Curing Cancer blog – part 9 – How cancer kills

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March 22, 2021

Revised 11Apr21

This blog discusses curing cancer based on the principles of complexity theory. Follow this blog at **https://natpernickshealthblog.wordpress.com** and join our Curing Cancer Network to receive weekly status updates by clicking **here** (note: this project is independent of PathologyOutlines.com).

Our **strategic plan** is to reduce US cancer deaths from 600,000 in 2021 to 100,000 by 2030. To do so, we must better understand how cancer actually kills people. We conclude that cancer often kills by promoting marked physiologic disruptions in life's essential networks and by creating a sense of futility, which causes individuals and the medical system to give up the fight. Other direct mechanisms include hemorrhage, infection, side effects of therapy, central nervous system changes and organ failure.

1. Life requires a sophisticated web of stable biologic networks

To understand death, we must understand life's requirements. To live, we require adequately functioning organs and organ systems within a supportive and stable biologic environment that these organ systems themselves help create and maintain through a sophisticated web of network interactions.

Life follows the principles of complex systems in that the properties of the entire system are greater than the sum of the properties of each part due to interactions between the parts (**Pernick 2017**). This synergy gives us a greater capability than we might imagine from studying each organ system separately but also creates difficult problems when multiple interdependent systems go awry.

Our cells function optimally only when supplied by blood with adequate oxygen and glucose and when the concentration of essential blood components is maintained within a narrow range. These include sodium and potassium (electrolytes), calcium and other minerals, acidity (pH) and nutrients. In addition, the immune system must limit destructive infections and their toxins, the coagulation system must preserve blood flow and prevent hemorrhage and the kidney and liver must detoxify harmful substances and remove them from the body.

2. Cancer kills by promoting marked physiologic disruptions

We propose that cancer kills by promoting marked disruptions in life's essential biologic networks. Our organ systems have evolved to be tightly integrated with each other for optimal performance, to respond to the usual physiologic conditions and to correct small,

short term disturbances. This explains why humans typically have a prolonged lifespan that only occasionally requires significant medical intervention. Cancer risk factors cause sustained stress on the networks, leading to initially small, unnoticeable changes. However, self-organized criticality predicts that over long time periods, these small changes, acting in a nonlinear manner, may lead to an avalanche of changes (**Bak, How Nature Works 1999**), which may cause marked physiologic disturbances and unstable states involving tumor growth and spread, the release of cytokines, inflammation, immune system dysfunction and other changes to the metabolic milieu. These "cancer attractor" states are difficult to normalize, even with intensive medical therapy and ultimately may lead to a downward spiral causing death.

Cancer risk factors and the malignant process create disruptions by several mechanisms: (a) they promote continuous activation of the inflammatory system, which is unstable and transmits this instability to the many networks with which it interacts (**Pernick 2020**); (b) tumor growth destroys normal tissue, which diminishes the effectiveness of organ systems and their cooperation with other organ systems or even causes organ failure; (c) growing tumors cause increased metabolic demands, which challenge network functioning; (d) tumors secrete products which disturb physiologic functions; (e) tumor growth may, over time, induce network changes that trigger cellular activities typically repressed in adults, such as unicellular programming for cells and embryonic differentiation; (f) tumor growth may create immune system dysfunction that leads to tolerance of cells with malignant properties that would otherwise be destroyed. Together, these mechanisms may lead to a dominance of cancer attractor networks which preserve malignant properties in organ systems, even against treatment, and are ultimately incompatible with life.

Our organ systems are interdependent so that disturbances in one system may cripple many systems. For example, cancer causes disturbances in the blood calcium level that affects the kidney, gastrointestinal tract, central nervous system and skeletal system (**Zagzag 2018**). Cancer or its treatment may damage the bone marrow, leading to anemia, bleeding or infections, all of which similarly degrade the functioning of multiple organs and organ systems.

3. Countering cancer related disruptions is difficult

In general, human physiology or medical practitioners are capable of countering slow declines in the functional capacity of organs, particularly when there are deficiencies in only one organ system, due in part to organ system redundancy and reserve. However, cancer kills patients because (a) systems fail quickly, challenging our ability to respond promptly and appropriately; (b) it is difficult to adequately respond when multiple critical organ systems fail simultaneously because the usual treatments for single system failure may be inadequate; (c) even before the rapid decline, these organ systems were slowly diminishing due to tumor related destruction or age related changes.

When multiple organ systems are working harmoniously, we marvel at the wonders of life. However, dysfunction in multiple systems produces not just abnormal lab values that threaten life, as assessed by medical scoring of physiologic instability (**Mattia 1998**, **Pollack 1996**), but the inability to easily return these physiologic measures to normal.

It is important to note that cancer typically does not kill by destroying the functional capacity of organs to the extent that they no longer sustain life. When people die of cancer, particularly if this occurs rapidly after diagnosis, they usually have adequate reserves of function in their organs or these reserves can be supplemented by technology.

Rapid cancer deaths have similarities to diabetic ketoacidosis in that both are lethal primarily due to abrupt physiologic changes, not because the patient is terminally ill. In diabetic ketoacidosis, insulin deficiency transforms an orderly physiology into chaotic, life threatening disturbances in many essential networks. Merely giving insulin does not fix the problem – instead, a sophisticated system of treatment and monitoring is required **(Fayfman 2017**) that is so complicated that simulations are often used in training (**Roberts 2020**).

Similarly, we suggest that rapid cancer deaths could be reduced with a sophisticated system of treatment and monitoring. The initial concern should be countering the tumor's disruptive effects on network related stability so that medical therapy can restore viable physiologic characteristics and maintain life. Subsequent treatments can focus on killing the bulk of the tumor cells and achieving long term survival.

4. A sense of futility is another major cause of cancer death

Another major mechanism of cancer death is futility, the belief that there is no reasonable hope for a cure or benefit to continued treatment. With advanced cancer, the physiologic changes are persistent, but not necessarily rapid; although medical science can halt them temporarily, patients and their physicians may believe it is futile to aggressively manage what is clearly a downhill process.

Even with progression, life can continue as long as there are no rapid instabilities and if patients and their physicians rationally believe there is hope to continue. If cancer is viewed as a chronic disease that can be managed (even if not cured) and as newer treatments improve our ability to hold it in check, then we can limit this sense of futility and diminish cancer related deaths, at least for some time. Anti-tumor treatment may incorporate the principles of adaptive therapy, which uses more dynamic treatment protocols, such as (a) suppressing the growth of resistant phenotypes, (b) creating an initially small resistant tumor cell population that is eradicated by a second treatment, (c) designing a "resistance management plan" and (d) at some point, assessing the success of treatment in each patient and determining what could be improved for future patients (**Stanková 2019**).

6. Occasionally, cancer does kill directly

Cancer can kill directly by eroding blood vessel walls, leading to lethal hemorrhages, which either damages vital brain functions or causes loss of blood flow throughout the body, starving cells of oxygen and nutrients. In addition, brain tumors can cause increased intracranial pressure, leading to brainstem herniation, which blocks the nerve signals to the lungs for breathing. Cancer treatment or its persistence can damage immune system and bone marrow function, leading to life threatening infections, anemia or coagulation disturbances, which also cause death.

In summary, we propose that to prevent cancer related deaths, cancer treatment must also focus on countering the physiologic disruptions it creates. In addition, cancer should be viewed as a chronic disease that although sometimes curative, often will not disappear but can be managed for long periods of time.

Thanks to Philip Agop Philip, MD, PhD, FRCP, Professor of Oncology and Pharmacology, Karmanos Cancer Institute / Wayne State University, for his careful and constructive review (FRCP: Fellow, Royal College of Physicians).