

How to Cure Cancer

Arthur M. Diamond, Jr.

Department of Economics
University of Nebraska Omaha
Omaha, NE 68182-0048

(402) 554-3657

adiamond@unomaha.edu

Academic Web Site: <http://cba.unomaha.edu/faculty/adiamond/web/diahompg.htm>

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Abstract

Medical central planners have been declaring war on cancer since the 1960s, but have not achieved the unconditional surrender that they seek. To speed future cures, we need to look at the traits of medical entrepreneurs who achieved breakthroughs in the past, and learn what institutions and policies enabled, or blocked, their progress. For example, Emil Freireich cured childhood leukemia and Vincent DeVita cured Hodgkin's Lymphoma, by pursuing quick trial-and-error experimentation in their anti-cancer chemical cocktails. But FDA regulations, often defended as exemplars of the precautionary principle, greatly restrict such pursuits by medical entrepreneurs, thereby delaying cancer cures and costing lives.

(101 words; 716 characters)

1. Introduction

Health care and education are two of the areas of the economy that are most important to human well-being, and yet have seen the least institutional changes over the past several decades (Bush and Baker 2014, pp. 61-62). Rigid hierarchies in both areas, restrict innovative entrepreneurship, limiting the pace and scope of innovations. In this section of the concluding chapter, I argue that reducing the obstacles to innovative medical entrepreneurship will result in quickening the pace of finding cures for more kinds of cancer. My method is to examine important examples of breakthrough innovations in medicine and ask what sort of people made those innovations, and what sort of conditions enabled or obstructed their innovations.

The stakes are high. Gennawey (2011) discusses what Walt Disney might have achieved at Epcot if he had lived several more years. And what neat new device would Steve Jobs have given us next? We all know someone who has cancer, and we all fear that it may happen to us. Cancer takes away from us life that we thought we would have, and that we ought to have had.

2. Examples of Medical Entrepreneurship

Schumpeter saw the key role of the innovative entrepreneur as being the overcomer of resistance to innovations, which could come in a variety of forms, and from a variety of sources (Schumpeter 1950, pp. 132-133). In this section I briefly examine a variety of cases in which major medical advances occurred, to see what

obstacles were most binding on the medical innovators. The goal will be to see which obstacles can be reduced, in order to enable medical innovators to bring us innovations more quickly and in greater number.

Histories of medical innovations in general (Meyers 2007) and medical innovations in fighting heart disease (Miller 2000) and cancer (Mukherjee 2010) in particular, show that the innovators frequently resemble Schumpeterian entrepreneurs. They are outsiders from the mainstream, who have the courage and persistence to continue to pursue their innovations in the face of sustained opposition from powerful incumbent medical institutions. Several examples will be briefly discussed.

At the start of the Boston smallpox epidemic of 1721, it is surprising that it was Cotton Mather, of Salem witch trial fame, who wrote a letter to all of the physicians of Boston, suggesting that they start the practice of inoculating the well by exposing them to smallpox matter from the infected. Mather had published a small report in the *Philosophical Transactions* of the Royal Society in London, which at the time was one of the world's most distinguished scientific associations (Coss 2016). In the same issue as his report had been an article by a Greek physician, of Italian descent, reporting his success at performing smallpox inoculations in Constantinople (Coss 2016). Mather also discovered that one of his slaves had been successfully inoculated in Africa, which led him to seek, and to find, several other slaves in Boston who had been successfully inoculated in Africa. With one exception, the entire medical community of the city rejected Mather's evidence and suggestion.

The exception was a young surgeon named Zabdiel Boylston, whose father had been a physician who had observed the success of some American Indian therapies, and

so may have been more open than most to possible cures arising from non-European sources (Coss 2016). On June 26, 1721, Boylston inoculated his first three patients. Among them was Thomas, his youngest son. Boylston was ridiculed and threatened with bodily harm and possible imprisonment. Mather's house was fire-bombed, though the wick from the bomb fortunately fell out before the bomb could ignite. Boylston proceeded to inoculate those who sought inoculation. All those who started the procedure in good health, and without previous exposure to the smallpox, survived, suffered mild cases of smallpox, and were immune to the current and future epidemics of the disease. The handful of those who died after inoculation from Boylston, either were already in the early stages of natural infection from smallpox, or were already frail or infirm from age or other diseases. It would have been easier for Boylston to have refused inoculation to these patients, since he knew that he, and inoculation, would be blamed for their death. But he allowed the patient to decide what risk was worth taking with their life. Boylston's most vitriolic opponent was Dr. William Douglass, who viewed himself as the only true "physician" in Boston, since he was the only one who at received his medical training at a European medical school, instead of through a then-more-common apprenticeship. To Douglas, his inferior colleagues were "practitioners," not "physicians."

When Ignaz Semmelweis suggested that doctors wash their hands more often, the medical establishment ridiculed to the point where he suffered a breakdown, was put in a mental asylum, beaten, and two weeks later was dead (Ashton 2015, pp. 72-76). Australian Barry Marshall was ridiculed by the medical establishment for suggesting that ulcers were caused by bacteria, finally convincing some of them when

he drank a vial of the bacteria, and developed an ulcer (^Meyers 2007, pp. 103-113; Klein 2013, pp. 52-56). Min Chiu Li was fired by the U.S. National Cancer Institute (NCI) for continuing to administer chemotherapy after all tumors had disappeared, but before a key marker (the hCG level) had reached zero (^Mukherjee 2010, pp. 136-138). After several years, the NCI eventually noticed that another marker had also reached zero: the number of Li's patients who suffered relapses of their cancer. Stephen Rosenberg was slowed and discouraged by the continuous efforts of the U.S. Food and Drug Administration (FDA) to block his experiments to use the body's own immune system to fight cancer (^Rosenberg and Barr 1992). As part of a private start-up, the undercredentialed Craig Venter, used a sequencing technique rejected by the medical establishment, to greatly speed up the sequencing of the genome compared to the pace of the government sequencing effort led by James Watson (^Shreeve 2004; ^Venter 2007).

Judah Folkman's research on a submarine led to his insight on developing drugs to cut off blood vessels to tumors (^Cooke 2001; ^Kounios and Beeman 2015, pp. 20 and 135-136; ^Ashton 2015, pp. 60-65). For a long time, many of Folkman's papers and grant applications were rejected by the medical establishment. Eventually his angiogenesis theory was recognized as important. And his entrepreneurial perseverance and independence may have contributed to his taking a chance on hiring the undercredentialed Robert Langer, who later established an M.I.T. lab, where he made major advances at his M.I.T. lab, including polymers to aid targeted drug delivery (^Wilkinson 2015, pp. 169-170). (Examples of advances from emergency/extreme medicine can be found in ^Fong 2014.)

Sidney Farber is credited with founding chemotherapy by showing that aminopterin could produce temporary remission in childhood leukemia. His path was difficult. He had to scrounge clinic space in a back room near the bathrooms, with his staff assigned to back rooms and stairwell shafts (Mukherjee 2010, pp. 34-35). The incumbent medical cancer establishment banned pediatric interns from assisting in Farber's unit (Mukherjee 2010, p. 34).

Paul Carbone, correctly believing that chemotherapy could aid in treating breast cancer, was caught in a surreal catch-22 situation. The medical establishment would not let him practice his treatment without first conducting a substantial double-blind study. But at that time breast cancer patients were primarily the patients of surgeons, and very few surgeons were willing to enroll their patients in such a study, perhaps because the likely results of the study would be to reduce the role of surgery in breast cancer treatment (Mukherjee 2010, pp. 219-220). Such medical turf protection also occurred when Vincent DeVita, then head of the NCI, suggested that based on the evidence, post-operative radiation for breast cancer should be reduced, because it was not improving patient outcomes. A radiologist came up to him complaining that much of the radiologist's practice was post-operative breast cancer radiation, and if that was reduced, she would have to fire one of her radiotherapy technicians (DeVita and DeVita-Raeburn 2015, pp. 182-183)¹. Turf protection also occurred when Bernard Fisher wanted to test whether radical mastectomy actually had better outcomes than more modest lumpectomies. His research was substantially delayed because of the resistance of American surgeons to allowing their patients to participate (Mukherjee 2010, p. 200). After he finally completed his research, breast cancer surgeons almost

succeeded in quashing publication of his article in which he presented evidence that lumpectomies were just as effective as radical mastectomies (^DeVita and DeVita-Raeburn 2015, pp. 182-183; see also pp. 222-223).

Emil Freireich was so aggressive in fighting cancer that he was threatened with firing, but he proceeded anyway. He said that he wouldn't want to work at a place that wouldn't let him do all he could do to save lives (^DeVita and DeVita-Raeburn 2015, pp. 55-56). Week-by-week his team (that one medical intern affectionately called the "Society of Jabbering Idiots") adjusted the dose and composition of the chemical mixture they were developing to fight childhood leukemia (^DeVita and DeVita-Raeburn 2015, pp. 63-64). Most advances in the treatment of cancer have been in terms of months or a few years of longer life. But their work resulted in a rare instance where a type of cancer can frequently and routinely be cured.

Vincent DeVita was a young member of Emil Freireich's team, who soon went on to use the same approach to develop a cure for the cancer known as Hodgkin's lymphoma. DeVita later tried to change institutions to increase the pace of cancer innovation, first as head of the NCI, and eventually as physician in chief of the Memorial Sloan Kettering Cancer Center. He left the NCI in part from his frustration at having to fight the bureaucracy and special interests within the government (^DeVita and DeVita-Raeburn 2015, pp. 188-189). But he also experienced frustration in the quasi-governmental, non-profit hospital, where entrenched medical incumbents defended their turf against innovations that would save lives. When he was fired from that position, his boss told the hospital board: "the problem with Vince is that he wants to cure cancer" (^DeVita and DeVita-Raeburn 2015, pp. 227-228).

DeVita offers an extended critique of current medical institutions in the United States. He points out that incentives and regulations strongly constrain physicians to follow established protocols. But the kind of entrepreneurial advance achieved by Freireich and his Society of Jabbering Idiots, was achieved through alert, extended trial and error, and could not have been achieved by following the then-mandated protocols. Freireich in part survived long enough to cure leukemia through the “umbrella” protection of the administrator Tom Frei, who had the courage and skill to sufficiently protect Freireich from the incumbent interests that want to rein him in (^DeVita and DeVita-Raeburn 2015, p. 94).

Today DeVita blames a dominant research methodology that says that research proposals need to be carried out as originally approved, even when (as should and does happen) the research process leads the researcher to conclude that the procedures need to be modified (^DeVita and DeVita-Raeburn 2015, pp. 196-197). This slows progress and loses lives. He also blames the FDA for restricting cancer researchers’ ability to experiment with different drug and dose combinations, in the way that led Freireich and his Society to cure leukemia (^DeVita and DeVita-Raeburn 2015, pp. 8, 192 and 254). The FDA slows progress in another way, by refusing to approve drugs that slow aging, on the grounds that aging is not a disease, and that the only drugs that should be approved are those that are effective against disease (^Anton 2013; ^Pontin 2007, p. 3).

3. Generalizations and Implications for Policy

From prominent cases of medical breakthroughs, I highlight four generalizations, and policy implications that are suggested by these generalizations.

Breakthrough innovators are outsiders. George Gilder observes that most innovative entrepreneurs are not successful credentialed insiders, but are the unproven, uncredentialed outsiders (Gilder 1990, pp. 113-114). (E.g., Cohendet et al. 2016, where the authors describe the “underground” of innovators in Montreal.) Gilder's point is re-affirmed in the history of advances of medicine, where breakthrough medical innovations are frequently achieved by outsiders to the incumbent medical establishment. Examples of outsiders in medical innovation include Zabdiel Boylston, Emil Freireich, Jonas Salk, Barry Marshall, Vincent DeVita. These outsiders have fewer and less prestigious past credentials, and have lower funded and less prestigious current positions. Sometimes they are not even in the incumbent disciplines the experts have assigned to the problem.

These claims can be illustrated by many examples. Emil Freireich had been a street kid (Gladwell 2013). Vincent DeVita had not attended a prestigious medical school (DeVita and DeVita-Raeburn 2015). In the cancer realm, there are many other examples (Mukherjee 2010). Ditto for Jonas Salk, and his first independent lab, where he did most of his research to develop the polio vaccine, was not prestigious (Jacobs 2015). John Hill, who documented that tobacco use increases the chances of cancer, was viewed as a “buffoon” by the medical establishment (Mukherjee 2010, pp. 239-240). Zabdiel Boylston was ridiculed by Dr. William Douglass [sic] for being

a "practitioner" instead of a physician, since Boylston had received his medical knowledge through the apprenticeship method rather than by attending a European medical school, as Douglass had (^Coss 2016). Australian Barry Marshall was ridiculed by the medical establishment for pointing out evidence that ulcers were caused by bacteria; the ridicule ceased when he swallowed a vial of the bacteria, and developed an ulcer (^Meyers 2007).

The contributions of outsiders are often prominent, not just for practical therapies, but also for fundamental advances in biological knowledge. One of the most fundamental advances in our genetic understanding, was first established by the modest monk Gregor Mendel, publishing in a modest regional publication, and long ignored by the biology establishment (^Wagner 2014). Antoine van Leeuwenhoek who first identified microbes, was a cloth merchant and minor city official, not an academic (Snyder 2015, p. 1). Galileo was supported by Medici bankers, not by incumbent academics (Westfall 1985). Craig Venter was viewed as an under-credentialed eccentric, as compared to his government-sponsored rival, the Nobel-Prize-winner James Watson (^Shreeve 2004).

Peter Thiel observes that the most important ingredient for successful entrepreneurship is not intelligence, but courage (^Thiel and Masters 2014, p. 5). Since the medical establishment protects its own turf (^Bush and Baker 2014; ^DeVita and DeVita-Raeburn 2015; ^Topol 2012), the success of the less-credentialed has frequently required persistence and courage.

Implications: we should not give too much power to the prestigiously credentialed gate-keepers. We should not marshal resources in a centrally organized plan.

Breakthrough innovations are often achieved by ‘seeing what others don’t.’

You might say that it was serendipitous that Robin Warren saw the bacteria that cause ulcers. But it is his co-author Barry Marshall who is perhaps better remembered for the discovery. It was he who drank the cocktail of the bacteria, and developed an ulcer. But if “serendipity” implies the good luck to experience a rare event, then that is not quite right for the ulcer case. The bacteria were there for others to see too, and there are published pre-Warren-and-Marshall photographs where we now can identify them, but they were not “seen” by the photographers (Marshall 2001). Daniel Kahneman has noted that we see what we expect to see. One example is what he calls “theory-induced blindness” (2011, pp. 10, 277, 280, 286-287, and 290). “Serendipity” involves seeing the unexpected. But it involves more. It involves seeing and remembering and having the resources and courage to stick with it, while others are denying it.

When Galileo argued for his views of the heavens with the clerical and academic incumbents of his day, he invited some of them to look through his telescope to see for themselves. Some did not look (Bucciantini et al. 2015, pp. 101-102). What was radical about Galilean science was not the individual assertions about the heavens, but that they were to be judged by one’s own eyes rather than by the authority of the credentialed. The Royal Society’s motto “Nullius in Verba” embraces this method:

belief should be based on evidence, not on the words of authorities (^Rosen 2010, p. 68).

In the United States, the economic Crisis of 2008 came as a surprise to most, including those who were credentialed as authorities in finance and economics. Since 2008, the conscientious have gone through a soul-searching quest to discover what went wrong, and why it had not been more widely expected. *The Big Short* suggests that much of the evidence was out in the open, but that the credentialed and uncredentialed refused to look; in some cases, they were bullied and obfuscated not to look, by the reassurances and confusing constructs of those who were trusted to know (^Lewis 2011, p. 56).

Breakthrough medical entrepreneurs are frequently in a similar situation. They have the courage and persistence to look, sometimes in straightforward ways, sometimes in non-mainstream ways.

Implications: opportunities for longer-term projects, and multiple funding sources and self-funding, are desirable. (E.g., see: Wang, Veugelers and Stephan 2016.) We should tolerate and maybe even value, cognitive diversity. (In *The Big Short* those who saw what was happening with the mortgage crisis, tended to have what are sometimes identified as Asperger's symptoms.)

Breakthrough innovations often come from nimble trial and error. Outside of medicine, Walter Isaacson's book on *Steve Jobs* documents (^2011) the importance of nimble trial and error in the development of his signature innovations such as the iPhone. The frequent procedure would be for him to have his team present him with four or five versions of a particular product. He would evaluate them and pick the best

for further development. When he was dying of cancer, he was having trouble breathing and the medical staff tried to put an oxygen mask over his face. He stopped them, gasping that he did not like the design of the mask. He then went on to gasp that they should bring him four or five versions of the mask, and he would pick the best. In the area of cancer research, Min Chiu Li was fired from the National Cancer Institute, because he believed that elevated levels of something called hCG, indicated that cancer was still lurking at low levels not evidenced by cancer symptoms. His patients did not suffer relapses of their cancers, and he is now viewed as the first to have shown that chemotherapy can cure cancer. Vincent DeVita feels guilty that he had learned that the chemotherapy needed to be applied longer, to save his friend. But he stuck with the protocol, and his friend died. Is that good science? Is that how to treat our fellow human beings?

Implication: we should not fund or regulate on the basis of rigid adherence to pre-established protocols.

Breakthrough innovations are often achieved at great risk, sometimes even of injury and death. (A few died from Boylston's smallpox inoculations, and even from the later and safer smallpox vaccinations. But many more lives were saved than lost. And, at least with the inoculation cases, the risks mainly were taken voluntarily.)

A growing obstacle to medical innovation has been the growing advocacy and implementation of the "Precautionary Principle," which states that new innovations should not be allowed to proceed until it has been shown that they cause no harm (^Sunstein 2005). Perhaps one reason that medical advances have sometimes arisen in war theaters or emergency medicine, is that the Precautionary Principle is **not**

implemented in those settings. For instance, Nobel-Prize winner Alexis Carrel honed his technique for re-attaching small blood vessels in the crucible of WWI² (Friedman 2007). Examples of advances from emergency/extreme medicine can be found in Fong (2014).

Such cases show that exemption from the Precautionary Principle allows for quick and substantial experimental trial-and-error that can speed innovation. They do not provide a justification for war, but they do suggest the pursuit of other ways to counter the Precautionary Principle. These might include patients voluntarily signing waivers to accept experimental treatments, either because they know that no other treatment is available to them, or because they have made a conscious decision to accept risk for the goal of advancing medicine (DeVita and DeVita-Raeburn 2015). If we allow extreme athletes to accept risks for the sake of “flow” or the adrenaline rush (Kotler 2014), should we not also allow thoughtful patients to accept risks for the sake of advancing medical knowledge?

Implication: we must reject the Precautionary Principle that is increasingly behind regulation of innovations.

4. How to Cure Cancer

Nixon predicted in the 1960s that cancer could be eliminated within a generation. He and others declared a "war" on cancer. In the United States after World War II, science and technology policy were heavily influenced by Vannevar Bush, who believed that science and technology should be funded by the government,

but that decisions on what research to pursue should be left mainly to academics. Among those who wanted the government to more actively central plan was Mary Lasker, who thought that since the government had succeeded in the centrally planned Manhattan Project, it could also succeed with central planning in other areas, such as in a war on cancer (^Mukherjee 2010, pp. 118-121). Lasker and Bush were each partly right and partly wrong. Lasker was right that progress would be enhanced if researchers were primed with problems---that way they might be alert to serendipitous solutions. But she was wrong to think that you could assign them problems and "plan" the solution of those problems. While Bush was right that the Manhattan Project had succeeded because the basic, hard problems had already been solved. But he was wrong to think that scientists pursuing anything that they were randomly curious about, would be the best way to reach rapid progress.

The "war" analogy may be useful in arguing for a high intensity of effort and funding. But often it is taken further to suggest that the effort to cure a disease should be commanded by a centrally planned hierarchy, based on the common assumption that real war is best fought by hierarchies that centrally plan. (This common assumption has actually been disputed, in different ways, by books such as *Corps Business* (^Freedman 2000), *Start-up Nation* (^Senor and Singer 2011), and *The Generals* (^Ricks 2012).)

Using the war analogy as a guide to medical policy for curing diseases is based on the idea that a centralized hierarchy can predict the right approach, and marshal resources to achieve it, like a conquering army. But a centralized approach will only work when there is clarity on how to solve the problem, and all that remains is to

marshal resources to execute the solution. But with cancer there have been a variety of approaches with varying degrees of success, including surgical excision, radiation therapy, chemotherapy, angiogenesis, and immunotherapy. Some have predicted that cancer would not be cured by a particular medical technology, but by restricting cancer-causing agents, such as tar in cigarettes, or certain viruses. This has had some success, but many cancers have no known external agents causing them.

One assumption of all of these approaches has been that cancer is one disease that can be cured by the successful pursuit of one common best technology, although there have been major differences on just what that one common best technology is. In contrast, a current approach, one that had not been predicted by the experts from decades past, is that what we call "cancer" may turn out to be several different diseases, with different medical technologies curing different variants.

Those advances against cancer, and other diseases, that have occurred have often been the result of serendipitous events observed by alert medical outsiders (^Meyers 2007; ^Root-Bernstein and Root-Bernstein 1997). If the path of technical progress in medicine is in fact predictable, then centralized policies, such as President Richard Nixon's past declaration of a "war on cancer" or President Barack Obama's current establishment of a "Cancer Moonshot" are plausible (^Kolata and Harris 2016, p. A17). If, on the other hand, technical progress is not predictable, and depends on alertness to serendipitous events, then it might be wiser to follow the policy attributed to Mao to 'let a thousand flowers bloom' (^Meyers 2007, p. 173).

5. The Road Ahead

If we take these steps, how much will we speed up cures for cancer? That is impossible to predict because we do not know what breakthrough innovations, innovative medical entrepreneurs will achieve. We do know, based on past experience, that the pace and number of breakthrough innovations will increase. And we do know that Vincent DeVita, who himself is in a position to know, says that if we allowed practicing physicians to act more entrepreneurially, the immediate effect would be that thousands of those who will otherwise die of cancer in the next year, will live.

Prometheus was punished for bringing fire to humanity. In reality, as in myth, the medical benefactors of humanity often have been punished. They have been ridiculed, defunded, fired, and ignored. If we unbind the entrepreneurs of medical innovation, we will be treating our benefactors more justly, and we will be allowing them to achieve even greater innovations. We may expect that they will respond by bringing us better health and longer lives.

Walt Disney died of cancer at the age of 65. Steve Jobs died of cancer at the age of 56. When the cancer killed their bodies, it also killed their dreams. Cancer is now killing your neighbor, your friend, your co-worker, or your family member. Disney and Jobs had flourished as innovative entrepreneurs because we did not bind innovative dynamism in entertainment or computers. If we had unbound innovative dynamism in medicine, cancer could have been cured in time to save Jobs, and maybe even Disney. If we unbind innovative dynamism now, it may be in time to save your neighbor, your friend, your co-worker, your family member, or even you.

Footnotes

* The current version of the paper is much evolved from a paper presented at the biennial meetings of the International Schumpeter Society in Montreal in 2016.

¹ DeVita does not specify the gender of the radiologist.

² Gerhard Domagk who discovered one of the first antibiotics, became convinced of the importance of antibiotics through observing infections kill those operated on during WWI. (But the war's contribution to his eventual innovation was more due to the building of motivation than from the building of relevant experiences.) [Hager 2007, pp. 18-20]

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