

Cowpox virus: Old friend but new foe

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The observation that milkmaids are frequently infected with cowpox but rarely catch smallpox is generally credited to the English doctor Edward Jenner. Although Jenner might not have been the first person to notice the correlation, he was the first to make use of it: in 1796 he "vaccinated" children with material from cowpox blisters and showed that they became immune to smallpox. Jenner's work led directly to the development of a smallpox vaccine and less than 200 years later the disease was eradicated. Jenner's initial vaccine presumably came from an English strain of cowpox and it was generally assumed that commercial vaccines are derived from this. Recent findings from an international consortium including the group of Norbert Nowotny at the University of Veterinary Medicine, Vienna challenge this view and suggest that smallpox vaccines come instead from central or eastern Europe. The results have recently been published in the prestigious online journal *PLoS One*. The work is not merely of historical interest: since the cessation of smallpox vaccination there has been a rise in cases of related diseases and pox viruses once again represent a serious threat to public health.

The family of orthopox viruses is generally considered to comprise vaccinia virus, variola virus (which causes smallpox), cowpox virus and at least six other species. The various pox viruses are named after their usual hosts but this nomenclature may give rise to a false sense of security: most of them seem to have fairly catholic tastes and cowpox is able to infect not only cows but also a variety of other animals, ranging from mice to elephants as well as man.

Despite the importance of cowpox in human medicine the virus has attracted relatively little attention and how the many forms of cowpox are related was until recently a matter of conjecture. The issue has been clarified by a large international consortium headed by Darin Carroll at the [Centers for Disease Control and Prevention](#) in Atlanta, Georgia and including Jolanta Kolodziejek and Norbert Nowotny of the University of Veterinary Medicine, Vienna. The scientists compared the complete genome sequences of twelve different isolates of the cowpox virus, using sophisticated computer methods to prepare a phylogeny or family tree of the various forms.

Their first finding was that "cowpox" may actually comprise a number of distinct species. The researchers found a high degree of variation between samples, with the sequences clustering into five distinct "clades" or groups, each of which could be considered to represent a separate species. This is in contrast to prevailing wisdom, which considers cowpox to be a disease with a single causative agent. The second surprising finding was that the strains used in smallpox vaccines were most closely related to cowpox virus isolates from Russia, Finland and Austria rather than to samples from England. This suggests that commercial smallpox vaccines were not derived from Jenner's original strain but instead from somewhere in central or eastern Europe.

The last reported case of smallpox was in 1977 and in 1979 the World Health Organization declared that the disease had been eradicated. To date, smallpox is the only human viral disease to have been fully eradicated. Because smallpox is no longer a threat and because vaccination against it was occasionally associated with unpleasant side-effects, wide scale vaccination ceased in the early 1980s and fewer people are now immune to [smallpox](#) and related viruses, such as monkeypox and cowpox. As a consequence, these diseases are increasingly recorded in man. The incidence of monkeypox in the Democratic Republic of the Congo (the country with the most cases) has

risen twenty-fold since the 1980s and 2003 saw a serious outbreak of the disease in the US.

As Jenner noted in the 18th century, the cowpox virus is also readily transmitted to man. Despite its name, cowpox no longer occurs in cows but wild mice and voles represent a source of infection: Nowotny cites a recent study in Austria that revealed that "about 1 in 6 mice carries the cowpox virus. As a result, the virus can be transmitted to domestic cats (at least, to those that hunt mice) and we and others have shown that it can then be passed on to humans" and the decades since the cessation of vaccination have witnessed a significant rise in the incidence in humans. The majority of cases stem from Great Britain (a nation of dog-lovers, perhaps, although cats are also popular pets) with the remainder restricted to Europe, apart from a single case in Israel. The disease is unpleasant but not generally fatal, except in immunocompromised patients. As Nowotny says, "diagnosis of cowpox is relatively straightforward – in humans as well as in animals – but it is important that doctors and vets consider the possibility when they see patients with lesions."

More information: Chasing Jenner's Vaccine: Revisiting Cowpox Virus Classification by Darin S. Carroll, et al.

www.plosone.org/article/info

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