

**A CONCISE HISTORY ON CHEMOTHERAPY****Paulo Nuno Martins**

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ABSTRACT

Chemotherapy is a therapy used for the treatment of cancer, particularly since the 1940s. This essay aims to be a contribution to the study of this subject, namely in the description of its history, indicating the main types of regimens and treatments in chemotherapy.

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INTRODUCTION

The main objective of this brief essay is to describe a concise history of the discovery and evolution of chemotherapy over time. There are references to the existence of cancer in ancient Persia, and the search for a rudimentary chemotherapy cure has begun in the nineteenth century, although it was only in the 1960's that this method became indispensable in the treatment of cancer [1].

Chemotherapy is a therapy that uses chemical agents to cure or control some diseases, such as mental illness or kill malignant cancer cells. There are several techniques of chemotherapy that might be prescribed by an oncologist physician with the intention of curing, being adjuvant or only palliative. In this regard, I have to mention that alongside the technical procedure for curing cancer, physicians have sought to ensure the quality of life of patients due to side effects of chemotherapy treatment, such as, hair loss, nausea, vomiting [2].

METHODS

In this brief essay on the concise history of chemotherapy, I collected and analyzed the main scientific books and technical articles on this research area that are available in academic libraries in order to be useful to the reader who intends to have a succinct idea on this subject, but maintaining the scientific of my research. Thus, I selected a sample composed of the 20 most important items on this

topic, based on the "impact factor" of the article, and the "reference" books on the subject.

RESULTS AND DISCUSSION

The results of my research work on the concise history of chemotherapy lead me to say that around 1910, the word "chemotherapy" was coined by Paul Ehrlich who aimed to treat syphilis. Later, this term was used as a cancer treatment technique through chemical agents [3]. In this regard, I have to mention that the use of animal models in the early period of cancer drug development is a milestone in the history of chemotherapy. In fact, in the 1910s Georges Clowes performed the pioneering transplantable tumor in rodents that led to the development of several model systems that have been used with chemical agents in the fight against cancer. So, Furth and colleagues published an article on the mechanism of unfoldment of transmission of leukemia in mice, while Charles Huggins and his team studied the relationship between level of androgen and the occurrence of prostate cancer in dogs [4].

On the other hand, during World War II, it was found that people exposed to nitrogen mustard have reduced the number of white blood cells which led some researchers, such as Alfred Gilman and Louis Goodman to study the therapeutic effects of nitrogen mustard agents in the treatment of lymphomas in rabbits and a mouse [5]. Thus, Gilman and Goodman showed their data to surgeon Gustaf Lindskog who worked together to provide a cancer patient

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with the first experimental chemotherapy [6]. In 1946, experimental results of this chemotherapy were published and showed that tumors could be reduced in size, although the inability of mustard gas to produce lasting remissions has led to some pessimism during the 1950s [7]. Most positively, in 1948, Farber and his colleagues developed antifolate compounds (known as methotrexate) that were tested in children with leukemia, who had shown a remission of their disease after this treatment [8]. In this regard, I have to mention that the first description of the first tumor to be effectively cured was actually performed by Min Chiu Li, in 1958 [9].

In the 1960s, a major milestone occurred in the cure of cancer through the combination of several drugs in the chemotherapy regimen, namely the program known as VAMP (vincristine, amethopterin, 6-mercapto-purine, prednisone) [10], followed by MOMP (nitrogen mustard, vincristine, methotrexate, prednisone) and MOPP (nitrogen mustard, vincristine, procarbazine, prednisone) which were developed by pioneering physicians Frei, Freireich, DeVita, Moxley, among others [11] who have allowed a more effective treatment of cancer, since that time. Another success achieved in this decade was the understanding of the relationship between the kinetics of cancer cells and the mechanisms of action of different chemotherapeutic agents [12]. Indeed, the chemotherapeutic drugs could be classified according to the phase cell cycle in which they are active. For example, there are agents that have a linear dose response curve with respect to the cell cycle-phase (e.g. alkylating agents), while there are agents whose cell ability killing will not increase with further increase in drug dosage. So, it has been developed several types of chemotherapy regimens, namely, single-agent therapy (in the 1940s and 1950s, it started to be used with nitrogen mustard), combined therapy (in the 1960s, it started to be used with VAMP, MOMP and MOPP), adjuvant therapy (in the 1970s, it started to be used with L-PAM, CMF together with surgery and/or radiotherapy) [13] and targeted chemotherapy (in the 1980s and 1990s, it started to be used with Monoclonal Antibodies).

Furthermore, I have to mention the name of various types of chemotherapy treatments that might be prescribed by the physician to the oncological patient, namely Induction (high doses of drugs for cancer remission), Consolidation (repetition of the previous treatment to ensure total cancer remission), Intensification (application of a final treatment after cancer remission to ensure complete success), Maintenance (maintain chemotherapy treatments over time after cancer remission), Salvage (performed when there was no success with other treatments), Palliative (prolong the life of an oncological patient with no hope of cure) [14].

On the other hand, in the 1970s, another chemotherapy regimen was used as adjuvant to surgery and/or radiotherapy in order to obtain better results in relation to the previous regimes, and very suitable for several types of cancer or metastases. Examples of application of adjuvant chemotherapy programs are the cases of L-PAM (L-phenylalanine mustard) and CMF (cyclophosphamide, methotrexate, 5-fluorouracil) [15] performed by pioneering

physicians Bernard Fischer, Paul Carbone, Gianni Bonadonna, among others [16].

From the 1980s to the 1990s, targeted chemotherapy using monoclonal antibodies (Mabs), such as Bcr-Abi (tyrosine kinase inhibitor) was developed, and this treatment regimen is known as the new adjuvant chemotherapy. In fact, this chemotherapy regimen has allowed the increase of the success rate or even the total remission in the treatment of certain types of cancer, such as ovaries, lymphoblastic and myelogenous leukemias, gastrointestinal, among others [17]. In this regard, I have to mention that since the year 2000 many chemotherapeutic drugs have been developed, such as Topotecan, Pegylated liposomal doxorubicin, Bandamustime which have a specific profile compared to other alkylating agents in chemotherapy treatment [18].

CONCLUSIONS

As a summary of this essay, I want to mention that chemotherapy has proven to be increasingly an effective way to treat cancer (cure or palliative) as a complementary method to radiotherapy and/or surgery [19]. Furthermore, early diagnosis and prevention has also been an effective means of combating cancer because it is known that some cancers can be prevented through proper diet, namely, avoid red meat, sugars tobacco and simultaneously promote the practice of physical exercise [20]. All these factors combined together have made fighting cancer more effective.

References

1. Mukherjee, S. 2010. *The Emperor of All Maladies: A Biography of Cancer*. Simon&Schuster.
2. Pazdur, R. 2009. *Cancer Management: A Multidisciplinary Approach*. Cmp. United Business Media.
3. Papac, R. 2001. Origins of cancer therapy. *Yale Journal of Biology and Medicine*, 74:391-398.
4. ElBagoury, M. and Koth, M. 2018. Chemotherapy over the Years. *Journal of Pharmaceutical Sciences and Research*, 10(2):316-318.
5. Gilman, A. and Goodman, L. 2011. *The Pharmacological Basis of Therapeutics*. Mc Graw-Hill.
6. Karnofsky, D. and Burchenal, J. and Ormsler, R. and Corman, I. and Rhoads, C. 1947. Experimental observations on the use of nitrogen mustard in the treatment of neoplastic diseases. In: *Approaches to tumor chemotherapy*. American Association for the Advancement of Science.
7. Gilman, A. 1946. Symposium on advances in pharmacology resulting from war research: therapeutic applications of chemical warfare agents. *Federation Proceedings*, 5: 285-292.
8. Farber, S. and Diamond, L. and Mercer, R. et al. 1948. Temporary remissions in acute leukemia in children produced by folic acid antagonist, 4-aminopteroyl-glutamic acid (aminopterin). *New England Journal of Medicine*, 238: 787-793.
9. Li, M. and Hertz, R. and Bergenstal, D. 1958. Therapy of choriocarcinoma and related trophoblastic tumors with folic acid and purine

- antagonists. *New England Journal of Medicine*, 259:66-74.
10. Freireich, E. and Karon, M. and Frei, E. 1964. Quadruple combination therapy (VAMP) for acute lymphocytic leukemia of childhood. *Proceedings of the American Association for Cancer Research*, 5:20
 11. DeVita, V. and Moxley, J. and Brace, K. and Frei, E. 1965. Intensive combination chemotherapy and X-irradiation in the treatment of Hodgkin's disease. *Proceedings of the American Association for Cancer Research*, 6:15.
 12. Olson, J. 1989. *The History of Cancer: An Annotated Bibliography*. Greenwood Press.
 13. Przespolewski, E. 2017. *Principles of Chemotherapy*. The Jonah Center for Oncology and Hematology.
 14. Page, R. and Takimoto, C. 2008. Principles of Chemotherapy. *Chemotherapy*, 21(3):21-37.
 15. Canellos, G. and DeVita, V. and Gold, G. and Chabner, B. and Schein, P. and Young, B. 1974. Cyclical combination chemotherapy in the treatment of advanced breast carcinoma. *Proceedings of the American Association for Cancer Research*, 15:148.
 16. Fisher, B. and Ravdin, R. and Ausman, R. and Slack, N. and Moore, G. and Noer, R. 1968. Surgical adjuvant chemotherapy in cancer of the breast: results of a decade of cooperative investigation. *Annals of Surgery*, 168:337-356.
 17. DeVita, V. and Chu, E. 2008. History of Cancer Chemotherapy. *Cancer Research*, 68 (21): 8643-8653.
 18. Knop, S. *et al.* 2005. The efficacy and toxicity of Bendamustine in recurrent multiple myeloma after high-dose chemotherapy. *Haematologia*, 90(9):1287-1288.
 19. Baguley, B and Kerr, D. 2001. A brief History of Cancer Chemotherapy. In: *Anticancer Drug Development*. Academic Press.
 20. Gingras, D. and Béliveau, R. 2006. *Foods that fight Cancer: Preventing cancer through diet*. Mc Clelland & Stewart.
