

CHAPTER - HISTORY OF MEDICINE

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Introduction

Across the vast epochs of time, the story of medicine has unveiled itself, revealing an intricate tapestry, woven with the threads of exploration, ingenuity, and human perseverance. From the ancient rituals of tribal healers to the sterile halls of modern hospitals, the grand history of medicine serves as humanity's unwavering quest for understanding, healing, and alleviating suffering. Within this chapter, we delve into a captivating journey, tracing the paths of visionary individuals, groundbreaking discoveries, and the evolution of knowledge that have led us to where we are.

Ancient Medicine

In the distant past, healers made strides to comprehend and battle diseases as civilizations sought ways to understand medicine. Imhotep rose to notoriety in Egypt around 2600 BC as the leading figure seen as the earliest physician. His scientific work into strategies and remedies, documented in the distinguished Edwin Smith Papyrus, was devoted to both surgical operations and alternative cures. This paper methodically details multiple ailments such as wounds, fractures, dislocations, and tumors, underlining Imhotep's incredible medical knowledge for the period. Furthermore, the priests and physicians in historic Egypt provided crucial insights into the nuances of the human anatomy via procedures like mummification and the revelation of surgical tools.¹

Beyond Egypt, between 2000 and 1600 BCE, Mesopotamia also thrived in the pursuit of medical knowledge. Healers in this region embraced a holistic approach to healthcare, drawing extensively from nature's resources. Their healing practices relied on remedies derived from plants and herbal medicines, harnessing the inherent power of natural substances. Mesopotamian healers believed in minimizing human intervention, allowing the body's innate healing mechanisms to take precedence. Among their significant contributions was the Babylonian Diagnostic Handbook, an inclusive compilation detailing symptoms, diseases, and corresponding treatments, which laid a strong foundation for the accumulation of medical knowledge in written form. The utilization of antiseptics can be traced to the civilizations of the Egyptians and Greeks, who utilized substances such as vinegar, wine, and specific plant extracts to counter wound infections.²

Emerging from the depths of history, Ayurveda, the ancient and deeply rooted medicinal system of India, traces its origins to 5000 years ago.³ Practitioners of Ayurveda held it in high regard as a comprehensive form of healing, dedicating their practice to divinity and recognizing the paramount importance of health in human existence. The written documentation of this traditional medical approach dates back to a period between 4500 and 1600 BCE,⁴ with one of the earliest texts being the revered Charak Samhita, authored by the esteemed Maharishi Charak.⁵ The Charak Samhita provides profound insights into diagnosis and preventive medicine, meticulously cataloging over 2000 medicinal herbs and their therapeutic uses.⁶ Sushruta, another visionary of Ayurvedic medicine, is widely acclaimed as the 'Father of Surgery.' Notably, he accomplished the world's first plastic surgery approximately 2800 years ago.⁷ India's advancements in this ancient era extended to surgical innovations, herbal remedies, and an unparalleled understanding of human physiology and anatomy, leaving an enduring mark on the annals of medical history.

During the period from 1600 BCE to 220 AD, another Asian country situated north of India, namely China, also experienced significant flourishing in the field of medicine.⁸ The traditional concept of medicine in China was intricately intertwined with Taoist philosophy, emphasizing the attainment of balance and harmony within the body.⁹ Chinese physicians during this era utilized herbal medicine, acupuncture, and moxibustion to restore the flow of vital energy, known as qi.¹⁰

One of the prominent ancient Chinese treatises, the Huangdi Neijing, expounds on diagnostic methods, herbal treatments, and lifestyle recommendations. This text stands as a testament to the profound medical knowledge cultivated in ancient China.¹¹

Birth of Scientific medicine

During the emergence of scientific thought in ancient Greece around the 5th century BCE, the advent of scientific medicine marked a transformative period in the history of healing practices. Central to this development was the Greek emphasis on rationality, observation, and critical thinking, which laid the cornerstone for medical thought. Among the notable visionaries of this era was Hippocrates, revered as the 'Father of Medicine.' His invaluable contributions included promoting clinical observation as a fundamental diagnostic tool and formulating the humoral theory of health and disease. According to the humoral theory, a person's well-being depended on the balance of four bodily humors: blood, phlegm, yellow bile, and black bile. Any imbalance in these humors was believed to lead to illness. Further, Hippocrates theorized that illnesses had physical causes, in contrast to the notion that they occurred as a result of divine rage or mysterious forces. Subsequently, he opened the door to a logical procedure of comprehending and caring for health difficulties. His teachings were documented in the Hippocratic Corpus, a much-respected compilation of medical writings that carried medical information throughout the ages.¹²

Building on the foundation of Hippocrates, the physician Galen accomplished considerable progress in anatomical exploration during the 2nd century CE in the Roman era. His pioneering

endeavor in dissection and scrupulous observance of the human body revolutionized medical insight. Galen's ideas on the circulatory and nervous systems, among numerous others, left a long-lasting effect on medicinal contemplation for years to come, despite certain faults in his labor. His contributions were foundational in the progression of scientific medicine. The decline of the Roman Empire and the rise of religious dogma briefly hindered empirical approaches to medical inquiry. Hippocrates and Galen's ideas remained important as medicine emerged from the 5th century BCE to the 2nd century CE. Their principles prompted later medical progress, leading to the Renaissance and advancements in medieval medicine.¹³

Medieval Medicine

During the captivating embrace of medieval times, medicine transformed significantly, and monasteries played a prominent role. Scattered across Europe and Asia, these sanctums preserved ancient medical texts during the early Middle Ages. Devoted monks served as skilled practitioners and scribes, diligently copying and safeguarding invaluable manuscripts. This remarkable phase, spanning from the 5th to the 15th century CE, witnessed the noble preservation of medical heritage.¹⁴ During this period, the 12th century CE marked the emergence of illustrious figures like Hildegard of Bingen. She rose to the forefront of medieval herbal medicine and natural remedies, making noteworthy contributions to the enrichment of medical knowledge.¹⁵ It was during these transformative years that Ayurveda attained its zenith, flourishing and diversifying to embrace comprehensive approaches to well-being, encompassing herbal therapeutics, dietary prescriptions, and even surgical interventions.¹⁶ Alongside these medical advancements, European history celebrates Roger Bacon, a brilliant figure of the 13th century, renowned for his revolutionary invention of spectacles. This solution brought relief to millions of people suffering from vision problems, granting them the gift of clear sight. Bacon's invention in 1268 CE became a significant milestone in the journey of ocular well-being.¹⁷

In the pursuit of knowledge and innovation, the medieval period witnessed momentous advancements in the domain of distillation, an art cultivated and refined by celebrated alchemist, Jabir ibn Hayyan (Geber).¹⁸ This transformative process empowered the extraction of quintessential oils from botanical wonders, giving rise to the splendid world of perfumery—a realm encompassing both olfactory allure and therapeutic potency in the annals of medicine. These essential oils emerged as crucial pillars of medicinal preparations and treatments, revealing previously unexplored realms of pharmacology and broadening the possibilities for healing.¹⁹

In the 14th century, a deadly pandemic called the Black Death hit Europe. *Yersinia pestis* bacterium was an etiology for this and caused a lot of death and catastrophe.²⁰ Medieval physicians in that time tried various treatments to fight the disease because its outbreak recurred. They employed herbal remedies, such as mixtures containing aromatic substances like camphor and vinegar, to cleanse the air and protect against the infection. Additionally, respiratory masks filled with fragrant materials were advised as a preventive measure, and attempts at quarantine were implemented to limit the spread of the plague.²¹ Despite earnest efforts, the understanding

of contagion and disease transmission remained limited, leading to largely ineffective medical responses. However, the devastating impact of the Black Death prompted later investigations into infectious diseases, eventually contributing to the development of public health measures in the following centuries. Simultaneously, the establishment of apothecaries and pharmacies marked an era of unprecedented accessibility and efficacy in medicinal formulations. Aptly called apothecaries, these skilled pharmacists expertly compounded and dispensed a variety of drugs and herbal remedies, ensuring precise dosing and efficacious formulations, thereby elevating medical care to unparalleled heights.²²

Renaissance and the Birth of Modern Medicine

Throughout the centuries, humanity has advanced significantly in its understanding of illness and treatments, particularly in the timespan during the 14th to 17th centuries. During this era, medical societies and organizations held to a great extent a momentous role in stimulating joint ventures between medical experts and distributing medical know-how, leading to tremendous improvements in understanding and treating diseases.²³

Paracelsus, an authoritative Swiss doctor, and alchemist, contributed significantly to the revolution of medicine in the 16th century by integrating chemical medicine and advocating for the use of chemical remedies and alchemical principles. His ingenious methodology concerned understanding diseases as imbalances of chemicals within the body.²⁴ Paracelsus amalgamated chemistry with organic medicine, laying the foundation for pharmacology being a distinct specialty and steering a different direction for medical practice.²⁵ The innovative discoveries in the 16th and 17th centuries gave rise to the emergence of iatrochemistry, blending chemistry into medicine for curing illnesses with chemical remedies. This alteration broadened inner medical solutions, exploring chemical substances with curative properties, signifying the future of medical treatment and marking the way for inventive pharmaceutical breakthroughs.²⁶

In the 17th century, two significant breakthroughs transformed the history of medicine. The first was the introduction of quinine, derived from the cinchona tree's bark, which effectively combated deadly malaria, offering hope to countless individuals and improving patient outcomes. This success highlighted the importance of exploring natural remedies in the search for effective treatments.²⁷ The second breakthrough was the practice of variolation (inoculation) against smallpox, introduced to England by Lady Mary Wortley Montagu after witnessing it in the Ottoman Empire. Variolation involved infecting individuals with a milder form of smallpox to confer immunity, paving the way for future investigations into disease prevention.²⁸

Age of Enlightenment and Medical Achievements

During the Age of Enlightenment, mankind embraced knowledge and reason, building on top of the epochs of transitioning characterized by the Renaissance. In 1628, William Harvey revealed pulmonary circulation, modifying our apprehension of the circulatory system.²⁹ Later, in 1666, Richard Lower's intravenous transfusion of blood opened up the possibility of novel medical treatments.³⁰ Robert Hooke's microscope in 1665 gave insight into the world of cells,³¹ and in 1683, Antonie van Leeuwenhoek's revelation of bacteria revolutionized the face of medicine.³²

The Enlightenment encouraged progress, maneuvering the path of medicine and beckoning humanity's quest for healing.

Edward Jenner's momentous revelation in 1796 acted as an integral leap forward, introducing the primary smallpox vaccine that was obtained from cowpox. This innovation ended the threat of smallpox and spurred further studies into manufacturing other vaccines for contagious ailments, ultimately making vaccination one of the most impressive techniques for preserving public health.³³ In 1882, the renowned German physician and microbial specialist Robert Koch identified *Mycobacterium tuberculosis* as the cause of tuberculosis, a major breakthrough in determining and understanding the illness. This revelation allowed for the progression of effective treatments and well-being protocols to prevent the transmission of the disease.³⁴

In the middle of the 19th century, the English medical practitioner Joseph Lister founded the use of antiseptic procedures. He advocated utilizing carbolic acid to decontaminate medical implements and dress wounds, thereby reducing the number of diseases and surgical issues.³⁵

The Scottish surgeon John Hunter made an enormous contribution to the domain of surgery. He enhanced the management of wounds, brought knowledge surrounding inflammation, and made advances in surgical tactics. Moreover, his emphasis on precise observation and recording provided the foundation for today's surgical procedures.³⁶

20th Century and Modern Medicine

Antibiotics

In 1928, Sir Alexander Fleming, a Scottish bacteriologist, made a groundbreaking discovery at St. Mary's Hospital in London. While studying bacteria, Fleming accidentally left a petri dish of *Staphylococcus* bacteria uncovered on his laboratory bench. Upon his return, he noticed that a mold called *Penicillium* had grown on the dish, inhibiting the bacterial growth around it. Fleming identified this mold as the source of a substance he named "penicillin."³⁷ In the relentless search for medical breakthroughs, streptomycin emerged as a pivotal discovery during a systematic exploration of antibiotic substances in soil microorganisms. American microbiologist Selman Waksman and his team, in 1943, identified streptomycin's efficacy against tuberculosis and other bacterial infections, marking a significant turning point in the battle against infectious diseases. Waksman's groundbreaking work with streptomycin not only reduced mortality rates from tuberculosis but also earned him the prestigious Nobel Prize in Physiology or Medicine in 1952.³⁸ Another vital antibiotic, chloramphenicol, was first isolated from the bacterium *Streptomyces venezuelae* found in a soil sample collected from Venezuela. Discovered in 1947 by American scientists David Gottlieb, Rachel Storm, and Julian Suschitzky, chloramphenicol showcased a broad-spectrum activity that rendered it invaluable in treating various infections. However, its association with rare but severe side effects necessitated restrictions on its usage in many countries.³⁹ Tetracycline, another widely used broad-spectrum antibiotic, emerged from a soil sample collected in Missouri, USA, specifically from the bacterium *Streptomyces aureofaciens*. Its discovery in 1948 by American botanist Benjamin Minge Duggar significantly expanded the range of infections that could be effectively treated before newer antibiotics were

developed.⁴⁰ In 1952, J.M. McGuire and his colleagues made a remarkable discovery during a systematic screening of soil bacteria – erythromycin. This antibiotic with a unique chemical structure proved to be a vital alternative to penicillin, particularly for patients with penicillin allergies, significantly enhancing the antibiotic arsenal.⁴¹ Metronidazole, a product of a research program seeking new medications against *Trichomonas vaginalis*, was discovered in the 1960s by researchers at Rhône-Poulenc in France. Its distinctive mode of action targeting anaerobic organisms and parasites made it an invaluable addition to the antibiotic arsenal.⁴² In the late 1950s, Anthony Alfred Walter Long and John Herbert Charles Nayler developed amoxicillin by adding an extra hydroxyl group to the structure of ampicillin, a broad-spectrum penicillin. This modification resulted in amoxicillin's improved stability and efficacy against many bacteria, solidifying its position as one of the most commonly prescribed antibiotics.⁴³ Azithromycin, discovered in the 1980s by researchers at Pliva, a Croatian pharmaceutical company, emerged as a formidable option for treating respiratory and sexually transmitted infections. Derived from erythromycin through chemical modifications, azithromycin offered enhanced tissue penetration, a prolonged half-life, and the convenience of once-daily dosing.⁴⁴ The relentless pursuit of potent and diverse antibiotics has etched these discoveries in the annals of medical history, shaping the course of medicine and saving countless lives worldwide.

Analgesics

In ancient civilizations like the Egyptians, Greeks, and Chinese, natural remedies like opium poppy and various herbs were used to alleviate pain. These remedies served as some of the earliest forms of analgesia, providing relief from discomfort and easing suffering.⁴⁵ In 1804, German pharmacist Friedrich Sertürner achieved a significant breakthrough by isolating morphine from opium. This marked the first isolation of a powerful alkaloid with extraordinary pain-relieving capabilities. Morphine's discovery laid the foundation for the development of more targeted and potent analgesics.⁴⁶ Later in the same century, French chemist Charles Frederic Gerhardt synthesized acetylsalicylic acid, later known as aspirin. Aspirin exhibited both anti-inflammatory and analgesic properties, making it an invaluable pain reliever, especially for conditions involving inflammation.⁴⁷

In the early 20th century, significant advancements were made in the field of analgesics and pain management. Barbiturates were introduced as sedative-hypnotic agents in the early 1900s, initially used for pain relief and anesthesia but limited due to their potential for addiction and severe side effects.⁴⁸ In the mid-20th century, nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and naproxen were developed as effective analgesics with anti-inflammatory properties.⁴⁹ Around the same time, opioid analgesics derived from natural or synthetic sources underwent significant advancements and became crucial for managing severe pain, albeit with concerns of dependence and abuse.⁵⁰ Also, during the mid-20th century, acetaminophen (Paracetamol) emerged as a widely used analgesic with limited anti-inflammatory effects.⁵¹ Throughout the 20th century and beyond, ongoing pharmaceutical research led to the development of new analgesics, including selective COX-2 inhibitors, tramadol, and modified

opioid formulations to reduce abuse potential.⁵² Alongside drug development, advancements in medical techniques introduced improved pain management options, such as nerve blocks and epidurals, providing alternative and targeted approaches to alleviate pain in various conditions, thereby enhancing patient care.⁵³

Antiseptics

The use of antiseptics can be traced back to ancient civilizations such as the Egyptians and Greeks. They applied substances like wine, vinegar, and certain plant extracts to prevent infections in wounds.⁵⁴ In the 19th century, Dr. Ignaz Semmelweis introduced hand washing with lime water to reduce infection deaths in maternity wards during childbirth.⁵⁵ His work laid the foundation for modern antiseptic practices, saving countless lives. British surgeon Joseph Lister is credited with popularizing antiseptic surgery. Building on the work of Louis Pasteur, who proposed the germ theory of disease, Lister successfully used carbolic acid (phenol) as an antiseptic during surgeries to prevent infections. This significantly lowered post-operative infection rates and revolutionized surgical practices.⁵⁶ Over time, various antiseptic techniques were introduced. These developments encompassed the introduction of various antiseptic agents and practices. Iodine solutions became a popular choice for disinfecting wounds and surgical sites due to their broad-spectrum antimicrobial properties.⁵⁷ Hydrogen peroxide was also embraced for its effectiveness in killing bacteria and preventing infection.⁵⁸ Additionally, alcohol-based solutions gained prominence as effective hand sanitizers, proving crucial in maintaining hygiene and preventing the spread of pathogens in medical settings.⁵⁹ These diverse antiseptic techniques continue to be refined and adapted, playing a vital role in modern infection control measures.

Anesthesia

In the 20th century, anesthesia underwent a transformative evolution, introducing safer and more advanced techniques that revolutionized patient care during surgical procedures. In the year 1847, inhalation anesthetics like chloroform were introduced, proving more potent than ether but with higher risks, and gradually declined in use.⁶⁰ Later, in the 20th century, specifically in the 1950s, halothane, a new inhalation anesthetic, was developed, providing greater control over anesthesia depth and fewer side effects.⁶¹ During the 1970s, isoflurane and other modern inhalation anesthetics came into use, further refining anesthesia practices.⁶² In 1977, the intravenous anesthetic propofol was introduced, revolutionizing rapid induction and recovery times.⁶³ These advancements in anesthesia contributed significantly to patient safety and comfort during surgical procedures, marking a turning point in the evolution of modern anesthesiology. The 20th century witnessed substantial progress in anesthesia, making it safer and more specialized. Anesthesia monitoring and equipment, such as pulse oximeters and capnographs, enhanced patient safety during surgery.⁶⁴

Regional anesthesia techniques, like epidurals and spinals, became common for pain management during childbirth and surgery.⁶⁵ The field of anesthesiology emerged as a specialized medical discipline, leading to advanced research, training, and improved patient care.

Antidiabetic drugs

Diabetes, a metabolic disorder characterized by high blood sugar levels, has seen significant advancements in treatment over the years. The discovery of insulin in the 1920s revolutionized diabetes management, providing life-saving treatment for type 1 diabetes.⁶⁶ Additionally, the introduction of sulfonylureas in the 1950s paved the way for oral medications that stimulate insulin production.⁶⁷ Metformin, a widely prescribed biguanide in the 1970s, became a cornerstone of type 2 diabetes treatment.⁶⁸ Alpha-glucosidase inhibitors, developed in the 1980s, helped slow carbohydrate absorption.⁶⁹ In the 1990s, thiazolidinediones (TZDs) improved insulin sensitivity, and incretin-based therapies emerged in the 2000s.⁷⁰ The 2010s brought sodium-glucose co-transporter 2 (SGLT2) inhibitors, which increase glucose excretion in the urine, further expanding the arsenal of diabetic medications.⁷¹ This continuous progress underscores the commitment to finding effective solutions for diabetes management.

Drugs for asthma

Asthma, a respiratory condition with airway inflammation and narrowing, can be deadly due to severe attacks leading to respiratory failure. In the 19th century, theophylline, a natural compound found in tea leaves, served as a bronchodilator to relax airways.⁷² Synthetic beta-agonists like isoproterenol emerged in the 20th century with improved potency and fewer side effects.⁷³ The introduction of albuterol in the 1960s marked a significant advancement in targeted asthma treatments.⁷⁴ Corticosteroids were discovered around the same era, reducing inflammation and preventing attacks.⁷⁵ Later, combination inhalers with LABAs and corticosteroids became standard, improving symptom control. Alternative options like leukotriene modifiers and monoclonal antibodies, such as omalizumab, were developed.⁷⁶ Ongoing research explores biological therapies for severe cases, enhancing global asthma management and quality of life.

Chemotherapy

Cancer is a complex and devastating disease characterized by the uncontrolled growth and spread of abnormal cells in the body. The history of chemotherapy, the use of drugs to treat cancer, can be traced back to ancient times when different techniques were employed to alleviate cancer symptoms. Around 3000 BCE, ancient Egyptian texts documented the early use of such practices.⁷⁷ However, the modern era of chemotherapy began during World War II when, in the 1940s, researchers discovered nitrogen mustard gas as a potential cancer treatment.⁷⁸

In the 1960s, a significant advancement in cancer treatment occurred with the development of Tamoxifen, a hormone therapy drug that became a major treatment for breast cancer.⁷⁹ Moving into the 1970s, the discovery and approval of Doxorubicin, a widely used chemotherapy drug,

further expanded the arsenal of cancer treatments.⁸⁰ The 1980s saw the development of Interferon and interleukins as immunotherapy treatments for specific types of cancer, bringing a new approach to combating the disease.⁸¹ In the 1990s, Rituximab, a monoclonal antibody, received approval for the treatment of non-Hodgkin lymphoma, offering another targeted therapy option.⁸² The 2000s marked a revolution in cancer treatment with the introduction of targeted therapies like imatinib (Gleevec) and trastuzumab (Herceptin), which showed remarkable efficacy against certain cancer types.⁸³ In the 2010s, a breakthrough came in the form of immune checkpoint inhibitors, such as pembrolizumab (Keytruda) and nivolumab (Opdivo), emerging as powerful immunotherapies for various cancers, opening new avenues of hope for patients worldwide.⁸⁴ The history of chemotherapy has seen remarkable progress and innovation, transforming the landscape of cancer treatment and offering renewed optimism for the future.

Antihypertensive drugs

Hypertension, commonly known as high blood pressure, is a prevalent and severe medical condition characterized by elevated blood pressure levels in the arteries. The history of hypertension treatment dates back centuries, with ancient healers using herbal remedies and lifestyle changes to manage the condition.⁸⁵ However, the modern era of hypertension management began in the mid-20th century when effective antihypertensive drugs were introduced. In the 1950s, reserpine emerged as one of the first widely used medications, derived from the Indian snakeroot plant.⁸⁶ Subsequently, in the 1960s, thiazide diuretics gained prominence by promoting increased urination to lower blood pressure effectively.⁸⁷ These years also saw the rise of beta-blockers, targeting the heart and circulatory system to reduce blood pressure,⁸⁸ followed by the development of calcium channel blockers, which helped relax and widen blood vessels, offering additional treatment options.⁸⁹ Moving into the last few decades of the 20th century, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) emerged as key players, effectively targeting the renin-angiotensin-aldosterone system to regulate blood pressure.⁹⁰ In the 2000s, a combination therapy approach gained traction, where multiple antihypertensive medications were prescribed together to achieve better blood pressure control.⁹¹ As we progressed into the 21st century, newer classes of antihypertensive drugs, like direct renin inhibitors and aldosterone antagonists, were developed to further enhance hypertension management.^{92,93} These advances in hypertension research and pharmacology have significantly improved the prognosis for individuals with high blood pressure, reducing the risk of serious complications such as heart attacks, strokes, and kidney damage. Continued research and innovation offer hope for even better treatments in the future, aiming to reduce the global burden of hypertension and its associated health risks.

To conclude, the phenomenal expansion in the journey of medical history driven by increased human understanding and modernization of technology has led to remarkable scientific progress in the modern era. This historical perspective guides us to confront challenges, showcases the advancement in the field of medicine, and facilitates improved healthcare for all. It reminds us to

widen our horizons in medical education, aiming for better treatment and the overall well-being of society as a whole.

References:

1. Barton M. Imhotep – The first physician. *Past Medical History* 2016;2.
2. Mark JJ. Medicine in Ancient Mesopotamia. *World History Encyclopedia* 2023;687.
3. Guha A. Where does Ayurveda come from? *Taking charge of your health & wellbeing*
4. Kala CP. Preserving ayurvedic herbal formulations by Vaidyas: The traditional healers of the Uttaranchal Himalaya region in India. *American Botanical Council* 2006; 70: 42-50.
5. Mishra L, Singh BB, Dagenais S. Ayurveda: Ahistorical perspective and principles of the traditional healthcare system in India. *Altern Ther Health Med* 2001;7(2):36-42.
6. Bhavana KR, Shreevathsa. *Medical geography in Charaka Samhita*. *Ayu* 2014;35(4):371-7. doi: 10.4103/0974-8520.158984.
7. Singh V. Sushruta: The father of surgery. *Natl J Maxillofac Surg* 2017;8(1):1-3. doi: 10.4103/njms.NJMS_33_17.
8. Zeng H, Qiao Y, Luo X, Chen X, Wang Z, Pan H, Wang Q, Zheng GQ. History and development of TCM case report in a real-world setting. *Evid Based Complement Alternat Med* 2021;2021:7402979. doi: 10.1155/2021/7402979.
9. Ping, Z., & Dong, Z. (2021). Taoist Medicine. *Interdisciplinary Journal for Religion and Transformation in Contemporary Society*, 7(2), 398-405. doi.org/10.30965/23642807-bja10026
10. Marshall AC. Traditional Chinese Medicine and Clinical Pharmacology. *Drug Discovery and Evaluation: Methods in Clinical Pharmacology* 2020;2:455–82. doi: 10.1007/978-3-319-68864-0_60.
11. Curran J. The yellow emperor’s classic of internal medicine. *BMJ* 2008;336(7647):777. doi: 10.1136/bmj.39527.472303.4E.
12. Kleisaris CF, Sfakianakis C, Papathanasiou IV. Health care practices in ancient Greece: The Hippocratic ideal. *J Med Ethics Hist Med* 2014;7:6.
13. National Library of Medicine. Greek Medicine. [Internet] 2012 [Last updated 2015, July 16]
14. Black, Winston. *The Middle Ages: Facts and Fictions*. ABC-CLIO, 2018,169–190.
15. Hildegard of Bingen Medicine. Healthy Hildegard.
16. Jaiswal YS, Williams LL. A glimpse of Ayurveda - The forgotten history and principles of Indian traditional medicine. *J Tradit Complement Med* 2016;7(1):50-53. doi: 10.1016/j.jtcme.2016.02.002.
17. Crowley T. Roger Bacon. *Encyclopedia Britannica* [Internet]. 2023
18. Amr SS, Tbakhi A. Jabir ibn Hayyan. *Ann Saudi Med* 2007;27(1):52–3. doi: 10.5144/0256-4947.2007.53.
19. Ramsey JT, Shropshire BC, Nagy TR, Chambers KD, Li Y, Korach KS. Essential oils and health. *Yale J Biol Med* 2020;93(2):291-305.

20. Glatter KA, Finkelman P. History of the plague: An ancient pandemic for the age of COVID-19. *Am J Med* 2021;134(2):176-181. doi: 10.1016/j.amjmed.2020.08.019.
21. Chen W, Vermaak I, Viljoen A. Camphor--a fumigant during the black death and a coveted fragrant wood in ancient Egypt and Babylon-A review. *Molecules* 2013;18(5):5434-54. doi: 10.3390/molecules18055434.
22. Apothecaries from the eighteenth century onward: England. Center for the History of Medicine. [Internet].
23. Toledo-Pereyra, Luis H. Medical renaissance. *Journal of Investigative Surgery* 2015; 28 (3): 127–130.
24. New World Encyclopedia. Paracelsus. [Internet]. New World Encyclopedia; c2008-2023
25. American Association for the Advancement of Science. Paracelsus: The Man Who Brought Chemistry into Medicine. [Internet].
26. Wikipedia. Iatrochemistry. [Internet]. Wikipedia, The Free Encyclopedia; <https://en.wikipedia.org/wiki/Iatrochemistry>
27. Achan J, Talisuna AO, Erhart A, Yeka A, Tibenderana JK, Baliraine FN, et al. Quinine, an old anti-malarial drug in a modern world: Role in the treatment of malaria. *Malar J* 2011;10:144. doi: 10.1186/1475-2875-10-144.
28. Time. Mary Montagu: The Woman Who Discovered Smallpox Variolation. [Internet]; 2019
29. Friedland G. Discovery of the function of the heart and circulation of blood. *Cardiovasc J Afr* 2009;20(3):160.
30. Fastag E, Varon J, Sternbach G. Richard Lower: The origins of blood transfusion. *J Emerg Med* 2013;44(6):1146-50. doi: 10.1016/j.jemermed.2012.12.015.
31. National Geographic Education. Cell Theory. [Internet]. National Geographic Society;
32. Lane N. The unseen world: Reflections on Leeuwenhoek (1677) ‘Concerning little animals’. *Phil Trans R Soc B* 2015;370: 20140344.
33. Riedel S. Edward Jenner and the history of smallpox and vaccination. *Proc Bayl Univ Med Cent* 2005;18(1):21-5. doi: 10.1080/08998280.2005.11928028.
34. Cambau E, Drancourt M. Steps towards the discovery of Mycobacterium tuberculosis by Robert Koch, 1882. *Bacteriology* 2014;20(3). doi: 10.1111/1469-0691.12555.
35. Michaleas S N, Laios K, Charalabopoulos A, et al. Joseph Lister (1827-1912): A Pioneer of Antiseptic Surgery. *Cureus* 2022;14(12): e32777. doi:10.7759/cureus.32777
36. Britannica, The editors of encyclopaedia. "John Hunter". *Encyclopedia Britannica* 2023. <https://www.britannica.com/biography/John-Hunter-British-surgeon>.
37. American chemical society international historic chemical landmarks. Discovery and development of penicillin.
38. Woodruff HB, Selman A, Waksman, Winner of the 1952 Nobel prize for physiology or medicine. *Appl Environ Microbiol.* 2014;80(1):2-8.
39. Dinos GP, Athanassopoulos CM, Missiri DA, Giannopoulou PC, Vlachogiannis IA, Papadopoulos GE, et al. Chloramphenicol derivatives as antibacterial and anticancer agents: Historic problems and current solutions. *Antibiotics* 2016;5(2):20. doi:10.3390/antibiotics5020020.

40. Chopra I, Roberts M. Tetracycline antibiotics: Mode of action, applications, molecular biology, and epidemiology of bacterial resistance. *Microbiol Mol Biol Rev* 2001;65(2):232-260. doi: 10.1128/MMBR.65.2.232-260.2001.
41. Cyphert EL, Wallat JD, Pokorski JK, von Recum HA. Erythromycin modification that improves its acidic stability while optimizing it for local drug delivery. *Antibiotics* 2017;6(2):11. doi:10.3390/antibiotics6020011.
42. Cudmore SL, Delgaty KL, Hayward-McClelland SF, Petrin DP, Garber GE. Treatment of infections caused by metronidazole-resistant trichomonas vaginalis. *Clin Microbiol Rev* 2004;17(4):783-793. doi: 10.1128/CMR.17.4.783-793.2004.
43. Fischer J, Ganellin CR. Analogue-based drug discovery. *John Wiley & Sons* 2006; 490. ISBN 978-3-527-60749-5.
44. Sandman Z, Iqbal OA. Azithromycin. [Updated 2023 Jan 15]. In: StatPearls [Internet].
45. Bandyopadhyay S. An 8,000-year history of use and abuse of opium and opioids: How that matters for a successful control of the epidemic? *Neurology* 2019;92(15).
46. Krishnamurti C, Rao SC. The isolation of morphine by Serturmer. *Indian J Anaesth* 2016; 60(11):861-862. doi: 10.4103/0019-5049.193696.
47. Higuchi S, Osada Y, Shioiri Y, Tanaka N, Otomo S, Aihara H. The modes of anti-inflammatory and analgesic actions of aspirin and salicylic acid. *Nihon Yakurigaku Zasshi* 1985;85(1):49-57. doi: 10.1254/fpj.85.49.
48. López-Muñoz F, Ucha-Udabe R, Alamo C. The history of barbiturates a century after their clinical introduction. *Neuropsychiatr Dis Treat* 2005;1(4):329-43.
49. Ghlichloo I, Gerriets V. Nonsteroidal anti-inflammatory drugs (NSAIDs) [Updated 2023 May 1]. In: StatPearls [Internet].
50. Bethesda. LiverTox: Clinical and research information on drug-induced liver injury *National Institute of Diabetes and Digestive and Kidney Diseases* 2012.
51. Freo U, Ruocco C, Valerio A, Scagnol I, Nisoli E. Paracetamol: A review of guideline recommendations. *J Clin Med* 2021;10(15):3420. doi: 10.3390/jcm10153420
52. Burgess G, Williams D. The discovery and development of analgesics: New mechanisms, new modalities. *J Clin Invest* 2010;120(11):3753-9. doi: 10.1172/JCI43195.
53. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. *Cochrane Database Syst Rev*. 2018;(5) doi:10.1002/14651858.CD000331.
54. Antoniewicz J, Jakubczyk K, Kwiatkowski P, Maciejewska-Markiewicz D, Kochman J, Rębacz-Maron E, Janda-Milczarek K. Analysis of antioxidant capacity and antimicrobial properties of selected polish grape vinegars obtained by spontaneous fermentation. *Molecules* 2021;26(16):4727. doi: 10.3390/molecules26164727
55. Pittet D, Allegranzi B. Preventing sepsis in healthcare - 200 years after the birth of Ignaz Semmelweis. *Euro Surveill*. 2018;23(18):18-00222. doi:10.2807/1560-7917.ES.2018.23.18.18-00222.
56. Michaleas SN, Laios K, Charalabopoulos A, Samonis G, Karamanou M. Joseph Lister (1827-1912): A pioneer of antiseptic surgery. *Cureus* 2022;14(12):e32777. doi:10.7759/cureus.32777.
57. Durani P, Leaper D. Povidone-iodine: Use in hand disinfection, skin preparation and antiseptic irrigation. *Int Wound J* 2008;5(3):376-87. doi: 10.1111/j.1742-481X.2007.00405.x

58. Juven BJ, Pierson MD. Antibacterial effects of hydrogen peroxide and methods for its detection and quantitation. *J Food Prot* 1996;59(11):1233-1241. doi: 10.4315/0362-028X-59.11.1233.
59. McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. *Clin Microbiol Rev* 1999;12(1):147-79. doi: 10.1128/CMR.12.1.147.
60. Khan KS, Hayes I, Buggy D. Pharmacology of anaesthetic agents II: Inhalation anaesthetic agents. *Contin Educ Anaesth Crit Care Pain* 2014;14(3):106-111. doi:10.1093/bjaceaccp/mkt038
61. Giesecke AH. First use of halothane in the United States. *Bull Anesth Hist* 2008;26(2):1,4. doi: 10.1016/s1522-8649(08)50011-4.
62. Chau PL. New insights into the molecular mechanisms of general anaesthetics. *Br J Pharmacol* 2010;161(2):288-307. doi: 10.1111/j.1476-5381.2010.00891.x.
63. Sahinovic MM, Struys MMRF, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. *Clin Pharmacokinet* 2018;57(12):1539-1558. doi: 10.1007/s40262-018-0672-3.
64. Pedersen T, Nicholson A, Hovhannisyan K, Møller AM, Smith AF, Lewis SR. Pulse oximetry for perioperative monitoring. *Cochrane Database Syst Rev* 2014 17;(3):CD002013. doi: 10.1002/14651858.CD002013.pub3.
65. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. *Cochrane Database Syst Rev* 2018;5(5):CD000331. doi: 10.1002/14651858.CD000331.pub4.
66. Vecchio I, Tornali C, Bragazzi NL, Martini M. The discovery of insulin: An important milestone in the history of medicine. *Front Endocrinol* 2018;9:613. doi: 10.3389/fendo.2018.00613.
67. Kalra S, Aamir AH, Raza A, Das AK, Azad Khan AK, Shrestha D, Qureshi MF, Md Fariduddin, Pathan MF, Jawad F, Bhattarai J, Tandon N, Somasundaram N, Katulanda P, Sahay R, Dhungel S, Bajaj S, Chowdhury S, Ghosh S, Madhu SV, Ahmed T, Bulughapitiya U. Place of sulfonylureas in the management of type 2 diabetes mellitus in South Asia: A consensus statement. *Indian J Endocrinol Metab.* 2015;19(5):577-96. doi: 10.4103/2230-8210.163171
68. Bailey CJ. Metformin: Historical overview. *Diabetologia* 2017 Sep;60(9):1566-1576. doi: 10.1007/s00125-017-4318-z.
69. Derosa G, Maffioli P. α -Glucosidase inhibitors and their use in clinical practice. *Arch Med Sci* 2012;8(5):899-906.
70. Lazar MA. Reversing the curse on PPAR γ . *J Clin Invest* 2018;128(6):2202-04. doi: 10.1172/JCI121392
71. Bays H. Sodium glucose co-transporter type 2 (SGLT2) inhibitors: Targeting the kidney to improve glycemic control in diabetes mellitus. *Diabetes Ther* 2013;4(2):195-220. doi: 10.1007/s13300-013-0042-y
72. Barnes PJ. Theophylline. *Pharmaceuticals (Basel)* 2010;3(3):725-747. doi: 10.3390/ph3030725.
73. Barisione G, Baroffio M, Crimi E, Brusasco V. Beta-adrenergic agonists. *Pharmaceuticals (Basel)* 2010;3(4):1016-1044. doi: 10.3390/ph3041016.
74. Stein SW, Thiel CG. The history of therapeutic aerosols: A Chronological review. *J Aerosol Med Pulm Drug Deliv* 2017;30(1):20-41. doi: 10.1089/jamp.2016.1297

75. Barnes PJ. How corticosteroids control inflammation: Quintiles prize lecture 2005. *Br J Pharmacol* 2006;148(3):245-254. doi: 10.1038/sj.bjp.0706736
76. Pelaia C, Crimi C, Vatrella A, Tinello C, Terracciano R, Pelaia G. Molecular targets for biological therapies of severe asthma. *Front Immunol* 2020;11. doi:10.3389/fimmu.2020.603312
77. Faguet, G.B. A brief history of cancer: Age-old milestones underlying our current knowledge database. *Int J Cancer* 2015; 136:2022-36.
78. Papac RJ. Origins of cancer therapy. *Yale J Biol Med* 2001;74: 391-398.
79. Goetz MP. The development of endoxifen for breast cancer. *Clin Adv Hematol Oncol* 2018;16(2):102-5.
80. Thorn CF, Oshiro C, Marsh S, Hernandez-Boussard T, McLeod H, Klein TE, Altman RB. Doxorubicin pathways: Pharmacodynamics and adverse effects. *Pharmacogenet Genomics* 2011;21(7):440-6. doi: 10.1097/FPC.0b013e32833ffb56
81. Akbulut H. Immune gene therapy of cancer. *Turk J Med Sci* 2020;50(SI-2):1679-90. doi: 10.3906/sag-2005-327.
82. Maloney DG. Newer treatments for Non-Hodgkin's Lymphoma: Monoclonal antibodies. *Oncology* 1998;12(10)
83. Ross JS, Schenkein DP, Pietrusko R, Rolfe M, Linette GP, Stec J, Stagliano NE, Ginsburg GS, Symmans WF, Puztai L, Hortobagyi GN. Targeted therapies for cancer. *Am J Clin Pathol* 2004;122:598-609. doi: 10.1309/5CWPU41AFR1VYM3F
84. Jaber N. Study details long-term side effects of immune checkpoint inhibitors. *National Cancer Institute* 2021.
85. Saklayen MG, Deshpande NV. Timeline of history of hypertension treatment. *Front Cardiovasc Med* 2016;3:3. doi: 10.3389/fcvm.2016.00003
86. Lobay D. Rauwolfia in the treatment of hypertension. *Integr Med (Encinitas)* 2015;14(3):40-6
87. Roush GC, Abdelfattah R, Song S, Ernst ME, Sica DA, Kostis JB. Hydrochlorothiazide vs chlorthalidone, indapamide, and potassium-sparing/hydrochlorothiazide diuretics for reducing left ventricular hypertrophy: A systematic review and meta-analysis. *J Clin Hypertens (Greenwich)* 2018;20(10):1507-15.
88. Wiysonge CS, Bradley HA, Volmink J, Mayosi BM, Opie LH. Beta-blockers for hypertension. *Cochrane Database Syst Rev* 2017;1(1):CD002003. doi: 10.1002/14651858.CD002003.pub5.
89. Godfraind T. Discovery and development of calcium channel blockers. *Front Pharmacol* 2017;8:286. doi: 10.3389/fphar.2017.00286
90. Acharya KR, Sturrock ED, Riordan JF, Ehlers MR. Ace revisited: A new target for structure-based drug design. *Nat Rev Drug Discov* 2003;2(11):891-902. doi: 10.1038/nrd1227
91. Guerrero-García C, Rubio-Guerra AF. Combination therapy in the treatment of hypertension. *Drugs Context* 2018;7:212531
92. Ram CV. Direct renin inhibitors: a new approach to antihypertensive drug treatment. *J Clin Hypertens (Greenwich)* 2007;9(8):615-21.
93. Ross S, Macleod MJ. Antihypertensive drug prescribing in Grampian. *Br J Clin Pharmacol* 2005;60(3):300-5