

## HISTORY OF MEDICINE

### Measles in antiquity and the Middle Ages

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Although no longer a formidable epidemic disease, measles is still responsible for up to 2 million deaths per annum – mainly among children in developing countries. It is an ancient disease, long confused with smallpox, from which it was clearly differentiated only in the 10th century. In this paper, the place of measles in the medical history of antiquity and the Middle Ages is reviewed.<sup>1</sup>

#### Modern understanding

##### Pathogenesis

Measles is caused by a paramyxovirus (RNA family) closely related *inter alia* to the viruses causing canine distemper and rinderpest in cattle. The antibody response to its infection causes lifelong immunity. There are no known extra-human reservoirs of the virus, and infected fluids quickly lose their infectivity on drying outside the body. The virus was first identified by Enders and Peebles in 1954.<sup>1,2</sup>

Infected particles enter the patient mainly via the respiratory tract and conjunctiva, from where the virus rapidly spreads through the body. Previously infected pregnant women pass the antibody to the fetus, and the newborn are then immune for a few months. Average survival time of the virus in the human body is approximately 2 weeks.<sup>1</sup>

##### Epidemiology

The disease is highly infective, rapidly spreads through a virgin community, and typically infects young children. The patient transmits the virus to others during the incubation period and up to the end of the rash. Typically, the highest attack rate is at the school-going age of approximately 6 years. Infections tend to be more serious in malnourished communities and young adults rather than children. In modern societies, approximately 90% of individuals are immune by age 20.<sup>1</sup>

For measles to remain endemic in a community, a population density of at least 260 000 people and 40 000 births per year

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are required. Such communities tend to experience minor epidemics at 2-yearly cycles.<sup>1,2</sup> Of interest is that the smallpox virus needs a lower population density for long-term survival, partly because the virus survives in the body for a longer period.<sup>3</sup> Even in modern times, measles epidemics in previously unexposed (virgin) societies may lead to high mortality. In 1954, the mortality of a measles epidemic in a virgin community of Brazil was 27%.<sup>1</sup>

Mass vaccination introduced in the early 1960s has greatly diminished the international impact of measles as an epidemic disease, but it nevertheless remains a significant paediatric illness.<sup>1</sup>

##### Clinical picture<sup>4</sup>

After an incubation period of 10 - 14 days, a week-long prodromal phase characterised mainly by fever, non-productive cough and conjunctivitis follows. On the 2nd or 3rd day, so-called Koplik spots appear that last for up to 4 days: tiny white lesions on the mucosa of the mouth and vagina. With the Koplik spots still present, the typical maculopapular red rash appears – initially behind the ears and on the face, from where it then spreads to the trunk and limbs. Occasionally, lymphadenopathy and splenomegally occur. In partially immune persons, the clinical picture may be atypical.

In the absence of complications (which are most common in malnourished patients), mortality is very low. Encephalitis, occurring in less than 0.1% of patients, carries a mortality of 10 - 20%, and is commonly followed by permanent neurological defects. In 1:100 000 cases, the organism remains in the neurological system as a 'slow virus', causing debilitating subacute sclerosing panencephalitis (SSPE). In approximately 15% of patients, significant bacterial infection may lead to pneumonia, otitis media or adenitis. In the USA, current measles mortality is 0.6% but in developing countries still reaches 10% or more.<sup>1</sup>

##### History

###### In antiquity

The measles virus probably descended from the ancestors of the modern canine distemper and/or rinderpest viruses, a process which may be dated back to the Epipalaeolithic Age (approximately 10 000 BC), when man started domesticating dogs and cattle in the Middle East.<sup>2</sup> It has been suggested that measles probably became a human disease in Mesopotamia during the 4th millennium BC, whence it gradually spread with the evolution of civilisations. Cliff *et al.*<sup>1</sup> postulate that it reached the Indus civilisation in India by 2 500 BC, Asia Minor and the Levant 1 000 years later, and the Egyptian and Ganges civilisations by 1 000 BC. They believe that China and Japan in the Far East housed endemic measles only much later in the

Christian era. If we accept McNeil's estimate of a population of around 500 000 inhabitants for the Tigris-Euphrates valley by 3 000 BC, endemic measles could then well have been supported.<sup>5</sup> Cliff *et al.*<sup>1</sup> suggest that measles reached Italy and the Greek city states by 1 000 BC. It could then have occurred as isolated epidemics, but at that stage the local population was too low to sustain endemic disease. It was only by the 1st century BC that Rome's population (always much greater than that of Athens) had grown large enough to maintain endemic measles.<sup>6</sup>

During antiquity, measles was almost certainly confused with smallpox and not clearly differentiated from the latter before the 10th century. Undisputed early evidence of the occurrence of measles is fragmentary.<sup>1</sup> There is no description of a disease compatible with measles in early medical writings from Mesopotamia or Egypt. Egyptian mummies of the 2nd millennium BC show evidence of smallpox, but measles does not leave palaeopathological evidence in human remains. However, DNA studies might in future reveal evidence of whether measles existed in Pharaonic Egypt and elsewhere in the early Middle East, as hypothesised by Cliff *et al.*<sup>1</sup> The relative absence of written records in the rest of Africa prevents an assessment of the presence of measles in this region. The sparse African populations would not have supported endemic disease.<sup>1</sup>

There is very limited written evidence of epidemic disease in classical Greece, with the exception of the Athenian epidemic of 430 - 426 BC. Although measles has been mentioned as a possible cause of this catastrophe, smallpox was most probably responsible.<sup>2,7</sup> Hippocrates (mainly 5th and 4th centuries BC) does not mention a measles-like disease, which is probably to be expected in view of the fact that the Greek populations of the time were not big enough to sustain epidemic disease. Periodic epidemics like that of 430 - 426 BC could of course still occur.<sup>1,2</sup> The Bible mentions many 'plagues' of obscure nature. There is no evidence that the epidemics which struck armies at Syracuse in 413 BC and 396 BC were measles.<sup>1,7</sup>

In contrast, early Roman records mention many epidemics, progressively decreasing from 9 in the 5th century, to 4 in the 1st century BC. Poor or absent descriptions of clinical features make the identification of diseases, and measles in particular, very difficult. Later, during the Roman Empire, periodic epidemics continued and disease descriptions improved. The population of Rome was now big enough to sustain an endemic disease such as measles. Smallpox was almost certainly responsible for many of the epidemics (e.g. 54, 125, 161 - 180, 321 - 313), but it is possible that measles could have caused the epidemic of 54 AD. The so-called epidemic of Cyprian (251 - 266), which ravaged Italy, North Africa and Syria, had characteristics suggesting measles, but the absence of a recorded skin rash is against this diagnosis. Recognised physicians of the era, such as Soranus, Galen, Rufus of Ephesus, Aretaeus of Cappadocia and Caelius Aurelianus, did not describe measles. In 455 - 456, an epidemic originating near present-day Vienna was characterised by severe respiratory infection, inflammation of the eyes and reddening of the skin over the entire body. This could well have been measles.<sup>7,8</sup>

## Middle Ages

Cliff *et al.*<sup>1</sup> postulate that the large population of the Indus civilisation could well have harboured endemic measles by the 3rd millennium BC and the Ganges civilisation by 1 000 BC, but the first written record of measles in India dates from the 8th century AD, when the *Nidana* of Madhavakar included a description of it. In subsequent Hindu symbolism, a goddess of measles was recognised.<sup>3</sup>

Grmek<sup>9</sup> postulates that measles has occurred in China since time immemorial. However, Cliff *et al.*<sup>1</sup> state that measles infiltrated China by the 3rd century AD, and McNeil<sup>5</sup> suggests that it only reached that country by the 7th century (carrying a very high mortality). Measles was possibly recognised by Chinese doctors of the latter era who exchanged knowledge with Arab counterparts. Whether measles was discussed is not known. In Japan, measles was clearly described by 998. It was considered a new disease, causing regular epidemics.<sup>1,3</sup>

Measles was probably brought by a Persian army in 616 to Egypt, where an Alexandrian Christian priest, Aaron, differentiated measles from smallpox in 622 AD (although the description was vague). During the 6th century, smallpox and possibly measles played a decisive role during the siege of Mecca (Elephant War of 569) and decimation of the Abyssinian population.<sup>1,10</sup>

The Islamic philosopher-physician Rhazes made a crucial contribution by clearly differentiating between measles and smallpox in his *Treatise on Smallpox and Measles* of 910. This description by one of the outstanding physicians of the Middle Ages proved a landmark in the understanding of measles, permanently influencing subsequent medicine.<sup>1,10</sup>

During the Middle Ages, measles became established as an endemic disease throughout the Middle East, North Africa and the Old World. In England, the term *mezils* appeared in the 13th century, initially referring to both measles and forms of leprosy. In the British Isles, 49 'plagues' of uncertain nature, but probably including measles, struck between 526 and 1087. In 1546, the Veronese physician Fracastero wrote a classic description of measles, which he attributed to 'seeds' (*seminaria*) of illness spreading from person to person. In London, Sydenham left a very clear description of a measles epidemic which struck the city in 1670 but, unlike Fracastero, he attributed it to toxic *miasms* (vapours) arising from the ground, and not person-to-person spread.<sup>1</sup>

Spanish explorers took measles and smallpox to the New World, where it caused devastating epidemics in the early 16th century. Smallpox was evident in Mexico in 1515 and among the Incas by 1524. Measles probably appeared later, in 1529.<sup>3,10</sup>

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