

HISTORY OF MEDICINE

Breast cancer in antiquity

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Breast cancer is one of the first recognisable cancers described in history, and we trace its recognition and treatment through antiquity. Galen saw cancer of the breast as the most common cancer of his time (and is still the most common cancer among South African women). Hippocrates in the 5th century BC possibly first described it. The *Corpus Hippocraticum* recorded a single case but mentioned no specific treatment. It was noticed that the cancer (*karkinôma*; *carcinoma* in Latin) could be preceded by an occult cancer (*karkinos kruptos*). Standard dogma through antiquity for close on a millennium was that all tumours resulted from an inflammatory process caused by an abnormal flux of tumours, in which an excess of black bile was crucial.

For centuries after Hippocrates, and through the Hellenistic period, no further cases of breast cancer were recorded. However, physicians during this time must have encountered the common tumour regularly and evolved therapies. Cato (2nd century BC) advocated cabbage poultices as a panacea for tumours, and breast cancer in particular.

Breast cancer re-appeared in the medical literature of the 1st century AD; Aëtius of Amida probably first described Paget's cancer of the nipple. Treatment now comprised a combination of systemic and topical medicaments, venesection, surgery and cautery. Although the prognosis of breast cancer treatment with drugs was accepted to be poor, certain preparations, like that of Paccius Antiochus, were said to be curative. Galen, in particular, put great value on venesection for ridding the body of black bile. Surgical resection as first described by Celsus and later by Leonides, usually combined with cautery, proved curative when performed at an early stage of the disease.

Breast cancer is still the most common malignancy among women in South Africa, with a crude incidence rate of 18.5/100 000; its probability rises with age, with a mean age of 60 - 61 years. Male breast cancer is very rare (1% of the incidence of females), commonly presents at a more advanced stage, and has a worse prognosis.^{1,2}

Ancient concept of tumours

The concept that tumour formation was part of the inflammatory process involving a 'flux of humours' and resulting in the formation of localised growths or swellings in regions of the body, was

postulated by Hippocrates in approximately the 5th century BC, and changed little during the next millennium up to the end of Graeco-Roman antiquity. It was thought that the nature of tumours depended on mixtures of humours (blood, phlegm, yellow bile and black bile) and their response to stimuli such as fever, injury, fractures and over-exertion, present in a particular region of the body. Tumours arose when hormonal flux caused exudation of fluid from veins into the parenchymal components of the body. When these accumulated, extravascular fluids were not broken down to a fully concocted mixture (*materia pecans*) and re-absorbed or discharged (as in an abscess), and the remains formed a tumour (*onkos*) which could have various characteristics. The Hippocratic and other writings refer to a variety of such tumours:

- *Karkinos, karkinôma* (Latin: *canrum, carcinoma*). A flux of blood and black bile was said to cause scirrhus, and black bile unmixed with blood converted this to *karkinôs*, which was commonly found in the female breast. The name was derived from the Greek for crab, because of a fancied resemblance of this firm, fixed tumour with the rough, hard exterior of the crab and its long projections (feet and claws), which enabled it to cling to the environment.
- *Phuma*. An inclusive term which encompassed many tumours, which we would probably classify as non-malignant or inflammatory lesions. It included small breast tumours, called tubercula, associated with lactation which might have been fibroadenosis or retention cysts.
- **Other.** *Oidêma* were soft, non-tender tumours, often pitting on pressure, and which possibly included gross oedema of the body. Whereas *karkinos* arose from excess black bile, *oedêma* was caused by excessive phlegm. Several other terms associated with tumours, but with little reference to the breast, included *struma, melicerides, condyloma* and *occalescit*.

The ancients did not differentiate between benign and malignant tumours, but recognised the ability of tumours like *karkinoi* to infiltrate neighbouring tissue. The words *deina* and *kakoêthês* furthermore referred to ominous changes in lesions, suggestive of malignant transformation. Bacchius (3rd century BC) commented on a Hippocratic document, *On Carcinosis*, but this no longer exists.^{3,4}

Breast cancer: historical overview

There is no clear evidence of breast cancer in the medical writings of ancient Mesopotamia.⁵ Evidence of cancers in the Egyptian papyri is very uncertain, but the occurrence of the word *weshau* (eating) may on occasion be interpreted as indicative of malignancy, and breast cancer might have been recognised.⁶

Possibly the first reference is from the 6th century BC Herodotus.⁷ He described that a Greek doctor, Democedes, then captive of the Persian king, Darius the Great, managed to cure a *phuma* in the breast of the king's wife, Atossa, which erupted and grew in size. Democedes was evidently able to cure the lesion quite readily though it is not known how this was done. However, the relatively benign nature of this *phuma* would suggest that it was a benign tumour, or more likely a breast abscess, rather than a cancer.

Hippocrates (5th - 4th centuries BC) probably described the first true case of breast cancer in history in a woman from Abdera.⁸ She presented with a chest wall tumour associated with bleeding from the nipple, and was diagnosed to have a *karkinôma* (cancer). When

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the bleeding stopped, she died. Hippocrates also described the occurrence of *phumata sclera* (hard tumours) in breasts, which he claimed could turn into *karkinoi kruptoi* (occult cancers). This could well have represented fibrous dysplasia known to be pre-malignant.³

We have no record of breast tumours described during the Hellenistic Period.

Celsus⁹ (1st century AD) described breast cancer as appearing in stages of development, only the first of which (*cacoethes*) was curable. Celsus consequently used the Latin term *cacoethes* with a meaning differing from Hippocrates' Greek term *kakoëthês*. The lesion then progressed to *carcinoma* when the swelling became irregular and fixed to surrounding tissues, with numbness and a prickling sensation of the overlying skin, which also developed prominent veins. Still later, the lesion became painful and could ulcerate through the skin. He warned, however, that it was very difficult to determine clinically when the cancer was incurable. Celsus' *therioma*, sometimes associated with malignancy, fits in better with severe, spreading infection.

By the 1st century AD, breast cancer, as described by Celsus, was a well-recognised condition, but views on treatment varied considerably. Pliny the Elder¹⁰ stated that childbirth aggravated breast cancer.

Galen^{3,11} (2nd century) largely confirmed the views of Hippocrates and subsequent authors, stressing the concept that certain benign hard breast lesions, which he called *karkinoi genomoi*, could become cancers. He considered breast cancer to be the most common cancer, stating that it usually developed after the menopause.

Aëtius of Amida¹² (6th century) based his authoritative writings on breast cancer on the views of two well-known physicians of earlier years: Archigenes of Apamea (late 1st century), often quoted by Galen, and the surgeon, Leonides (also called Leonidas) of Alexandria. He stated that although breast cancer could occur in male breasts, it was most commonly found in large, fleshy female breasts. He differentiated between ulcerated and non-ulcerated tumours, but otherwise confirmed characteristics as previously described by Celsus. He also identified a cancer localised to the nipple area, which had a good prognosis.

Soranus of Ephesus¹³ (turn of the 1st century AD) left us an extensive contribution on diseases of women, but there is no description of breast cancer in his surviving works. Neither does Caelius Aurelianus¹⁴ extensive Latin translation of Soranus' works on acute and chronic diseases (probably 5th century) include a contribution on this disease.

Treatment

Hippocrates (5th - 4th centuries BC) did not relate how the *karkinôma* of the woman from Abdera was treated. Virtually no information on the handling of breast cancers is found in the *Corpus Hippocraticum*. However, the advice in *Aphorisms* that deep-seated cancers should not be treated at all, as treatment shortened the patient's life, confirms that cancer therapy was in vogue.³ Although surgery comprised an extensive and excellent component of the *Corpus*, there is no mention of mammary surgery.¹⁵

In his *De Agricultura*, Cato¹⁶ (234 - 149 BC) proposed cabbage (especially the small variety), that should be crushed and applied as a poultice twice a day, as a panacea for contusions, dislocations, wounds and sores, and ulcer or cancer of the breast in particular. In the centuries after Hippocrates, many animal, vegetable and mineral products, besides cabbage, were used as anti-tumour therapy, and elements of surgery and cautery were gradually introduced. However, the first available systematic recording of such treatment for breast cancer dates from the 1st century A.D.

Celsus⁹ stated that only the earliest stage of breast cancer (*cacoethes*) could be cured but, because it was clinically very difficult to distinguish this from more advanced tumour (*carcinoma*), caustic medicaments should be applied when there was doubt. If this relieved the tumour, treatment should be advanced to excision and cautery. He also advised that even incurable lesions could find long-lasting benefit from soothing applications such as fig plasters or rose cerate mixed with powder from a blacksmith's crusted earthenware pot. With considerable growth of the tumour, a mild caustic such as copper scales could be tried.

Like Plinius the Younger¹⁷ (1st century AD), Scribonius Largus¹⁸ (1 - 50 AD) wrote that breast cancer could not be cured, but nevertheless mentioned that he had 'cured' a patient by means of Paccius Antiochus' plaster, *emplastrum album*. This was almost certainly a transdermal anaesthetic containing *inter alia* mandrake. Unlikely to cure breast cancer, the plaster possibly acted as a narcotic to relieve pain.

The original works of Archigenes of Apamea (1st century AD) and Leonides of Alexandria (probably late 2nd century AD) are lost to posterity, but we know their contribution to the management of breast cancer through the quotations of Aëtius of Amida (6th century AD).^{4,12,15} Leonides is largely credited with the surgical component of Aëtius's treatment schedule, but Archigenes was also known for his surgical skills. Aëtius emphasised the surgical removal of mammary tumours, after the patient's general health had been optimised with good food, selected medications and instituting proper bowel movements. He probably first described Paget's cancer of the nipple. Cancer surgery was recognised as causing serious haemorrhage, while removing non-cancerous tumours was associated with much less bleeding. With the patient lying on her back, an incision was made through healthy tissue surrounding the cancer, and the cut surface immediately cauterised with a hot instrument to stop bleeding. The procedure was repeated until the tumour was resected, when the whole cut surface was cauterised again. Care was taken that no abnormal tissue remained behind. Linen bandages and plasters containing *inter alia* plantain, knotgrass, honey, lentils, milk, sesame and bread flour, were applied until the scabs came off. For suppuration, rose oil and milk applications were applied. The patient was kept in a warm room, as cold was thought to cause convulsions. Wine, cold water and unmixed foods were avoided. When the wound was healed, general bodily health had to be improved with proper exercise and good food in a pleasant environment. When surgery was not indicated, the patient's health was optimised, and medications such as theriac, goose blood as hot drink, and mixtures of bitumen, trefoil, pennyroyal, mallows, rue and asses' blood in water, taken. This was continued until the cancer proved inactive. Non-ulcerated tumours could also be treated with specified poultices to keep the breast warm. Archigenes and Theodorus applied extremely complex specialised poultices to ulcerated tumours.¹²

Authors like Riddle¹⁹ and Bonet¹⁷ have reviewed the extensive subject of substances with claimed anti-tumour effects used in antiquity. In his *Materia Medica*, Dioscorides²⁰ (1st century AD) referred to squirting cucumber and water figwort as having anti-tumour affinities; orobos (lathyrus) and chamaipus (*ajuga*) were considered specifically beneficial against hard lumps in the breast, and asklepias (milkweed) against malignant breast sores.

Galen^{3,11} (2nd century AD) strongly supported the Hippocratic concept of excessive black bile being fundamental to the development of malignancies. He therefore believed that breast cancer at an early stage could be cured by venesection (even free bleeding) to rid the body of excess black bile, and topical remedies applied to the breast. He supported the Hippocratic suggestion that deep-seated cancers

should not be disturbed, but nevertheless taught that breast cancers not cured by these conservative measures should be resected and cauterised; bleeding could be a major problem. Tumour resection was followed by appropriate medicaments applied to the wound, and systemic medicines. Cancers adhering to the thoracic wall could not be resected. Galen also advocated an extensive list of anti-cancer medicaments derived from plant, animal and universal origins.

Rufus of Ephesus (1st century) and Cassius Felix (2nd century) were of the opinion that breast cancer could not be cured.¹⁷

Bonet¹⁷ states that, during the Graeco-Roman period, magic and superstition did not play a significant role in the management of breast cancer. Harstad²¹ shows that, during the subsequent Byzantine era, the Christian culture of the Eastern Roman Empire fostered the creation of biographies based on the lives of saints. These biographies were often melds of fact and fiction, and included a 7th century text where the miraculous cure of breast cancer was mediated by the Saints Cosmas and Damian. At the sanctuaries of Asklepius,²² this disease hardly featured on the votives and inscriptions left by satisfied patients over the centuries. Given the poor prognosis of breast cancer, this is not surprising.

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