



Mucosal Immunology with Historical Aspects

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Histories testis temporum, lux veritatis, vita memoriae, magistra vitae, nuntia vetustatis. (History is that the witness of your time, the sunshine of truth, the essence of remembrance, the teacher of life, the messenger from times past.)

For millennia, the empirical experience of past generations suggested that those that survived certain diseases became immune to repeated attacks. For example, plague survivors could attend to the needs of the sick and deceased without becoming sick again (Thucydides, fifth century BC; translated complete works of Thucydides, 1951). The earliest recorded and surprisingly successful plan to enhance resistance to a harmful substance—in this case, a plant poison—was described in great detail by the king of Pontus (a territory on the Black Sea Coast of Turkey), Mithridates VI–Eupator (about 132–63 BC) (Reinach, 1890). To protect himself against a highly probable attempt on his life by numerous adversaries to his rather despotic rule, Mithridates invented a universal antidote to the then commonly used plant-derived poisons. The formula found in his archives in his own handwriting consisted of two dried nuts, two figs, and 20 leaves of rue (an aromatic Eurasian plant, the “herb-of-grace” from which essential oil utilized in ancient medicine are often expressed), which were crushed and mixed with salt [1]. More importantly, the blood of ducks fed unspecified poisonous weeds was added before ritual ingestion of this mixture every morning. Although the poison from an equivalent vial was lethal for his daughters Mithridatis and Nysa, the king survived. Whether the dose was insufficient (he shared it with two additional persons) or Mithridates was “immune” to the poison remains disputable. In desperation, the unfortunate king ordered his Gallic mercenary Bituit to stab him shortly before being captured by mutinous soldiers. These dramatic events captured the eye of the prolific French playwright Racine (1639-1699) and inspired him to write down the famous tragedy Mithridate (1673). A century later, Wolfgang Amadeus Mozart (1756-1791) composed at the age of 14 his highly successful youthful opera seria Mithridate, Re di Ponto, which premiered in December 1770 in Milan. Thus, the story of Mithridates, understandably barren of its immunologic undertones, survives for posterity.

In the fifth century AD, wise men highly venerated for their experience, judgment, and wisdom—called sages—recommended in the Babylonian Talmud for the treatment of rabies that “if one is bitten by a mad dog, he may eat his liver and be cured”. According to other sources, the diaphragm of a rabid dog should even have been ingested. Although there are no reports suggesting the success of such treatment, based on the current knowledge, it is not surprising that this recommended practice was not widely accepted and remained of historical interest [2].

The roots of mucosal immunity can also be traced to documents dated around 900 AD. The Chinese developed a secret ritual to keep off the dreaded scourge of their time, smallpox, which we now know was caused by the smallpox virus. As a part of this Chinese ritual, the scabs of healed pustules were ground up and used as an inhalant. In many instances, this earliest sort of nasal immunization worked so well that the practice made its way into India. However, in some instances, this risky practice resulted during a fatal infection. Nevertheless, modifications of the practice spread from India to Turkey, where in 1717 Lady Mary Wortley Montagu (1689–1762) learned of it and

brought the practice of variolation back to England. Her adaptation, although still risky, worked in many instances. Later in that century, Dr Edward Jenner (1749–1823), who knew of and practiced this method of treatment, worried about the inherent risks of spread of the disease. He astutely recognized that milkmaids often developed handsorens closely resembling smallpox pustules; however, the lesions healed and altogether cases they were resistant to smallpox [3]. As we now appreciate, the cowpox lesions were caused by Vaccine virus, which, although associated with the variola virus, was much less virulent for humans. The infection, however, did induce immunity to smallpox. The actual practice of using Vaccinia (from the Latin vacca, meaning “cow”) was adapted to describe use of attenuated bacteria or viruses, or inactivated bacterial toxins or recombinant proteins as vaccines, which in fact is that the accepted terminology today. Interestingly, 1996 was proclaimed the year of the vaccine in recognition of Jenner’s contributions 200 years earlier. A complete worldwide vaccination program by the planet Health Organization and other health agencies resulted in eradication of smallpox in 1979 [4].

Mucosal Microbiota

Based on Pasteur’s work on the microbial nature of fermentation, it had been widely believed that the presence of bacteria within the intestine was essential for the lifetime of the host. However, tended to regard the intestinal “flora” as hostile, inducing toxemia in the host, and proposed that the process of premature aging could be prevented by altering the intestinal micro biota. Surprisingly, this doctrine found a fertile ground within the early twentieth century and drastic sorts of treatment, including high enemas or maybe therapeutic colectomies, were wont to prevent intestinal auto-intoxication. On the opposite hand, many workers devoted themselves to determining whether life might be maintained with a sterile intestinal tract. One of the primaries, who were ready to rear chicks under sterile conditions. Achieved some success with mammals: they removed embryonic guinea pigs by cesarean delivery and maintained them uncontaminated for several weeks. The conclusion was that bacteria within the intestinal tract weren’t necessary for mammalian life, when an appropriate diet was provided. Finally showed that “prolonged” life was possible within the absence of gut bacteria by rearing chicks for up to 40 days under germ-free (GF) conditions [5].

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Conflict of interest

None

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