# New ideas about cancer

natpernickshealthblog.wordpress.com/2021/07/04/new-ideas-about-cancer/

July 4, 2021

4 July 2021

This essay lists my new or “not generally accepted” ideas about cancer:

**How cancer arises**

1**. Complexity science is more important than reductionism.** We cannot understand cancer through reductionist thinking, which states that life is just a sophisticated machine that can be analyzed by breaking everything down into smaller and smaller discrete parts. In fact, the behavior of the whole is greater than the sum of the behavior of the parts. This “extra behavior” is due to interactions between the parts, often described as emergent behavior, which is unpredictable and nonlinear (**Pernick, The Laws of Complexity and Self-organization: A Framework for Understanding Neoplasia 2017**).

**2. It is important to assess cancer in terms of network activity.** In textbooks, a biologic pathway is often depicted as an assembly line of activity, with a beginning and end that are connected. However, each pathway is affected by numerous other pathways, meaning that the overall function resembles a web of activity. This has several consequences for cancer, including (a) blocks to any pathway can be bypassed through other pathways on the web; (b) networks have generic features that are independent of the details; (c) understanding changes in network behavior may be more important than identifying mutations (**Pernick, Curing Cancer – Part 4 – Principles of curative treatment, 2021**).

**3. Coordination of network activity is a basic physiologic mechanism disrupted by malignancy.** Isolated network activity can be useful or destructive, depending on its context, but for sophisticated processes to be successful, such as inflammation and embryogenesis, groups of networks must work together in a specific, prescribed manner (**Pernick, How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**). This coordination also extends to ending patterns of network activity. Inflammation and embryogenesis both have features of malignancy, but their physiologic triggers also initiate the process of their resolution. Risk factors associated with malignancy activate these same networks but through a non coordinated process that has no programmed pathway to turn them off.

**4. Malignant change occurs through bursts of network activity, not through gradual change.** Nature often does not operate through gradual and stepwise change. Both complexity science and the related theory of self-organized criticality (**Bak, How Nature Works, 1999**) describe how small changes occur slowly over years, often unnoticed, until a critical point arises in which they reorganize with a burst of activity causing enormous transformations. In cells, cancer risk factors or random events trigger different patterns of

network activity that accumulate and ultimately burst into intermediate states (premalignant conditions) that often are identifiable microscopically, such as a colonic adenoma (polyp), but may be identifiable only as altered patterns of molecular or network expression (**Pernick, Focusing on Preinvasive Neoplasia, 2018**). These intermediate states may then undergo additional changes until they burst into overt malignancy (**Pernick, Curing Cancer – Part 7 – Random chronic stress / bad luck as a major cause of cancer, 2021**).

**5. Cancer is an inevitable tradeoff of human biologic design.** Cancer will always be with us, particularly as life expectancy increases. New cancer cases will continue to arise due to random chronic stress and behavior which promotes cancer (e.g. tobacco use, excess weight) which cannot be totally eliminated (**Pernick, Strategic Plan to Reduce Cancer Deaths, accessed 4 July 2021**). However, we can often prevent it, we can detect it earlier and we can treat it more effectively (**Pernick, How Cancer Arises Based On Complexity Theory, 2017).**

**6. Chronic cellular stress is the underlying cause of most cancers.** Chronic cellular stress disturbs the delicate balance that exists in our interconnected cellular networks between stimulating and dampening forces. In the correct context, it pushes susceptible stem or progenitor cells into increasingly dysregulated and unstable network trajectories that propagate throughout the cell, across adjacent tissues and systemically (**Pernick, The Laws of Complexity and Self-Organization: A framework for understanding neoplasia, 2011**). Ultimately, it may produce a cancer attractor, which is a cell with malignant properties that has mutually regulating genes that create a network stability that is difficult to disrupt. It is foreseeable that some chronic cellular stressors will cause cancer but which stressors will be important, where the cancers will arise and what their molecular and microscopic features will be is not predictable (**Pernick, How Cancer Arises Based On Complexity Theory, 2017**).

**7. Five "superpromoters" cause most adult cancers.** We initially identified nine chronic cellular stressors as the major cause of cancer: chronic inflammation (due to infection, infestation, autoimmune disorders, trauma, obesity and other causes), exposure to carcinogens; reproductive hormones; Western diet (high fat, low fiber, low consumption of vegetables and fruit); aging; radiation; immune system dysfunction; germ line changes and random chronic stress / bad luck (**Pernick, How Cancer Arises Based On Complexity Theory, 2017**). Recently, we condensed this list to 5 "superpromoters": chronic inflammation, DNA alterations (somatic or germline) / network rewiring, random chronic stress or bad luck, immune system dysfunction (individual or societal) and hormonal effects (**Pernick, How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**). Chronic inflammation includes components of diet, aging and carcinogen exposure. The DNA alterations / network rewiring category includes carcinogen exposure, radiation, germline changes and a component of aging.

**8. Random chronic stress or bad luck is a major cause of cancer death.** This is particularly true for nonsmokers who develop lung cancer (**Pernick, How Lung Cancer Arises, Based on Complexity Theory, 2021**) or pancreatic cancer (**Pernick, How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**). We propose that random chronic stress causes baseline rates of 2 cases per 100,000 people per year in the US for both lung and pancreatic cancer (**Pernick, Curing Cancer – Part 7 – Random chronic stress / bad luck as a major cause of cancer, 2021**).

**9. Cancer arises due to numerous changes in the immune system that evolve during the entire malignant process.** Targeting one aberrant pathway in the immune system is unlikely to be effective because it, like cell growth pathways, operates as a biologic web (**Pernick, How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**). In addition, a "runaway" immune system may play a prominent role in malignancies with no known risk factors such as classical Hodgkin lymphoma, nodular lymphocyte predominant Hodgkin lymphoma and glioblastoma **(Pernick, How cancer arises from chronic inflammation, based on complexity theory, 2020**).

**Treatment strategies**

**10. We need a strategic plan to substantially reduce cancer deaths.** Complexity theory recognizes that countering systemic diseases requires optimizing all factors affecting it, even if not directly part of the malignant process. Relying on a "silver bullet" or single solution is unlikely to be effective **(Pernick, Strategic Plan to Reduce Cancer Deaths**, accessed 4 July 2021). Our goal is to reduce annual US cancer deaths from 600,000 in 2021 to 100,000 by 2030. However, successful implementation requires that we focus on all important aspects of cancer, regularly track our progress and update the plan as needed.

**11. Cancer deaths cannot be reduced to zero.** Even with optimal treatment for a specific type of cancer, some patients will still die of cancer because of treatment refusal, compliance issues, medical conditions which interfere with treatment, treatment error, treatment failure for unknown reasons and development of additional cancers (**Pernick, Strategic Plan to Reduce Cancer Deaths**, accessed 4 July 2021).

**12. Successful cancer treatment requires combinations of drugs or other therapies because the malignant process constitutes a biologic web that has many pathways to bypass a specific block.** This web consists of networks associated with the cancer cells themselves, their microenvironment (surrounding tissues) and the systemic networks (including chronic inflammation, immune system, hormones) that support them.

**13. For each cancer histological type, we should identify 20-30 important malignant attributes and then identify or develop therapies with at least some effect for each attribute.** We have developed an initial list for pancreatic cancer, see **Pancreatic Cancer Treatment Targets.** Much work remains for investigators to find partially effective therapy directed against some of these malignant traits.

**14. We propose that our oncologists and pharmacologists can find combinations of 8-10 partially effective therapies against aggressive cancers that, as a combination, will be substantially effective** (**Pernick, Combinations of therapy to subsantially reduce cancer deaths, 2021**). The combinations, considered as a whole, will have behavior much greater than the sum of the behavior of the individual treatments.

**15. To have the greatest impact on reducing cancer deaths, we should focus on treatments for lung and pancreatic cancer and advanced cancers of the colon and breast, which cause the largest number of cancer deaths.** It may be difficult to target all cancer attributes because patients can only tolerate a limited number of therapies. Determining which combinations of therapies work together will require more aggressive enrollment of patients into clinical trials so physicians can learn and improve as much as possible.

**16. New therapies to be developed include: targeting networks, not just mutations; moving cancer cells that survive treatment into less dangerous pathways; attacking the microenvironment that nurtures the cancer; and identifying, monitoring and targeting systemic networks affecting the cancer.** To be successful, we need to target as many aspects of the malignant process as possible.

**17. It is important to study and reduce cancer deaths that occur soon after diagnosis due to treatment side effects, infections or life threatening disruptions to essential physiologic networks (Pernick, Curing Cancer blog – part 9 – How cancer kills, 2021**). It is also important to reduce cancer deaths due to a sense of futility which are based on expectations that may not be reasonable.

**Public health / prevention strategies**

**18. It is important to strengthen public health and preventative programs to promote a culture of being healthy and reducing risky behavior.** This includes promoting the **American Code Against Cancer** and other healthy lifestyle messages. At a societal level, our public health and medical care systems act as a "behavioral immune system" to reduce cancer risk factors and the incidence of cancer (**Pernick, How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**). Nonuse of screening is a major cause of cancer death (**Pernick, How colorectal cancer arises and treatment approaches, based on complexity theory, 2020**).

**19. Long term, we can reduce cancer deaths by 30-40% through prevention and improved screening.** We must reduce tobacco use to 5% or less of the population, improve diets to be predominantly plant based, reduce excess weight from 60% to perhaps 10% of the population and ensure that all Americans get adequate medical care including regular examinations to promote prevention and detect early disease.

**20. We should focus on improving screening programs that will reduce the most cancer deaths.** This includes screening for cancers with high mortality but effective treatment options when detected early; identifying premalignant or malignant lesions in both high risk patients and current cancer patients being monitored for relapse and identifying the most important screening programs for patients with cancer at risk for second cancers. We should also analyze whether testing or treatment for chronic inflammation associated with cancer is useful and if so, how best to do it.

**21. It is important to improve access to medical care.** We should determine the most effective types of medical intervention to reduce cancer deaths and how best to provide this care to needed patient populations.

**22. It is important to promote collaboration between physicians and scientists to create successful treatment combinations and change public policy to improve cancer screening and prevention.** Physicians and scientists must work together to exchange knowledge and develop treatments that combine their experience and expertise.