

# ORIGINAL ARTICLE

## Initial Thoughts about Serum Therapy

### Abstract

Immunology has played a prominent role in the history of medicine and considerable research has been conducted to explore the history of this science. However, the use of blood serum to treat diseases in pre-medieval times lacks a well-documented history. Despite this knowledge gap, Emil Adolf von Behring is recognized for his groundbreaking discovery of serum therapy. Serum therapy involves the administration of animal or human blood serums as a means of combating infections, paving the way for more effective disease management in the medical field.


This research, citing the book, *The Canon of Medicine*, written by Avicenna, states that there is evidence suggesting that serum therapy can be seen much earlier than its use in the Western world. In the discussion of poisonous animal bites, Avicenna first states the significance of fortifying the immune system to protect the body. In Avicenna's work on rabies, he states that if a patient bitten by a rabid dog eats the blood of the rabid dog that bit him, or eats the rabid dog's liver and heart, or puts it on his wound, especially if the liver and heart belong to the same dog that bit him, the patient will be healed. This early exploration of utilizing animal-derived substances to combat disease may be regarded as an antecedent to contemporary serum therapy, which was later developed by Emil Adolf von Behring.

This research reveals that Islamic scholars, especially Avicenna, through their clinical and practical experiences, possessed knowledge of the immune system and serum therapy long before the discoveries of Edward Jenner and Emil Adolf von Behring. Consequently, they were able to successfully apply this knowledge in treating patients well before the formal recognition of these principles in Western medicine.

**Key words:** Immunology, Serum Therapy, Serum, History of Medicine, Disease Management, Avicenna, *The Canon of Medicine*

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## Introduction

Serum therapy is a treatment approach wherein animal or human serums are administered to treat the infection. Most sera are obtained from animals vaccinated with the pathogen and the active agent in the serum therapy is antibody (Glatman-Freedman, and Casadevall, 1998, pp. 514-32; Beretta, 1891, pp. 1041–1042).

Today Serum therapy is recognized as an essential aspect of immunology. Immunology plays a prominent role in the history of medicine (Stiehm, and Johnston, 2005, pp. 458-67). So far, much work has been done to explore the history of immunology (Jafari, Ranjbar, and Farid Hosseini, 2019, pp. 344-352). For example, previous research suggests that the use of microbes to resist disease dates back thousands of years (Hutchings, Truman, and Wilkinson, 2019, pp. 72-80). However, the application of blood serum for therapeutic purposes in the pre-medieval era is not well documented. Behring's discovery of serum therapy in 1854 is often considered as the advent of the serum therapy approach. Behring found that the serum of infected animals contained antibacterial activity which is specific to the infectious agent (Kaufmann, 2019, p. 684; Winau, and Winau, 2002, pp. 185-188).

This article intends to specify part of the history of the discovery and widespread use of serum therapy in the Canon of Medicine of Avicenna.

Immunity is derived from the Latin name, *immunis*, which means “exempt”. *Immunis* was related to the tax-exempt status of Roman senators. However, in the context of classical immunology, it was related to the plague of Athens in 430 BC. This term was not used in medicine until the 19th and 20th centuries (Zanchin, 1992, pp. 91-95). Thucydides, the famous Athenian historian, made a significant observation during this time, noting that individuals who recovered from a previous illness could care for the sick without fear of reinfection. (Poole, and Holladay, 1979, pp. 282-300).

Before the discovery of the role of microbes in disease transmission, the “Miasma theory” was widely accepted in medicine. The word *miasma*, meaning pollution, is derived from ancient Greek. This theory was also known as the “bad air” or “night air” theory. It posited that diseases were caused by noxious air or environmental factors. After 1880, this theory was eventually developed and replaced by the disease microbial theory that certain microbes, not miasma, cause certain diseases. (Sterner, 1948, p. 747) This shift in understanding laid the foundation for advancements in immunology and the development of effective treatments and preventative measures against infectious diseases.

Immunity is defined as the body's ability to resist diseases, specifically infectious diseases. The collection of cells, tissues, and molecules that mediate resistance to infections is called the immune system, and the coordinated reaction of these cells and molecules to infectious microbes is the immune response. Immunology is the study of the immune system and its responses to invading pathogens. The physiologic function of the immune system is to prevent infections and eradicate established infections (Abbas, Lichtman, and Pillai, 2019).

In the pre-antibiotic era, passively administered immune animal sera, commonly referred to as serum therapy, was widely employed as the primary treatment for numerous infectious diseases, including diphtheria, tetanus, scarlet fever, pneumococcal pneumonia, and meningitis caused by *Neisseria meningitis* and *Hemophilus influenza* (Christian, 1944). Immune serum contained specific antibodies that mediated therapeutic effects via



various mechanisms, including opsonization, neutralizing toxins, or stimulating bacterial lysis with supplementation. (Kohler, and Milstein, 1975, pp. 495-497)

The field of immunology has been shaped by the invaluable contributions of numerous scientists throughout history. Notable pioneers include Edward Jenner, often referred to as the father of immunology and prevention (1732-1849); Louis Pasteur (1822-95), the French scientist, made groundbreaking discoveries in microbiology that have significantly impacted the medical field, including the development of vaccines for anthrax and rabies; and Emil von Behring (1917-1854), the father of serum therapy. Emile von Behring won the first Nobel Prize in Medicine and Physiology in 1901 for his work on serum therapy and in particular its use against diphtheria, which opened a new path in medical science, providing physicians with a powerful new tool to combat disease and death. Some of his findings were as follows: 1. Blood of rabbits safe from tetanus has the property of destroying tetanus toxin. 2. These properties are inherently stable and the effect remains in the body of other animals, thus offering therapeutic benefits through blood or serum transfusions. 3. The ability to neutralize tetanus toxin was not present in animals that had not developed immunity to the disease. (Winau, and Winau, 2002, pp. 185-188)

By looking at the medical texts of Iranian medicine, such as the Canon of Medicine of Avicenna, one can see the traces of serum therapy much earlier than those in the Western world.

Ibn Sina known as Avicenna in the West, was born on August 23, 980 95 CE in Afshaneh, a city in Persia. It is noteworthy that at the age of 16 years, he became a famous court physician who healed the Emir of Khorasan. (Hosseinzadeh, and Nassiri Asl, 2013, pp. 475-483)

Avicenna died in 1037 AD in Hamadan, Iran. Avicenna wrote several books on philosophy, the most significant of which was 'Kitab al Shifa' (The Book of Healing). He also wrote numerous medical books, and the most famous was the al-Qanun or Canon of Medicine or simply the Canon. It provides detailed descriptions of over 760 different drugs, including their properties, applications, and potential side effects.

The Canon of Medicine, authored by the eminent Persian physician Ibn Sina (Avicenna), holds profound significance in both the Islamic world and Europe.<sup>37,38,39,40</sup> This is truly a medical encyclopedia that systematically outlines all aspects of disease prevention and treatment. It is the most important work in his era. The Canon of Medicine greatly elevated the level of medical science and gained widespread recognition in Western Europe, approximately a century after Avicenna's passing. Thus, until the 18th century, the central universities in France, Spain, Italy, England, and Germany, studied the Canon of Medicine. The global impact of this influential text on medical education was solidified through numerous translations and publications. The first translation from Arabic to Latin was made by Gerard from Cremona (1114–1187) in the 12th century (by order of Frederick Barbarossa). The first printed edition of the Canon was published in 1473, followed by editions in Padua (1476–1479), Venice (1482–1500), Rome (1543 in Arabic), and France (1593). By the 17th century, around 40 complete editions of the Canon had been published. Over a span of 650 years, the Canon of Medicine had evolved into an indispensable guidebook for physicians worldwide and was considered equivalent to half of the medical school curriculum during that time. (Taheri-Targhi et al, 2019, pp. 1093-1098).



### Evidence of Serum Therapy in the Canon of Medicine

In discussing the bites of poisonous animals, Avicenna emphasizes the primary treatment approach: strengthening the immune system and stimulating its defensive capabilities.

In his Canon of Medicine on Rabies, he states a unique approach to counteracting the effects of a rabid dog bite. He proposes that ingesting the blood of the offending rabid dog may aid the patient's healing process. Furthermore, consuming the roasted liver and heart of the rabid dog, or applying the liver directly to the bite wound, could potentially enhance the therapeutic effects, especially if the liver is taken from the very same dog that inflicted the injury.

In the Canon of Medicine, Avicenna extends his exploration of unconventional treatments to include bites from various venomous animals, such as crocodiles, mink, vipers, scorpions, and other creatures with toxic venom (Avicenna, 1990).

Figure 1 is a manuscript of Avicenna's Canon of Medicine.

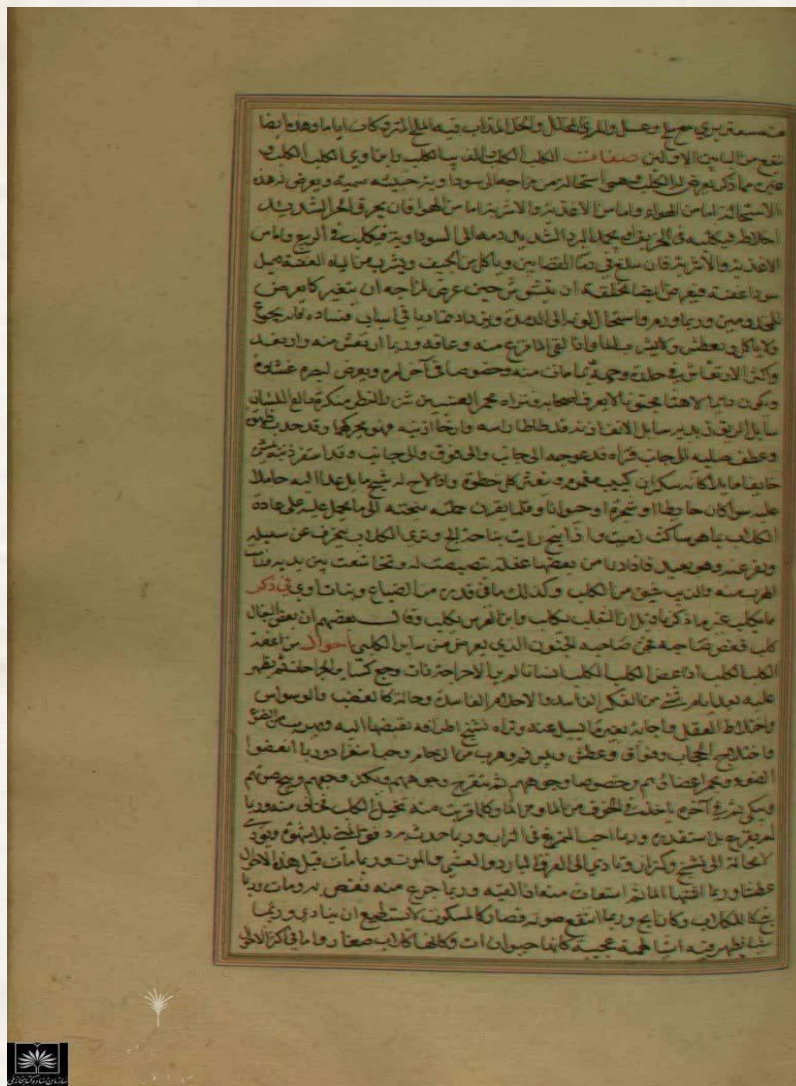


Figure 1. A page from the manuscript "The Canon of Medicine" by Avicenna (Avicenna, 1990)



### Conclusion

Islamic scholars like Avicenna (Ibn Sina) made significant contributions to medicine. These scholars, through their astute clinical observations and hands-on experiences, gained a deep understanding of the human immune system and pioneered treatments such as serum therapy.

Their knowledge and practices laid essential groundwork for later medical advancements and discoveries, including those made by Jenner and von Behring's work. Avicenna's recognition of the immune system's role in combating infectious diseases and his exploration of serum therapy demonstrate a level of insight that was well ahead of his time.

### Authors' Contribution

Zahra Ghahremani, Narges Tajik, Zahra Alamdar, Nafiseh Shabani and Mohammad Hossein Ayati contributed to the conception and design of the work. All authors read and approved the final version of the work.

### Conflict of Interest

None.

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