



# Understanding breast cancer – The long and winding road



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## ABSTRACT

**Background:** Despite a remarkable increase in the depth of our understanding and management of breast cancer in the past 50 years, the disease is still a major public health problem worldwide and poses significant challenges. The palpability of breast tumors has facilitated diagnosis and documentation since ancient times. The earliest descriptions of breast cancer date back to around 3500 BCE. For centuries to follow, theories by Hippocrates (460 BCE) and Galen (200 CE), attributing the cause of breast cancer to an “excess of black bile” and treatment options including the use of opium and castor oil, prevailed. Surgical resection was introduced in the 18th century. The advent of modern medicine led to the development of novel treatment options that include hormonal, targeted and chemo-therapies. There are still several therapeutic challenges including the treatment of triple negative breast cancer (TNBC), and overcoming drug resistance.

**Scope of review:** The increased incidence and awareness of breast cancer has led to significant changes in diagnosis and treatment in recent decades. But, mankind has come a long way. Herein, I have traced how our understanding of breast cancer has evolved from the early description of the disease around 460 BCE as “black bile-containing crab-like tumors” to the conventional as a heterogeneous disease with high degree of diversity between and within tumors, as well as among breast cancer patients. How is breast cancer treated today and how do risk factors, breast cancer subtype and drug resistance contribute to the therapeutic challenges at the turn of the 21st century?

**Major conclusions:** Breast cancer remains a serious public health issue worldwide. However, appreciable growth in our understanding of breast cancer in the past century has led to remarkable progress in the early detection, treatment and prevention of the disease. The clinical focus is shifting more towards tailored therapy as more targets are characterized and novel highly innovative approaches are developed.

**General significance:** Tracing the history of breast cancer, highlights how increased awareness of the disease, and progress in research and development have enhance our understanding of the disease.

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## 1. Introduction

Breast cancer is characterized by uncontrolled growth of malignant cells in the mammary epithelial tissue. The disease affects both genders. Breast cancer is the most frequent type of cancer in women worldwide, with an incidence that rises dramatically with age. Breast cancer reportedly accounted for 29% of all new cancer cases and 14% of all cancer-related deaths among women worldwide up to 2012 [1]. This translates into about 1.7 million new cases in women and an estimated 522,000 deaths in 2012 [2]. As alarming as it may seem, the mortality to incidence ratio for breast cancer is around 0.31, which is far more favorable than pancreas and liver cancers, with ratios of 0.98 and 0.95, respectively [2]. Breast cancer in the 21st century is therefore not necessarily terminal. Better therapeutic options and major improvements in public health and care have resulted in a dramatic reduction in mortality and a major increase in longevity. Breast cancer is rare in males, comprising 1% of all breast cancer diagnoses in the United States and less than 0.1% of cancer-related deaths in men [3].

Since 1999, incidence rates of breast cancer have stabilized among women aged 50 or over, which may reflect trends in mammography screening rates. Epidemiological data from the United States show that breast cancer death rates were stable from 1980 to 1989 for women aged 20 to 64 and increased for women aged 65 and over. In most countries, however, breast cancer incidence rates are increasing, including in countries with historically higher rates, such as those in Europe, as well as regions with historically lower incidence rates like many countries in Latin America, Asia, and Africa [4]. This rise is generally due to changes in reproductive patterns such as age at menarche, age at first pregnancy, number of births, and duration of breastfeeding [5]. The historically higher increase in breast cancer incidence in developed countries is largely due to factors associated with economic development and urbanization including obesity, consumption of processed foods, physical inactivity, and changes in reproductive patterns (delayed childbearing; having fewer children; earlier age at menarche; and shorter duration of breastfeeding). The rising incidence in

developing countries is likely due to the increasing adaptation of risk factors associated with the Western lifestyle [6].

Humankind has struggled to understand and treat breast cancer since the earliest documentation more than 3500 years ago. The visible signs and symptoms of breast cancer and the palpability and tangibility of the lumps at later stages of the disease have enabled easy diagnosis by physicians in almost every period of recorded history. Despite the noticeable manifestation of the disease since ancient times, e.g. the Pyramid Era, and the high mortality associated with the advanced form of the disease, cultural and sexual connotations regarding the breast have stigmatized discussions of the disease in the general public and limited its description to clinical journals and textbooks until recently. Besides, from the ancient civilizations and through the 18th and 19th centuries it was recognized that breast cancer could not be cured once the cancer had spread.

In many cultures, breast cancer is still considered a taboo subject. As a result, many patients are reluctant to candidly discuss their disease or its symptoms. However, moral and ethical reforms have been introduced in several societies and breast cancer topics are an open discussion in all forum or media today. Further, with the advent of electronic media and the Internet, online discussions on the awareness of the disease are now accessible even to the remote areas and cultures of the world. The pink symbol of breast cancer, adopted in the early 1990s, represents the international symbol of breast cancer awareness and is used by various breast cancer organizations to promote breast cancer awareness and to support fundraising campaigns.

Our clinical understanding of breast cancer dramatically improved from its early description around 460 BCE as “black bile-containing crab-like tumors” to the conventional or modern description as a heterogeneous disease that displays diversity in histopathology, genetic variation, molecular subtype and clinical outcome. In addition, scientific discoveries in recent decades have led to new and better ways to prevent, detect, diagnose, and treat breast cancer. This review traces the evolution of breast cancer through the various periods of recorded history. The historic milestones punctuating the progress of our

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