and might need to be repeated. The second produced a permanent correction, but there had been problems. The science was solid but there had been disturbing complications reported. The cosmoswide.net was whispering, ''Adenovirus/gene therapy 2000 repeated.'' It was a hard decision; she was from a medical family and believed in clinical trials, but . . . . And so she declined the trial, and six aberrant crypt foci, each less than 1 mm in size, were removed by virtual colonoscopy and laser capture removal. She would need a special limited PALS every 10 years, but that seemed like a small price to pay. After a long round of further discussions, she also entered a fourth-generation chemoprevention trial which randomised standard chemoprevention medicines to a seventh-generation nutraceutical difluoromethylornithine (DFMO) hybrid. She would receive the experimental drug via a transdermal patch for 10 years.

It is 2025. The concept of health has transcended any disease. Prevention and screening and early detection are a public health mandate for all, not just for the affluent.

In the year 2025 I will be 80 years old. It's almost eerie that every male in my father's genealogy for six generations has died at the age of 81 or 82. Perhaps with a little luck, I'll get to see the world of quantum computers, Maglev 5's and clinically applied artificial genomes.

I sure hope so.

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