

A Note From History: Landmarks in History of Cancer, Part 1

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Review of the earliest written descriptions and reports of cancer show that ancient physicians and surgeons made gradual progress in understanding cancer. It became clear to most of them that early detection and complete removal, before the cancer became ulcerated, afforded the best outcome. *Cancer* 2011;117:1097-102. © 2010 American Cancer Society.

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There is some truth to the old adage that cancer is as old as the human race, but paleopathologic findings indicate that tumors existed in animals in prehistoric times, long before men appeared on Earth. Let it be what it may, ultimate reliance in history requires written records. In medicine, the earliest written description of diseases and cancer, a breast cancer, is found in the Edwin Smith Papyrus that was written approximately 3000 BC. The writer concluded that bulging tumor of the breast was a grave disease and there was no treatment for it¹ (Fig. 1). The Ebers Papyrus, dated circa 1500 BC, contains the first reference to a soft-tissue tumor, a fatty tumor, and includes reference to possible cancers of the skin, uterus, stomach, and rectum.² The Egyptians attempted to treat tumors and cancers with cautery, knives, and salts, and introduced arsenic paste that remained in use as “Egyptian ointment” until the 19th century.³ The Sumerians, Chinese, Indians, Persians, and Hebrews of the same epoch were partial to herbal remedies such as tea, fruit juices, figs, and boiled cabbage, but in advanced cases, they did not hesitate to resort to solutions and pastes of iron, copper, sulfur, and mercury. Many of these concoctions remained in external and internal use, in various concentrations, for more than 3000 years.^{4,5}

The Greeks molded medicine into a mixture of art and science. Hippocrates (460-375 BC) and his disciples opposed superstitions as cause of cancer. They believed that cancer was initiated by natural causes. They rationalized that excess or deprivation of blood, mucus, bile, and other body secretions, particularly at old age, may induce cancer. Cancerous growths reminded Hippocrates of a moving crab, which led to the terms carcinoma (malignant tumor) and cancer (ulcerated malignant tumor). Scirrhus, or hard tumor, was separated from carcinoma and cancer, and listed as a tumor with uncertain malignant potential. Greek physicians knew about cancer of the skin, mouth, stomach, and breast. Hippocrates described anorectal condylomas and polyps and used a speculum for examination if the lesion was higher up in the colon. He regarded breast cancer and cervical cancer with bloody discharge as life-threatening tumors and applied only palliative care. Superficial and deep carcinomas and cancers were separate entities and were treated differently. Superficial lesions were treated with lotions and cautery, and deep tumors were either cut out with a knife or deemed untreatable^{5,6} (Fig. 2).

After Greece became part of the Roman Empire in 146 BC, Greek physicians were granted Roman citizenship and a place to settle in Rome. Among the new citizen-physicians was Aulus Celsus (25 BC-AD 50). Celsus became an influential Roman physician and made Latin the language of medicine. He continued the Hippocratic tradition by comparing cancer to a crab that adheres to surrounding structures with his claws. In his *De Medicina*, he described several varieties of superficial cancer, but he also mentioned cancers of visceral and parenchymal organs such as the stomach, colon, liver, and spleen.^{3,4} Celsus treated superficial carcinomas with a topical application of boiled cabbage and a salted mixture of honey and egg white. For cancers, he recommended early and aggressive surgical therapy. He knew that advanced breast cancers have a tendency to recur in the armpit, with or without swelling of the arm, and may cause death by spreading to distant organs^{5,7,8} (Fig. 3).

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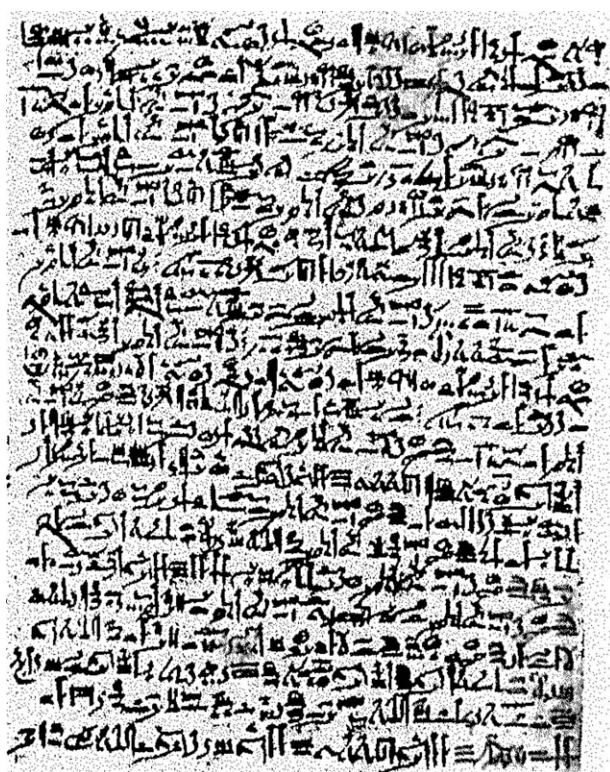


Figure 1. The Edwin Smith Papyrus was written about 3000 BC.

Remedies for cancer were compiled by Pliny the Roman (AD 23-79), in his *Materia Medica*. He recommended compound herbal and other remedies for internal use in advanced cancer before or after attempted surgery. His most highly praised prescription was a boiled mixture of ash of sea crabs, egg white, honey, and powdered feces of falcons.⁴

The first comprehensive description of symptoms, signs, and treatment of cancer of the uterus was rendered by Aretaeus (AD 81-138), who lived and practiced medicine in Alexandria, Egypt. He wrote, in his notes, that there were 2 distinct forms of cancer: one was firm to the touch and nonulcerated, whereas the other was foul smelling and ulcerated. Both tumors were associated with pain and swelling in the groin. He regarded both lesions as chronic and deadly, but the ulcerated one was worse without any chance of cure. He looked upon uterine bleeding in association with enlargement of the uterus as an incurable condition^{4,9} (Fig. 4).

Aretaeus is also remembered for his clinical description of elephantiasis, jaundice, and pleurisy, as well as the first accurate account of diabetes, to which he gave its

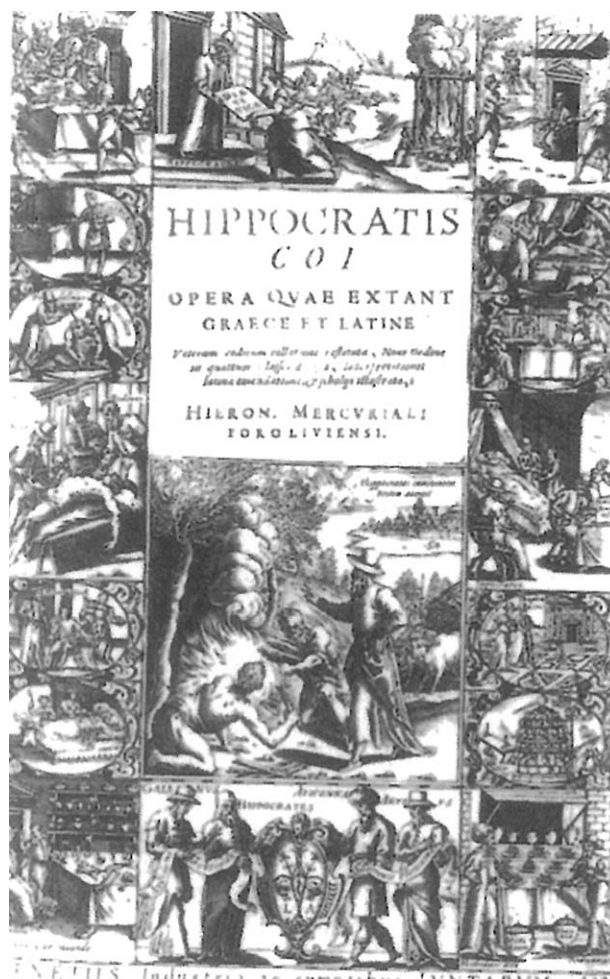


Figure 2. The collected writings of Hippocrates was printed in Venice in 1588.

present name. The Romans' thinking about cancer, as well as the whole known world at that time, came under the influence of Claudius Galen (130-200), a native of Greece, who practiced medicine in Rome.^{3,5,10} He believed that thick black bile caused ulcerated and incurable cancer, whereas thin yellow bile was responsible for nonulcerated and curable cancer. Despite being an appointed surgeon to the gladiators, he accepted the Roman prejudice against surgical treatment of cancer. Galen held that cancer was a disease of the sick and should be treated with purgatives to diminish the accumulation of black bile. He named swellings and fleshy tumors with the appearance of raw meat sarcoma. Galen was a prolific writer who wrote more than 100 notes on tumors and cancers, more than any of his predecessors (Fig. 5). His writings were translated from Greek into Latin and were widely distributed, in handwritten copies, in all known

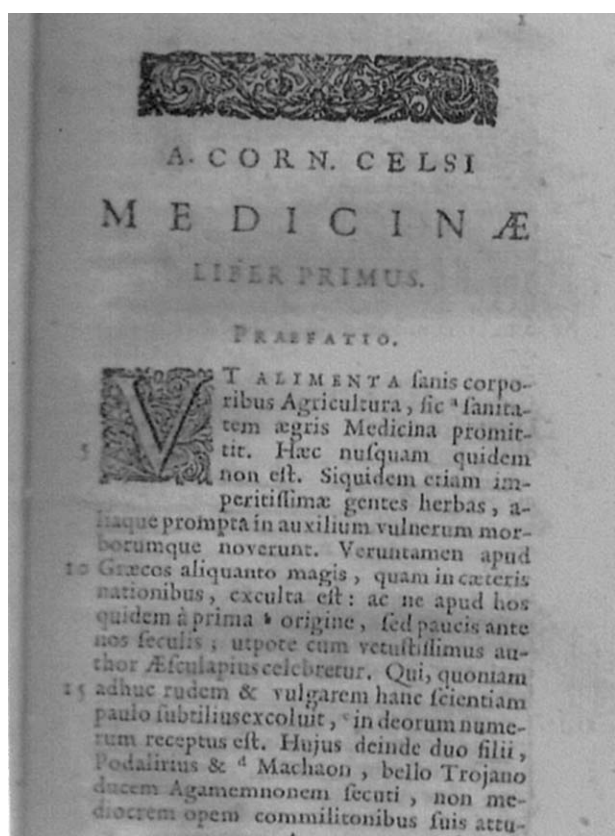


Figure 3. The first edition of *De Medicina* by Celsus was printed in Florence in 1478. It is known as the first medical book published by printing.

countries. His dogmatic theories well suited the Christian theology as well as Byzantine and Arabic teachings, and delayed advances in understanding the natural history of cancer and its treatment for several centuries.^{4,5,11}

After the decline of the Western Roman Empire, Constantinople and Baghdad became the centers of medical knowledge, and several physicians are renowned for their contributions to the advancement of medicine.⁵ Oribasius of Baghdad (325-403) noted that cancers were mostly painless and were not as red as inflammatory lesions. Cutting into cancers, he observed scirrhous (firm) tissue, black bile, and coarse soft material (necrosis). He admitted that he had no luck in curing ulcerated cancers. Treatment of breast cancer by amputation of the whole breast was introduced by Aetius (527-565), physician to Emperor Justinian in Constantinople.^{4,12} He treated nonulcerated lesions of the cervix, labia, and the anus with cautery, but he offered no treatment for ulcerated cancers. He recommended complete excision of tumors of the extremities by using elliptical incision¹³ (Fig. 6). Thyroid-

ARETÆI CAPPADOCIS
DE ACUTORVM, AC DI-
turnorū morborū causis & signis, Lib. IIII.
De acutorum, ac diuturnorum morborum cu-
ratione, Lib. IIII.
EX BIBLIOTHECA REGIA.



Βασίλει τ' ἀγαθῶ κρατερῶ τ' ἀχιμνῶ.
PARISIIS M. D. LIII,
Anno 1559. Typographū Regium.

Figure 4. *De Acutorum* by Aretaeus was published in Paris in 1559.

ectomy and nasal polypectomy were introduced by Paulus of Aegina (625-690). He knew about cancer of the liver and the intestines. He did not hesitate to excise cancers, but he advised that surgery be avoided if the cancer was insensible because it was incurable.⁴

Hippocrates and Galen were introduced to the Arabic world by Rhazes of Baghdad (860-932). He practiced surgery and introduced new operative techniques and instruments. In his *De Chirurgia*, he described jaundice as being caused by an obstruction of the bile duct. He relieved intestinal obstruction by surgical resection of the affected segment, but he warned surgeons that if the obstruction was caused by cancer, no surgery should be attempted unless the cancer can be excised completely.^{5,13} Avicenna of Persia (980-1037) introduced polypectomy by a wire loop that was made tighter each day until the tumor fell off¹⁴ (Fig. 7). Surgical treatment of cancer was introduced in Spain by Albucasis (1013-1106), the first Muslim physician in Europe. He practiced bloodletting before surgery and was an advocate of ligation of vessels only in severe hemorrhage. It is perhaps not a surprise that



Figure 5. The collected writings of Galen was printed in Venice in 1625.

he cautioned that extensive surgery should be used sparingly for treatment of cancer because surgery may kill the patient before the cancer does.^{3,4,15} The signs and symptoms of cancer of the esophagus were described by Avenzoar (1070-1162). He was a Jewish physician who practiced in Cordova, Spain. He invented esophageal and gastric cannulas for relief of strictures caused by cancer and for injection of nourishment. He knew about obstruction by rectal cancer and introduced hysterectomy for removal of uterine tumors.^{5,8}

In 1215, the Pope announced that the church abhorred bloodshed and prohibited surgical operation. However, the prohibition failed to restrain Theodoric (1205-1296), a bishop and physician, who practiced in Salerno, Italy. He knew that cancers, particularly the neglected ones, commonly involved muscle, vessels, and

AETII MEDICI
 GRAECI CONTRACTAE EX VETESTIBVS
 MEDICINAE TETRABIBLOS, HOC EST QUATERNIO,
 id est libri uniuersales quatuor, singuli quatuor sermones
 complectētes, ut sint in summa quatuor sermonum
 quaterniones, id est sermones xvi. per Iulium
 Cornarium Medicum Physi-
 cum Latinè conscripti.



BASILEAE M D XLII

Figure 6. Aetius' *Medicini*, was published in Basle in 1542.

كتاب القانون في الطب
 لاجوركي الشيخ الرئيس
 ابن سينا

مع بعض ما يعمد وهو علم المنطق وعلم الطبي
 وعلم الكلام



ROMAE,
 In Typographia Medicea .
 M.D.XCIII.
 Cum Licentia Superiorum.

Figure 7. Avicenna's *Canon of Medicine* was printed in Rome in 1593.

Table 1. Chronology of Discoveries, First Descriptions, New Terms, and Other Satient Events

Year	Medical History	Year	World History
3000 BC	Breast cancer described	3000 BC	Construction of Stonehenge
1500 BC	Herbal, mineral, and arsenic therapy, and soft tissue tumor described	1500 BC	Hebrews are in captivity in Egypt
375 BC	Cancer, carcinoma, scirrhous and condyloma introduced, skin, mouth, stomach and breast cancers, cautery	377 BC	Walls built around Rome
AD 50	Cancer surgery, breast cancer in axilla, lymphedema of arm, cancer of liver, colon and spleen, superficial and deep cancers, mixture of honey, egg white, and cabbage for inoperable cancer	AD 43	Roman invasion of Britain
79	Internal remedies before and after surgery, book on drugs published	68	Nero commits suicide
138	Nonulcerated and ulcerated uterine cancers	132	Seismograph developed in China
200	Sarcoma introduced, yellow and black bile, and, humoral theories, first pharmacy in Rome	200	Afghanistan invaded by Huns
403	Necrosis in cancer identified	403	Visigoths invade Italy
562	Mastectomy, cancer of cervix, vulva and anus described	571	Mohammed is born
690	Cancer of intestines described, cancer is painless	691	Dome of the Rock completed
932	Bile duct and intestinal obstructions	933	Algiers founded by Arabs
1037	Polypectomy by wire loop	1023	Paper money is printed in China
1080	Medical school in Salerno and Montpellier	1066	Norman conquest of England
1106	Bloodletting prior to surgery, no extensive surgery	1110	University of Paris founded
1162	Cancer of esophagus, esophageal cannula for stricture and injection of nourishment, rectal obstruction, hysterectomy	1149	University is founded at Oxford
1163	Holistic healing	1163	Notre Dame of Paris built
1215	The Pope prohibits surgery	1215	Magna Carta
1296	Cancer is locally invasive, wide excision, nasopharyngeal cancer; livid tumors are inoperable, general anesthesia with opium	1295	Marco Polo returns to Italy
1315	Clinical separation of benign and malignant breast tumors, surgeons learn regional anatomy	1314	Dante writes the Divine Comedy
1320	Scirrhous and carcinoma are cancers, classification according to size, site and depth, theory of external carcinogens in England	1319	Prosecution for body-snatching
1368	Cancers are cold, diet and purgatives for treatment	1369	Building the Bastille in Paris
1390	Anorectal cancers are firm and incurable	1388	Scotts defeat the English at Chevy Chase

nerves. Because of the unknown anatomic extent of tumors, he advised that cancers be excised widely with healthy tissue around them, but he regarded nasopharyngeal cancers and firm and livid tumors of the extremities inoperable due to local extent of invasion. He promoted thorough physical examination before surgery. During surgery, he used a sponge saturated with opium and mandragora juice for general anesthesia.^{8,9,15}

French surgery was founded by Lanfranc (1252-1315), a native of Milan who was driven out of Italy for political reasons. He practiced medicine and surgery in Paris and was an ardent opponent of the separation of medicine and surgery. He gave the first description of how to differentiate benign tumors of the breast from cancer. He advised surgeons to learn about the complex anatomic setting of vessels and nerves before they operate. Lanfranc summarized his thoughts about cancer in his 2 texts, *Chirurgia Parva* and *Chirurgia Magna*.^{5,10} Henri de Mondeville (1260-1320), a French physician, was the first to publicly reject Galen's nearly 1000-year-old theories. He simplified terminology by pointing out that scirrhous

and carcinoma had the same meaning and both of them were cancer. He divided cancers into simple and compound forms on the basis of history of prior lesions. He also introduced the classification of cancers with consideration of size, anatomic site, and whether the tumors were superficial or deep in location. Mondeville advanced the concept of external carcinogens and assumed that the carcinogens entered the body through orifices of glands.^{9,11,16}

Guy de Chauliac (1300-1368), a French surgeon, devoted one chapter in his book, *Chirurgia Magna*, to skin diseases and cancers. He distinguished hot and cold lesions. The hot tumefactions were pustules, abscesses, and gangrenes, and the cold ones were cancers. He treated operable cancers with wide excision.¹⁷ Patients with inoperable growths were treated with nutritive diet and purgatives. Anorectal lesions were the primary interest of John Arderne (1307-1390), who practiced in London and is remembered as the first proctologist. He noted that many anorectal benign lesions and cancers may present with identical symptoms but that most cancers could be felt

with the tip of the finger as hard indurations or irregular polypoid masses. He regarded blood, mucus, and constriction as cardinal signs of cancer. Despite his extensive surgical experience with anorectal lesions, he recommended only local excision for cancers because, as he wrote in his *De Arte Physicale et de Chirurgia*, he had never seen a person recover from cancer of the rectum.^{9,18}

The physicians and surgeons who cared for cancer patients during the 4000 years covered in this review were the pioneers in oncology. Despite their shortcomings, all contributed many ways to the detection, diagnosis, and treatment of cancer (Table 1).

CONFLICT OF INTEREST DISCLOSURES

The author made no disclosures.

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