Review Article

Immunity over inability: The spontaneous regression of cancer

Thomas Jessy

Department of Oral Medicine and Radiology, Dr. Syamala Reddy Dental College and Hospital, Marathahalli, Bangalore, Karnataka, India

Address for correspondence:
Dr. Thomas Jessy, D-203, Vineyard Gardens, RMN Main, Dodda Banaswadi, Bangalore – 560 043, Karnataka, India. E-mail: jesanil@gmail.com

Abstract

The spontaneous healing of cancer is a phenomenon that has been observed for hundreds and thousands of years and after having been the subject of many controversies, it is now accepted as an indisputable fact. A review of past reports demonstrates that regression is usually associated with acute infections, fever, and immunostimulation. It is stated that in 1891, William Coley of New York's Memorial Hospital developed the most effective single-agent anticancer therapy from nature, which faded into oblivion for various reasons. Cancer therapies have been standardized and have improved since Coley's day, but surprisingly modern cancer patients do not fare better than patients treated 50 or more years ago as concluded by researchers in 1999. This article peeks into the history of immunostimulation and the role of innate immunity in inducing a cure even in advanced stages of malignancy. The value of Coley's observation is that rather than surviving additional years with cancer, many of the patients who received his therapy lived the rest of their lives without cancer. In our relentless efforts to go beyond nature to fight cancer, we often overlook the facts nature provides to heal our maladies.

Key words: Acute infections, Coley's toxins, cancer, fever, immunostimulation, spontaneous regression

INTRODUCTION

The word spontaneous implies "without any apparent cause,"[1] and regression is defined as a decrease in the size of the tumor or in the extent of cancer in the body according to the national cancer institute (NCI).[2] Spontaneous regression occurs in most types of cancer and was recorded in the medical literature as early as 1742.[3] The standard definition of spontaneous regression as "the partial or complete disappearance of a malignant tumor in the absence of treatment or in the presence of therapy considered inadequate to exert a significant influence on the disease" was composed by Dr. Tilden Everson and Dr. Warren Cole in the 1960s,[4] with the further requirement that the original presence of cancer was proven by the microscopic examination of tissues.[5]

Access this article online	
Quick Response Code:	Website: www.jnsbm.org
	DOI: 10.4103/0976-9668.82318

Spontaneous regression of cancer is not a rare occurrence as thought to be; in an average month during 2002, medical journals published more than four articles on the subject.[6]

Cancer is probably the deadliest of human ailments. Cancer fatalities account for 12% of all deaths worldwide each year.[7] Across the globe, 10 million people are diagnosed with cancer annually and almost 7 million die from cancer. The global cancer rates could increase to 15 million by 2020.[8]

HISTORY OF SPONTANEOUS REGRESSION

Spontaneous tumor regression is a phenomenon that has been observed for hundreds if not thousands of years. Although the term spontaneous implies "without any apparent cause," a review of reports demonstrates that regression generally coincides with acute infections.[1] Savarrio *et al* claimed to report the first ever case of spontaneous regression of a neoplasm of the oral cavity

of the subset of non-Hodgkin's lymphomas known as Ki-1 anaplastic large cell lymphoma (ALCL). King *et al.* reported a case of complete spontaneous regression of metastatic cutaneous melanoma with parotid and neck lymph node metastases.[9]

The phenomenon of spontaneous regression is also known as St. Peregrine tumor. Peregrine Laziozi (1265–1345), a young priest, was afflicted with cancer of the tibia requiring amputation of the leg; the lesion grew to a point where it broke through the skin and became severely infected. Miraculously, by the time his operation was due his physician was astonished to observe that there were no signs of the tumor. St. Peregrine's tumor never returned.[7,10] Although numerous cases of spontaneous tumor regression have been published over the last several hundreds of years, such reports have become rare in the current medical literature;[1] virtually all of these reports note regression concomitant with infections including diphtheria, gonorrhea, hepatitis, influenza, malaria, measles, smallpox, syphilis, and tuberculosis as well as various other pyogenic and nonpyogenic infections. Observation of this non-specific effect led to the emergence of active cancer immunotherapies by the 1700s.[1,11]

In 1891, a young bone surgeon at New York Memorial Hospital began his search for a new approach to cancer treatment, after the loss of his very first patient to cancer. Serendipitously, he discovered the record of an immigrant patient who presented with an egg-size sarcoma on his left cheek.[10] The sarcoma was operated on twice and still recurred as a 4.5-inch grape-like cluster below his left ear. The extensive wound after surgery could not be closed and skin grafts were unsuccessful. Ironically, this failure to close the wound would play a key part in the patient's eventual cure. The tumor progressed and a final operation only partially removed the tumor; the wound became severely infected with erysipelas by *Streptococcus pyogenes* and the patient developed a high fever. Little could be done to stop the infection, yet surprisingly, after each attack of fever the ulcer improved; the tumor shrank, and finally disappeared completely. On a subsequent review, the patient, still bearing a large scar from his previous operations, had no trace of cancer and claimed excellent health since his discharge– 7 years previously.[10,12]

Coley suspected that somehow the infection was responsible for the miraculous cure. He later realized that the patient's activated immunity in response to the acute infection was the key factor in cancer regression. He decided to put his theory to the test and infected his next 10 patients with erysipelas.[12,13] Problems with this approach soon became apparent; sometimes it was difficult to induce an infection, other times there was a strong reaction and the disease regressed. However, occasionally, the infection was fatal. Due to its unpredictability, he developed a vaccine containing two killed bacteria, the Gram-positive *Streptococcus pyogenes* and the Gram-negative *Serratia marcescens*. Experimental work at the time suggested that the latter bacteria increased the virulence of the former.[14] In this way, he could simulate an infection with inflammation, chills, and fever without worrying about the risks of an actual infection. This vaccine became known as "Coley's toxins." Coley stressed that the technique of administration and the ability of the vaccine to induce mild to moderate fever was of paramount importance in the regression of cancer.[15,1] He successfully used his vaccine, in treating a man bedridden with an inoperable sarcoma involving the abdominal wall, pelvis, and bladder. The sarcoma regressed completely and the patient was followed up until his death from a heart attack 26 years later.[16]

Coley worked in the Department of Bone Service at the hospital, later becoming its chief in 1915, and her fathers discovery was further pioneered by Helen Coley Nauts Coley's vaccine was widely and successfully used by other contemporaries for sarcomas as well as carcinomas, lymphomas, melanomas, and myelomas.[17] Coley's immunotherapy regimen was so outstanding that even when applied to patients in their final stages of disease, some remarkable recoveries were obtained, with patients often outliving their cancer.[17,18] Coley was considered to have treated more sarcoma patients than any other physician up to that time.[17]

STIMULATED IMMUNOTHERAPY

Martha Tracy who formulated many of Coley's vaccine observed that the most effective formulation was the one that induced both local and systemic reactions.[19]

Coley considered several points crucial to a patient's survival. First and foremost was to simulate a naturally occurring acute infection, and thus, inducing a fever was essential. Injections were optimally administered daily or every other day for the first month or two. To avoid immune tolerance to the vaccine, the dosage was gradually increased over time depending on the patient response. The vaccine was injected directly into the primary tumor and metastases when accessible. Finally, a minimum 6-month course of weekly injections was followed to prevent disease recurrence. Ensuring a prolonged follow-up was the most difficult part of the treatment.[20]

In the past, coincidental infections had in fact inspired a wide variety of rudimentary cancer immunotherapies. Coley also discovered that many past physicians had

used these infections to the advantage of their patients. Cancer immunotherapy was practiced thousands of years ago. In the writings of the Ebers Papyrus (c 1550 BC), attributed to the great Egyptian physician Imhotep (c 2600 BC), the recommended treatment for tumors (swellings) was a poultice followed by an incision which would result in infection of the tumor and therefore its regression.[21] By the 1700 and 1800 AD, crude forms of cancer immunotherapy became widely known and accepted.[1]

Before Coley's discovery of his killed vaccines, using live bacteria to initiate an infection was a risky experiment between life and death. Coley emphasized that the induction of fever was the key aspect of his treatment, a strong febrile reaction was the symptom most associated with tumor regression. A retrospective study of the patients with inoperable soft tissue sarcomas treated with Coley's vaccine found a superior 5-year survival in patients whose fevers averaged 38–40°C, compared with those having little or no fever (38°C) during treatment (60% vs. 20%).[22]

The greatest value of Coley's Toxins is evident in the lives of patients who received the therapy. Rather than surviving additional years with cancer, many of these patients lived the rest of their lives without cancer.[23,24]

The last recorded use of Coley's Toxins anywhere in the world was in China in the 1980s as a primary therapy for cancer in an adult male who had terminal liver cancer involving large tumors in both lobes of the liver; he received 68 injections of Coley's Toxins in 34 weeks. By the end of this course of treatment, all of the tumors had completely regressed.[25]

To most members of the medical community, non-surgical approaches to the treatment of cancer were simply of little interest. While most readers ignored Coley's articles, a number of independently minded doctors began to make use of the new cancer treatment. Before the turn of the 20th century, at least 42 physicians from Europe and North America had reported cases of cancer that had been successfully treated with Coley's Toxins.[26]

Stimulated immunotherapies ran a natural death in the latter half of the 20th century due to a number of reasons. First, with the newer concept of asepsis, cancer surgery like any other operation became a sterile procedure with fewer postsurgical infections especially after Lister's aseptic techniques in the late 1800s. Second, by the time of Coley's death in 1936, radiotherapy was an established treatment for cancer and chemotherapy was slowly gaining acceptance. Such therapies though highly immunosuppressive could more easily be standardized than Coley's approach. Third, the administration of antibiotics further reduced the incidence of postsurgical infections and antipyretics came into routine use to eliminate fever and discomforting symptoms of an immune response, and the lastly due to an unfavorable approach of the medical industrial regulatory complex of the 1960s.[10,26]

Cancer therapies have been standardized and have improved since Coley's day, but these improvements in treatment have resulted for the most part in prolonging the disease rather than curing it. For example, when the American Cancer Society claims, "Today, far more than half of all cancers are curable,"[27] it is referring to the fact that about 60% of patients diagnosed with cancer during the period 1989–96 survived for at least 5 years.[28] According to the National Cancer Institute, the 5-year survival rate includes persons who survive for 5 years after diagnosis, whether in remission, disease-free state, or under treatment.[29] This concept is far away from the ideal of achieving a cure for a disease-free state.[30] To this day, earlier diagnosis is the single most important contributing factor in the observed increase in 5-year survival rates.[26] Presently, the medical literature has dropped its duration of cancer survival rates from an older standard of 5 years to a mere 3 years and hence is the increase in the percentage of survival rates.[31]

Though modern therapies have added some years to the life of the average cancer patient, they have not reduced the patient's chances of dying from the disease. In fact, a resident of the United States is more likely to die of cancer today (225.4 per 100,000) than in 1950s (195.4 per 100,000).[32,26]

The primary cancer therapies, namely, surgery, radiotherapy, and chemotherapy, widely accepted and practiced have their own pitfalls. The risks, deficiencies, cost, specialized skills, and medical ethics are often associated with these procedures. Even surgery, the most acceptable of the three in treatment of most tumors, has resulted in an ethical dilemma. Every time an incision is made into cancerous tumor, with even the least invasive type of incision called the needle biopsy, there is a risk of spreading the disease due to cancer cells entering the bloodstream or becoming implanted in the surrounding tissue. There are at least 10 published cases of tumors arising along the route taken by a biopsy needle.[26] Surgical excision usually done with an intention to cure also removes the protective barrier or the wall, body builds itself to protect itself from cancer metastasis. Surgery and the subsequent healing process greatly increases the risk of death by metastasis in certain cancer patients by disrupting tumor integrity, facilitating metastasis, directly seeding the tumor, inducing local

angiogenesis, immune suppression, and enhancement of tumor growth.[33] Surgical stress also greatly enhances metastasis by increasing the expression of proteinases in the target organ of metastasis, metastasis being the primary concern of fatality in cancer patients.[34]

The effects of radiation are often temporary and have little impact on survival rates. One study of 3,000 breast cancer patients found that those receiving radiation in addition to surgery did no better than patients who received surgery alone.[28] The great disadvantage of radiation therapy is the same as that with surgery; it is simply not effective in the control of widely spread cancer. Chemotherapy and radiotherapy to some extent are highly immunosuppressive and therefore infections in these patients do not lead to any immunostimulation. Addition of antibiotics further deprives these patients of the benefits of an immune response and subsequent regression if any.[26]

Chemotherapy for head and neck cancer may result in a temporary reduction in the tumor size but has not translated into increased survival, control of the primary tumor, or decreased incidence of metastasis.[31] The FDA has approved more than 80 anticancer drugs, 40 of which are chemotherapeutic agents. These drugs interfere with cell division, an essential activity of the immune system, thereby profoundly suppressing the magnitude and the effectiveness of immune responses.[35,36] Hence the ability of the body to protect itself against an existing cancer is weakened; they are also neocarcinogenic which can lead to the development of new cancers that did not exist prior to the administration of chemotherapy.[26]

To effectively control the spread of cancer after the destruction or removal of the primary tumor, a systemic therapy is needed that can be delivered to the entire body that can destroy cancer wherever it might be lurking. This can be delivered by an active immune system of the patient by activating its immense potential.

DISCUSSION

Spontaneous regression is a well-authenticated and natural phenomenon. Its study may lead us to a better understanding of the natural history of neoplastic disease which so commonly progresses but rarely regresses.[37] The comparative rarity of spontaneous regressions today may result from the immunosuppressive nature of conventional cancer therapies.[1] The spontaneous healing of cancer, after having been the subject of many controversies, is now accepted as an indisputable fact. The percentage of spontaneous regression as quoted by Boyers is 1 in 80,000 and 1 in 100,000 by Bashford; it may be subjected to criticism but proves a remarkable fact that cancer is not an irreversible process.[38]

Regression is more commonly associated with groups of tumors like the embryonal tumors in children, carcinoma of the female breast, chorionepithelioma, adenocarcinoma of the kidney, neuroblastoma, malignant melanoma, sarcomas, and carcinoma of the bladder and skin.[38]

The impediment toward the spontaneous healing of cancer is due to the failure of recognition of cancer cells as non-self and dangerous by our immune system and hence it's subsequent escape to establish the disease, as well as the nature of contemporary cancer therapies which trigger metastasis, suppress immune responses as well as compound any existing immune deficiency. The other major drawback is that primary cancer therapies especially the systemic ones are unable to differentiate between normal and abnormal, and therein lies their potential to harm.[26] The disturbance of tumor such as biopsy and surgical procedures cause a greatly increased number of cancer cells to enter the bloodstream, while most medical intervention (especially chemotherapy) suppresses the immune system. This combination is a recipe for disaster. It is the metastases that kill, while primary tumors in general, and those in the breast in particular, can be relatively harmless. These findings have been confirmed by recent research which shows that surgery, even if unrelated to the cancer, can trigger an explosive spread of metastases and lead to an untimely end.[39]

So how can we help our system recognize tumor cells as "tumor cells" and aid in natural and biologic defence against cancer.

Infectious agents are present in nature that can cause cancer but we should also remember the dual role they play in preventing cancer. Acute infectious agents are a natural source of immunostimulants that challenge our immune system from time to time as well as pep it up to confront newer challenges evolution brings about like cancer.[40,41] [Figure 1] Cancer is a disease that springs up from within; it is a disease of our genes and inherited or acquired deficiencies in genome maintenance systems contribute significantly to the onset of cancer.[42] Though all of us develop cancer cells in our life time, not all of us develop cancer. The proportion of risk of cancer varies from person to person and the individuals' exposure to common febrile infections as shown by epidemiologic studies. What helps the majority safe guard against cancer? Do acute infections have a direct and spontaneous role in the prevention and regression of cancer?[43]

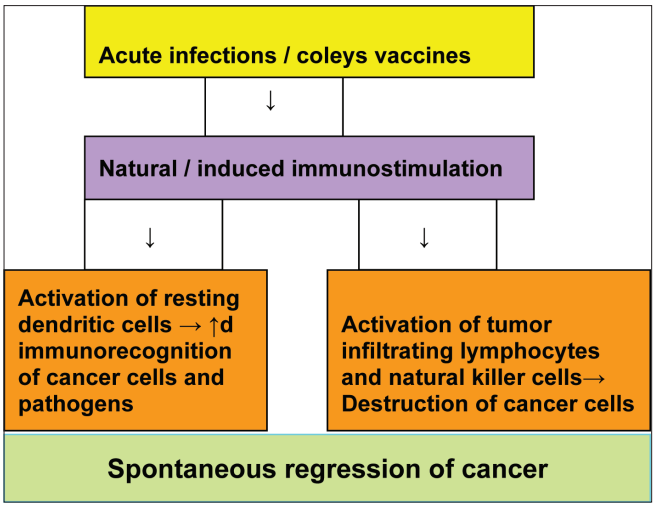

Figure 1: Immunostimulation in cancer regression

As early as 1899, British cancer researcher D'Arcy Power observed, "Where malaria is common, cancer is rare."[44] Between 1929 and 1991, at least 15 investigations including 8 case–control studies examined the link between infectious disease and cancer and all but one have found that a history of infectious disease reduces the risk of cancer.[41,28]

Since spontaneous regression is often associated with a previous history of acute infections and fever, it is likely that fever-causing pathogens have a beneficial role to play in activating and stimulating the immune defenses which battle the invading pathogens as well as gain a new-found recognition of cancer cells and attack them vigorously. Fever whether natural (acute infections) or induced (Coley's Toxins) stimulate a multitude of cascading, interlinking, and complex pathways of the immune system simultaneously releasing numerous products in the right quantity and qualities to combat the disease which may not be humanly possible to reproduce *in vitro*. This may explain why single cytokine therapy or immune products don't give desirable results in cancer therapy, besides being expensive, toxic, and at times fatal due to the unnatural challenge they pose to the human system.[40,10]

The evidence and observations of rapid tumor regression following infection sometimes within hours suggest that the innate rather than the adaptive immune response is a primary mediator of tumor regression in such cases.[10] Unfortunately, even during cancer immunotherapy, an acute febrile reaction is often regarded as an unwanted symptom rather than an integral and healing component of the immune response.[1]

A review of previous reports suggests that the occurrence of fever in childhood or adulthood may protect against the later onset of malignant disease and that spontaneous remissions are often preceded by feverish infections.

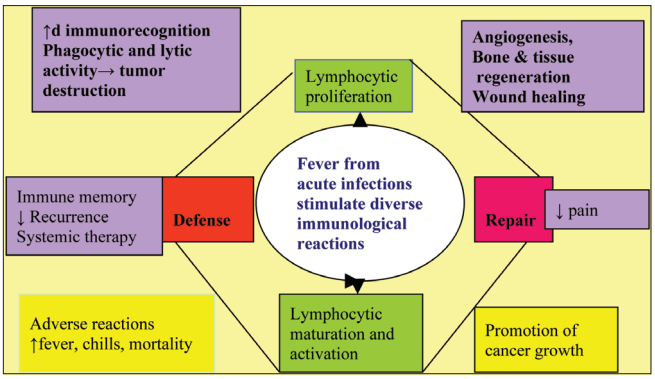

Figure 2: The dual nature of defense and repair of the immune system and its effects

Pyrogenic substances and a more recent use of whole body hyperthermia to mimic the physiologic response to fever have successfully been administered in palliative and curative treatment protocols for metastatic cancer.[40]

Acute infections and fever provoke an immediate and effective immune response that can fight infectious agents as well as cancer at the same time; similarly Coley's Toxins were a highly effective anticancer treatment because they worked by stimulating a powerful immune response. By itself, a powerful immune response is sufficient to cure some cancers in some patients but cannot cure all cancers in all patients. A powerfully stimulated immune system is only part of the answer because cancer cells are frequently able to hide from the immune system. The immune system cannot kill what it cannot see.[26] The failure of the immune system to recognize cancer cells in the system is the major setback we face in our fight against cancer and this is compounded by the duality of the immune system of defense and repair; in the reparative mode the immune system can promote cancer growth in its attempt to repair what it perceives as a "sterile wound."[Figure 2] This can be overcome by the generation of inflammatory products during an episode of fever, be it natural or simulated (Coley's Toxins), when the well-studied defensive role becomes active at the onset of an acute infection, where cytotoxic cells seek out and destroy invading pathogens.[1,45]

Uwe Hobohm has recently observed about Coley's Toxins that the following cascade might explain their effectiveness: *"Fever generates inflammatory factors with co-stimulatory activity, which activate resting dendritic cells (DC), leading to the activation of anergic T cells, maybe accomplished by a second process, where a possible physical damage of cancer cells leads to a sudden supply of cancer antigens to DC."* In other words, fever is a state in which body's own antigen recognition mechanism turns on to such a high level of activity that it becomes capable of recognizing cancer and microbial invaders. Specialized cells like the dendritic cells then communicate the identity of the pathogen to lymphocytes to establish active immunity against stealth

diseases. Fever plays a beneficial role when body's immunity is challenged, and helps in the natural destruction of cancer cells. Cellular damage occurs only at temperatures above 108°F, but much good is accomplished at lower temperatures.[16,46]

Acute inflammatory responses have also benefited terminal cancer patients in the reduction of cancer pain as well as fast wound healing. As observed by Coley, the immunological stimulation by his toxins led to a marked relief of pain, so that patients could often discontinue using narcotics. There was an extraordinary enhancement of wound healing and even bone regeneration when the toxins were injected into the tumors.[19] Similar observations on infectious amelioration of cancer pain and enhancement of wound healing have been reported by others.[47]

The recent 6-year Norwegian follow-up study on breast cancer in women also accepts the fact of natural regression in one-fifth of the untreated cases that were followed up; the authors concluded that this may reflect the fact that these cancers are rarely allowed to follow their natural course.[48]

It is interesting to note that the current primary cancer management procedures neither harness the benefits of patients' own immune system nor stimulate it to achieve tumor regression but actively suppress it; thus it does not run parallel to body's own defensive mechanisms but opposes its natural role. An ideal cancer management would involve the stimulation of the immune system, its complex effective and reproducible *in vivo* mechanisms that fight cancer. Acute infections are beneficial in the prevention and regression of tumors. In conclusion, childhood febrile infections can prevent cancer in adulthood. Asepsis, fever control, surgery, and immunosuppressive therapies are known to have an inverse relation to cancer regression, while acute infection, fever, and cancer vaccines by the virtue of immunostimulation induce regression of cancer even in the most advanced stage of disease and prove that cancer is not an irreversible process without a cure.[1,43]

REFERENCES

1. Hoption Cann SA, van Netten JP, van Netten C, Glover DW. Spontaneous regression: A hidden treasure buried in time. Med Hypotheses 2002;58:115-9.
2. Cancer. gov. United States: National cancer institute. Dictionary of cancer terms. Available from: http://www.cancer.gov/dictionary/?CdrID=46039. [Last accessed on 2010 Sep, cited 2010 Oct].
3. Le Dran HF. Traite des operations de chirurgie. Paris: C. Osmont; 1742.
4. Everson TC. Spontaneous regression of cancer. Prog Clin Cancer 1967;3:79-95.
5. Everson T, Cole W. Spontaneous Regression of Cancer. Philadelphia, PA: WB Saunders; 1968.
6. Pubmed.gov. United States: Search of PubMed database, web site of the National Institutes of Health, returned 302 articles published in 2010 including the terms "cancer" and "spontaneous regression." Available from: http://www.ncbi.nlm.nih.gov/pubmed. [Last accessed on 2010 Dec 30 and cited 2010 Jan 07].
7. Pakhmode VK. Understanding the possible mechanisms of spontaneous regression of oral cancer. J oral and maxillofac pathol 2007;11:2-4.
8. Who.int> W.H.O. cancer estimates 2003. Available from: http://www.who.int/mediacentre/news/releases/pr27/en. [Last accessed on 2010 Nov 30 and cited 2010 Dec 10].
9. Savarrio L, Gibson J, Dunlop DJ, O'Rourke N, Fitzsimons EJ. Spontaneous regression of an anaplastic large cell lymphoma in the oral cavity: First reported case and review of literature. Oral Oncol 1999;35:609-13.
10. Hoption Cann SA, van Netten JP, van Netten C. Dr William Coley and tumour regression: A place in history or in the future? Postgraduate Med J 2003;79:672-80.
11. Rohdenburg GL. Fluctuations in the growth energy of tumors in man, with especial reference to spontaneous recession. J Cancer Res 1918;3:193-225.
12. Coley WB. The treatment of malignant tumors by repeated inoculations of erysipelas, with a report of ten original cases. Am J Med Sci 1893;105:487-511.
13. Coley WB. Contribution to the knowledge of sarcoma. Ann Surg 1891;14:199-220.
14. Coley WB. Treatment of inoperable malignant tumors with toxins of erysipelas and the bacillus prodigiosus. Trans Am Surg Assn 1894;12:183-212.
15. Richardson MA, Ramirez T, Russell NC, Moye LA. Coley toxins immunotherapy: A retrospective review. Altern Ther Health med 1999;5:42-7.
16. Nauts HC. The beneficial effects of bacterial infections on host resistance to cancer: End results in 449 cases. 2nd ed. Monograph no. 8. New York: Cancer research institute; 1980.
17. Nauts HC, Fowler GA, Bogatko FH. A review of the influence of bacterial infection and of bacterial products (Coley's toxins) on malignant tumors in man. Acta Med Scand Suppl 1953;276:1-103.
18. Nauts HC. Immunotherapy of cancer by microbial products. In Mizuno D, editor. Host defense against cancer and its potentiation. Baltimorey, MD: Universit Park Press; 1975. p. 337-15
19. Beebe SP, Tracy M. The treatment of experimental tumors with bacterial toxins. JAMA 1907;49:1493-8.
20. Coley WB. Late results of treatment of inoperable sarcoma by mixed toxins of erysipelas and bacillus prodigiosus. Am J Med Sci 1906;131:375-440.
21. Ebbel B. The papyrus ebers: The greatest Egyptian medical documents. London: Oxford University Press; 1937.
22. Nauts HC, Pelner L, Fowler GA, sarcoma of the soft tissues other than lymphosarcoma, treated by toxin therapy: New York: Cancer Research Institute; 1969.
23. Nauts HC, Fowler GA, Bogatko FH. A review of the influence of bacterial infection and of bacterial products (Coley's toxins) on malignant tumors in man. Acta Med Scand Suppl 1953;276:28-30.
24. Coley WB. Late results of the treatment of inoperable sarcoma by the mixed toxins of erysipelas and Bacillus prodigiosus. Am J Med Sci 1906;131:398-9.
25. Nauts HC. Bacteria and cancer- antagonisms and benefits. Cancer Surv 1989;8:720.
26. MacAdam DH, Spontaneous Regression: Cancer and the Immune System, Xlibris: Philadelphia 2003. Available from: http://www.mbvax.com/pdf/book_excerpt.pdf. [Last accessed on 2009 June, Cited 2009 Sep].
27. Cancer.org. United States. American Cancer Society appeal for funding. Website of the Illinois State and University Employees Combined Appeal. Available from: http://www.secaillinois.org/acs.htm. [Last Accessed on 2002 Dec 17].
28. Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer Statistics, 2001. CA Cancer J Clin 2001;51:15-36.

29. Cancer.gov. United States: National cancer institute. Dictionary of cancer terms. Available from: http://www.cancer.gov/dictionary/?CdrID=597152. [Last accessed on 2010 Oct 30; cited 2010 Nov 29].
30. Thomas Allen and Son, Webster's Ninth New Collegiate Dictionary. Ontario: Markham; 1989. p. 316.
31. Epstein JB. Oral cancer. Greenberg, Glick, editors. Burkets textbook of oral medicine. 10th ed. Elseiver India: BC Decker Inc; 2003. p. 194-227.
32. Seer.cancer.gov. United States: National Cancer Institute. Cancer statistics Table I-2, National Cancer Institute website. Available from: http://www.seer.cancer.gov. [Last accessed on 2010 Oct 30: Cited 2010 Nov 29.]
33. van der Bij GJ, Oosterling SJ, Beelen RH, Meijer S, Coffey JC, van Egmond M. The perioperative period is an underutilized window of therapeutic opportunity in patients with colorectal cancer. Ann surg 2009;249:727-34.
34. Tsuchiya Y, Sawada S, Yoshioka I, Ohashi Y, Matsuo M, Harimaya Y, *et al*. Increased surgical stress promotes tumor metastasis. Surgery 2003;133:547-55.
35. Peen J. Cancer in immunosuppressed patients. Transplant Proc 1984;16:492-4.
36. Clegg LX, Li FP, Hankey BF, Chu K, Edwards BK. Cancer survival among US whites and minorities. Arch Intern Med 2002;162:1985-93.
37. Smithers DW. Spontaneous Regression of Tumors. Clin Radiol 1962;13:132-7.
38. Fauvet J; Campagne J; Chavy A; Piet G Cures, Regressions and Spontaneous Remissions of Cancer. La Revue du Praticien 1960;10:2349-84.
39. Tagliabue E, Agresti R, Carcangiu ML, Ghirelli C, Morelli D, Campiglio M, *et al*. Role of HER2 in wound-induced breast carcinoma proliferation. Lancet 2003;362:527-33.
40. Kleef R, Jonas WB, Knogler W, Stenzinger W. Review of fever, cancer incidence and spontaneous remissions. Neuroimmunomodulation 2001;9:55-64.
41. Abel U, Becker N, Angerer R, Frentzel-Beyme R, Kaufmann M, Schlag P, *et al*. Common infections in the history of cancer patients and controls. J Cancer Res Clin Oncol 1991;117:339.
42. Hoeijmakers JH. Genome maintenance mechanisms for preventing cancer. Nature 2001;411:366-74.
43. Hoption Cann SA, van Netten JP, van Netten C. Acute infections as a means of cancer prevention: Opposing effects to chronic infections? Cancer Detect Prev 2006;30:83-93.
44. Power D. The local distribution of cancer and cancer houses. Practitioner 1899;62:418-29; quoted in Graner J. History of infectious disease oncology, from Galen to Rous. Infectious Causes of Cancer. Goedert, James J, editor. Totowa, New Jersey: Humana Press; 2000. p. 16.
45. Wang R. Regulatory T cells and innate immune regulation in tumor immunity. Springer Semin Immunopathol 2006;28:17-23.
46. Hobohm U. Fever and cancer in perspective. Cancer Immunol Immunother 2001;50:391-6.
47. Quesnay F. Traite de la gangarene. Paris d houry;1749:313.
48. Zahl PH, Maehlen J, Welch HG. The natural history of invasive breast cancers detected by screening mammography. Arch Intern Med 2008;168:2311-16,2302-03.

How to cite this article: Jessy T. Immunity over inability: The spontaneous regression of cancer. J Nat Sc Biol Med 2011;2:43-9.

Source of Support: Nil. **Conflict of Interest:** None declared.