

# Chapter 1

## A Brief Overview of Cancer, Its Mechanisms, and Prevention Methods



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**Abstract** Cancer is a wide-reaching burden that affects differently diverse regions. In this chapter, the impact of cancer worldwide, main causes of cancer and most common types of cancer will be accessed. Moreover, the main treatments will also be addressed including surgery, radiotherapy, chemotherapy and immunotherapy. The understand of the causes of cancer, including environmental, genetic, and behavioral factors, will allow to better prevent cancer as well as to choose the most suitable treatment. In this regard, the use of some bioactives or nutraceuticals to prevent or combat cancer can be of great value. This book will update readers on the scientific evidence of different bioactive and nutraceuticals in the prevention and treatment of cancer.

**Keywords** Cancer · Prevention · Screening · Treatment · Radiotherapy · Chemotherapy · Immunotherapy · Bioactives · Nutraceuticals

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## 1 Cancer Over Time

Cancer, also called malignant tumour or neoplasm, is defined by the WHO as a “*large group of diseases that can start in almost any organ or tissue of the body when abnormal cells grow uncontrollably, go beyond their usual boundaries to invade adjoining parts of the body and/or spread to other organs*” (WHO 2020).

Cancer was firstly reported in the Edwin Smith Papyrus in 3000 BC, a surgical document. In this Papyrus, women with breast cancer were described (Kane et al. 2019). In 400 BC, Hippocrates has described different types of cancer. In the nineteenth century there was significant improvements in the treatment of cancer due to the better understanding of pathology at cellular level and the advances in antiseptics and anesthetics, which made possible the surgery involving the removal of the organ containing the tumour and lymph node drainage. The twentieth century replaced the complete removal of the affected organ by a combination of radiotherapy, selective surgery (just part of the affected organ was removed) and frequently adjuvant therapy (Sikora 2020).

The impact of cancer at pan level is impressive. Cancer is the second leading cause of death globally, accounting for an estimated 9.6 million deaths, or one in six deaths, in 2018 (WHO 2020). It is expected that in 2030, there will be around 25 million new cancer patients each year, most of them in countries with less resources for cancer control (Sikora 2020). According to WHO, 9.6 million people worldwide are estimated to die from cancer in 2018. It is the second leading cause of death globally. Although it affects more adults, 300,000 new cases of cancer are diagnosed each year among children aged below 19 years. It is estimated that about 30–50% of cancers could be prevented (WHO 2020).

The most common types of cancer differ between genders. In men the most prevalent are lung, prostate, colorectal, stomach and liver cancer. On the other hand, in women the most common are breast, colorectal, lung, cervical and thyroid cancer (WHO 2020). Over the past decade, the cancer incidence rate (2006–2015) was stable in women and declined by approximately 2% per year in men, whereas the cancer death rate (2007–2016) declined annually by 1.4% and 1.8%, respectively.

According to annual updates on cancer occurrence and trends annual report elaborated by the American Cancer Society (ACS), the Centers for Disease Control and Prevention (CDC), the National Cancer Institute (NCI), and the North American Association of Central Cancer Registries (NAACCR), between 2008 and 2014 the cancer incidence rate was stable in women and decreased about 2.2% per year in men in the United States (Cronin et al. 2018). The cancer death rate between 2007 and 2016 also decreased 1.4 and 1.8% in women and men, respectively, in the United States (Siegel et al. 2019). Cancer mortality is slowly decreasing, however there are more socioeconomic inequalities which are more notable in what concerns to preventable cancers (Siegel et al. 2019). The American Cancer Society also discusses the incidence and mortality of different types of cancer such as the colorectal cancer (Siegel et al. 2020) and specific age groups such as Adolescents and Young Adults (Miller et al. 2020).

Cancer does not only affect individuals physical and psychologically but also their families. Moreover, it has a high economic impact in the community and health systems. In fact, US\$ 1.16 trillion is the estimated total annual economic cost of cancer in 2010 (WHO 2020). In high income countries the survival rates of cancer are higher than in low- and middle-income countries thanks to the string health systems that allow early detection, effective treatment and survivorship care (WHO 2020).

Feng et al. (2019) reviewed several reports on cancer, including the Global cancer statistics 2018 and Cancer statistics in China, 2015, along with the GLOBCAN 2018 online database, to discuss possible differences of cancer patterns among the United States of America (USA), the United Kingdom (UK) and China. Compared to the USA and UK, China has lower cancer incidence than USA and UK however it has higher cancer mortality (30% and 40% more than the UK and USA, respectively). In China about 40% of the cancer-related deaths were from the digestive tract cancers (stomach, liver, and esophagus cancer) while in EUA and UK digestive cancer deaths only represent less than 5% of the total cancer deaths. In addition to a high occurrence of infection-related and digestive cancers, in China there has been a rapid increase of colorectal, prostate, female breast cancers due to the westernized lifestyle (Feng et al. 2019).

To accelerate the progresses to gain the battle against cancer burden, it would be of utmost importance to enlarge the coverage of effective screening programs, specially to low income population groups, to allow their access to basic health care, vaccination programs and educational programs in order to have smoking cessation and education on healthier lifestyle. In the human body there is about  $10^{13}$  cells and multiplication can face dysregulated cells that can multiply indefinitely (Sikora 2020). However, the biggest issue of cancer is not the local growth of tumour cells but their spread to other sites of the body through invasion or metastasis. Due to the impressive advances in the treatment of cancer, now it is possible the cure of this disease even if diagnosed in an advanced stage (Sikora 2020).

## 2 Cancer Prevention

Cancer prevention is better than cure. Although prevention of other deadly diseases has already been achieved, namely through the use of vaccines, the goal of cancer prevention is a tortuous path because many environmental, genetic, and behavioural factors contribute for different types of cancer (Bode and Dong 2009). In it generally accepted by the scientific community that to reduce the cancer risk worldwide is of utmost importance to avoid animal fat, reduce the intake of red meat, increase the consumption of fiber and of fruits and vegetables, eliminating exposure to carcinogens, such as alcohol and tobacco and to exercise in order to avoid obesity (McCullough and Giovannucci 2004; Umar et al. 2012).

Another cause of cancer are infections caused by virus, such as hepatitis B and human papilloma virus and bacteria such as *Helicobacter pylori* (Moore and Chang

2010; Moore and Chang 2017). The control of these infections can greatly reduce through the use of vaccines or through the control of the safety of all steps of food chain (Sikora 2020). The future of cancer prevention will lay on a personalized program based on lifestyle and environmental data.

Nowadays one of the tools to detect cancer in earlier stages is the use of screening tests. These are tests applied to an individual who does not require medical attention and should be simultaneously specific (avoid false results) and sensitive (detect all the cancers). Although the test can reduce cancer mortality due to allow earlier detection of the cancer, when the cancer is metastasised does not prolong survival (Sikora 2020).

It is important to define rational screening programs that allow to improve survival rates in certain types of cancer. Some papers report the rational used for targeting of population groups and residential areas for cancer, namely colorectal cancer (Strömberg et al. 2019), breast cancer. These should be adapted to the reality of each country and should have a cost that corresponds to the gain in survival rates (Sikora 2020).

Screening targets only few organs that are affected by tumors of sufficient prevalence to show cost-effectiveness at population levels. Therefore, most types of cancer are not screened. Ahlquist defends a multi-organ cancer screening considering its great advantages including to provide an “universalized” value because it can detect all cancer types and an “individualized” value because indicated the likely organ of origin when it gives a positive result (Ahlquist 2018).

Some cancers present various symptoms from early stages but others are asymptomatic and are only detected when they are spread. The diagnosis of cancer as an emergency is generally accompanying with a markedly worse prognosis; though, there is still lack of data on this subject, being this limited to data from developed countries which have examined frequency and aetiology of cancer (Zhou et al. 2017).

The diagnosis of cancer has greatly improved thanks to imaging, namely computed tomography (CT) and magnetic resonance imaging (MRI) and biomarkers. Several biomarkers have been used to diagnosis cancer as prostate specific antigen (PSA) for the prostate cancer diagnosis (Sikora 2020).

Le Duff et al. (2019) reported a project that aimed to evaluate the impact of the provision of a test in pharmacies to screening for colorectal cancer in Corsica. The paper describes the procedure used to mobilize the pharmacists of the territory, provide them the test kits and accompanies the participants in the test. According to the authors the project had a very positive impact with a realized rate of 36% over 9 months (Le Duff et al. 2019). In one decade, it is likely that tests based on cancer biomarkers are available in the pharmacy to diagnose the major cancers or that implanted devices can detect cancer at early stages and be monitored through a computer or mobile phone (Sikora 2020).

### 3 Treatment of Cancer

The main focus of cancer treatments are surgery, radiotherapy, chemotherapy and immunotherapy. Although the progresses, surgery is the most effective cancer treatment. Surgery advances between the nineteenth century and nowadays are impressive. Surgery started to be radical, i.e., with complete removal of the affected organ and of the lymph node(s) of the area, but nowadays is more conservative allowing to maintain organs through minimally invasive surgeries (Sikora 2020).

Radioterapy has also evolved significantly since its first use, over one century ago. This technique allows to destroy cancer cells and keep unaffected the normal cells through the use of radiation. The key factors for the effectiveness of the treatment with radiotherapy is the precise application of the radiation. This greatly improved thanks to computer-based imaging that allows deliver precisely the radiation according to the type, size and site of the tumour (Sikora 2020).

Radioterapy has many side effects and some of them can reduce the quality of life of patients. In this line intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) are now routinely used, in combination, in order to reduce the side effects of radiotherapy (Bujold et al. 2012; Samuelian et al. 2012; Sikora 2020).

Another factor that can reduce the lack of effectiveness of radiotherapy is the resistance to radiation. According to scientific evidence microRNAs modulate key cellular pathways that mediate response to radiation, so microRNAs might have potential as targets for the development of new therapeutic strategies to battle cancer (Mueller et al. 2016).

Immunotherapy is a cancer treatment that mobilizes immune system of the individuals in order to recognize and induce cancer cell destruction. This will stop or slow down the growth of the tumor, avoid cancer cells spread (metastasis) or aid immune system to better detect and destroy cancer cells (Dougan and Dranoff 2012; Sikora 2020). There are different types of immunotherapies. These include non-specific immunotherapies like interferon and interleukins (Bassiony et al. 2020; Sikora 2020). Also cancer vaccines are used as immunotherapies (Banchereau and Palucka 2018; Grenier et al. 2018; Hollingsworth and Jansen 2019). These can prevent cancer like human papillomavirus vaccine. This vaccine avoids the infection with human papillomavirus that is responsible for cervical cancer and other types of cancer. Other vaccines are used to target cancer cells in order to treat cancer. Sipuleucel-T is a licensed vaccine for the treatment of asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer (Caram et al. 2019; Hu et al. 2016; Wei et al. 2018).

Many studies have combined radiotherapy with immunotherapy and they have proven to be effective (Wang et al. 2018). The synergy between these two therapies allows to increase the visibility of tumor antigens, to activate the cGAS-STING pathway, and to modulate the tumor microenvironment. Immunotherapy can act as a “radiation sensitizer” improving tumor local control but to increase the

effectiveness of this combination of therapies it is necessary to optimize radiation dose and time and to identify potential biomarkers (Wang et al. 2018).

Monoclonal antibodies are proteins that fight infection because they attach to specific proteins in the cancer cell and they allow immune system to destroy cancer cells, deliver drugs directly to cancer cells, or deliver radiation to cancer cells (radio-immunotherapy: a radioactive molecule is attached to monoclonal antibodies). Also therapies with monoclonal antibodies also present side effects these are generally mild and most of times similar to an allergic reaction. (Sikora 2020; Zahavi and Weiner 2020).

Many drugs are used to treat cancer. The number of the approved drugs increases every year and they have very different cellular targets. These include cell-surface receptors, signal transduction cog molecules, transcription factors, apoptosis- stimulating proteins, growth factors and cell-cycle control proteins. Some cancers such as Hodgkin disease, childhood leukemia and testicular cancer respond very well to chemotherapy (Morton 2020). However, other types have low cure rates such as colon, stomach and lung cancer.

## 4 Natural Food Compounds and Cancer

Many food components have been associated with chemopreventive properties. These include lycopene from tomatoes (Paur et al. 2017), resveratrol from grapes (Berman et al. 2017), curcumin from curcuma (Hesari et al. 2019), omega-3-fatty acids from fish (Eltweri et al. 2017), among others. The present book dedicates to the update and discussion of the role of different food components in chemoprevention and chemotherapy of cancer based on scientific evidence. Bioactive compounds and nutraceuticals can be of great value in the prevention of cancer or for the effective treatment of cancer, mainly enhancing the effectiveness and/or minimizing the side effects of other therapies. In fact, some food components have already proved their effectiveness the combat against cancer in clinical trials.

## 5 Remarking Conclusions

While the number of cancer patients will continue to rise, the knowledge regarding the causes and the number of effective therapeutics against this global burden is also expanding. This chapter overviewed impact of cancer worldwide, main causes of cancer, most common types of cancer and main treatments, including surgery, radiotherapy, chemotherapy and immunotherapy.

As stated by Sikora, the “molecular signatures” of the cancer will determine the treatment choice (Sikora 2020). The tendency on the treatment of cancer is to have available therapies able to have specific targets (more selective), less toxic and with less side effects. In this regard, bioactive compounds present in food can have a

major role in the prevention and treatment of cancer, mainly enhancing the effectiveness and/or minimizing the side effects of other chemotherapies. This book updates the scientific evidence of different bioactive and nutraceuticals as potential munitions in the effort to minimize the burden of cancer.

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