

## SMALLPOX

ICD-9 050; ICD-10 B03

The last naturally acquired case of smallpox in the world occurred in October 1977 in Somalia; global eradication was certified 2 years later (1979) by WHO and sanctioned by the World Health Assembly (WHA) in May 1980. Except for a laboratory-associated smallpox death at the University of Birmingham, England, in 1978, no further cases have been identified. All known variola virus stocks are held under security at CDC, Atlanta GA, USA, or the State Research Centre of Virology and Biotechnology, Koltsovo, Novosibirsk Region, the Russian Federation. In response to concerns that live variola virus may be needed for research in the event that smallpox should re-emerge as result of accidental or intentional release, the WHA in May 1999 authorized that virus be retained at the laboratories in the Russian Federation and the USA for the purposes of essential research. The WHA reaffirmed that destruction of all the remaining virus stocks is still the Organization's ultimate goal and has appointed a group of experts to determine and oversee the research that must be carried out before the virus can be destroyed. WHO has also set up a biosafety inspection program for the 2 laboratories where official stocks are kept, in order to make sure they are secure and research can be carried out safely.

Because of increasing concerns about the potential for deliberate use of clandestine supplies of variola virus, it is important that health care workers become familiar with the clinical and epidemiological features of smallpox and how it can be distinguished from chickenpox.

**1. Identification**—Smallpox was a systemic viral disease generally presenting with a characteristic skin eruption. Preceding the appearance of the rash was a prodrome of sudden onset, with high fever (40°C/104°F), malaise, headache, prostration, severe backache and occasional abdominal pain and vomiting; a clinical picture that resembled influenza. After 2–4 days, the fever began to fall and a deep-seated rash developed in which individual lesions containing infectious virus progressed through successive stages of macules, papules, vesicles, pustules, then crusted scabs that fell off 3–4 weeks after the appearance of the rash. The lesions first appeared on the face and extremities, including the palms and soles, and subsequently on the trunk—the so-called centrifugal rash distribution—and were at the same stage of development in a given area.

Two types of smallpox were recognized during the 20th century: *variola minor* (alastrim), which had a case fatality rate of less than 1% and *variola major* with a fatality rate among unvaccinated populations of 20–50% or more. Fatalities normally occurred between the fifth and seventh day, occasionally as late as the second week. Fewer than 3% of variola major cases experienced a fulminant course, characterized by a severe prodrome, prostration, and bleeding into the skin and mucous membranes; such hemorrhagic cases were rapidly fatal. The usual vesicular rash did not appear and the disease might have been confused with severe leukaemia, meningococcaemia or idiopathic thrombocytopenic

purpura. The rash of smallpox could also be significantly modified in previously vaccinated persons, to the extent that only a few highly atypical lesions might be seen. In such cases, prodromal illness was not modified but the maturation of lesions was accelerated with crusting by the tenth day.

Smallpox was most frequently confused with chickenpox, in which skin lesions commonly occur in successive crops with several stages of maturity at the same time. The chickenpox rash is more abundant on covered than on exposed parts of the body; the rash is centripetal rather than centrifugal. Smallpox was indicated by a clear-cut prodromal illness; by the more or less simultaneous appearance of all lesions when the fever broke; by the similarity of appearance of all lesions in a given area rather than successive crops; and by more deep-seated lesions, often involving sebaceous glands and scarring of the pitted lesions (chickenpox lesions are superficial and chickenpox rash is usually pruritic). Smallpox lesions were virtually never seen at the apex of the axilla.

Outbreaks of variola minor (alastrim) occurred in the late 19th century. Although the rash was like that in ordinary smallpox, patients generally experienced less severe systemic reactions, and hemorrhagic cases were virtually unknown.

Laboratory confirmation used isolation of the virus on chorioallantoic membranes or tissue culture from the scrapings of lesions, from vesicular or pustular fluid, from crusts, and sometimes from blood during the febrile prodrome. Electron microscopy or immunodiffusion technique often permitted a rapid provisional diagnosis. Molecular methods, such as PCR, are now available for rapid diagnosis of smallpox and other orthopoxvirus infections. Should smallpox infection be suspected, immediate communication by national authorities with WHO is suggested for advice on appropriate laboratories for diagnosis.

**2. Infectious agent**—Variola virus, a species of *Orthopoxvirus*.

**3. Occurrence**—Formerly a worldwide disease; no known human cases since 1978.

**4. Reservoir**—Smallpox was exclusively a human disease, with no known animal or environmental reservoir. Currently, the virus is maintained only in designated laboratories.

**5. Mode of transmission**—Infection usually occurred via the respiratory tract (droplet spread) or skin inoculation. The conjunctivae or the placenta were occasional portals of entry.

**6. Incubation period**—From 7–19 days; commonly 10–14 days to onset of illness and 2–4 days more to onset of rash.

**7. Period of communicability**—From the time of development of the earliest lesions to disappearance of all scabs; about 3 weeks. The risk of

transmission appears to have been highest at the appearance of the earliest lesions, through droplet spread from the oropharyngeal enanthem.

**8. Susceptibility**—Susceptibility among the unvaccinated is universal.

**9. Methods of control**—Control of smallpox is based on identification and isolation of cases, vaccination (vaccinia virus) of contacts and those living in the immediate vicinity (ring vaccination), surveillance of contacts (including daily monitoring of temperature) and isolation of those contacts in whom fever develops.

Because of the relatively long period of incubation for smallpox, vaccination within a 4-day period after exposure can prevent or attenuate clinical illness.

Should a non-varicella, smallpox-like case be suspected, IMMEDIATE TELEPHONIC COMMUNICATION WITH LOCAL NATIONAL HEALTH AUTHORITIES IS OBLIGATORY. THESE SHOULD IMMEDIATELY INFORM WHO. Further information on <http://www.who.int/csr/disease/smallpox>.

## VACCINIA

ICD-9 051.0; ICD-10 B08.0

Vaccinia virus, the immunizing agent used to eradicate smallpox, has been genetically engineered into candidate recombinant vaccines (some are in clinical trials), with low potential for spread to nonimmune contacts. Vaccination with licensed smallpox vaccine is recommended for all laboratory workers at high risk of contracting infection, such as those who directly handle cultures or animals contaminated or infected with vaccinia or other orthopoxviruses that infect humans. It may be considered for other health care personnel who are at lower risk of infection, such as doctors and nurses whose contact with these viruses is limited to contaminated dressings. WHO does not recommend vaccination in the general public because the risk of death (1 per 1 000 000 doses) or serious side-effects is greater than the known risk of infection with smallpox. Vaccination is contraindicated in persons with deficient immune systems; persons with eczema or certain other dermatitis disorders; and pregnant women. Vaccine immune globulin can be obtained for laboratory workers, in the USA through CDC Drug Service (404 639-3670), and from public health agencies in other industrialized countries. Vaccination should be repeated unless a major reaction (one that is indurated and erythematous 7 days after vaccination), or "take" has developed. Booster vaccinations are recommended within 10 years in categories for which vaccine is recommended. WHO maintains a supply of the vaccine seed lot (vaccinia virus strain Lister Elstree) at the WHO Collaborating Centre for Smallpox Vaccine at the National Institute of Public Health and Environmental Protection in Bilthoven, The Netherlands. WHO also maintains a stockpile of vaccine should an outbreak occur.

## MONKEYPOX

ICD-9 051.9; ICD-10 B04

Human monkeypox is a sporadic zoonotic infection first identified (1970) from remote rural villages in central and western African rainforest countries as smallpox disappeared. Clinically the disease closely resembles ordinary or modified smallpox, but lymphadenopathy is a more prominent feature in many cases and occurs in the early stage of the disease. Pleomorphism and "cropping" similar to that seen in chickenpox are observed in 20% of patients. The natural history of the disease is unclear; humans, primates and squirrels appear to be involved in the enzootic cycle. The disease affects all age groups; children under 16 have historically constituted the greatest proportion of cases. The case-fatality rate among children not vaccinated against smallpox ranges from 1% to 14%. Smallpox vaccination protects against infection in some instances and in some others mitigates clinical manifestations. Between 1970 and 1994, over 400 cases were reported from western and central Africa; the Democratic Republic of the Congo (formerly Zaire) accounted for about 95% of reported cases during a 5-year surveillance (1981-1986). Poor public health infrastructure and other factors complicated accurate case reporting. Recently, a prolonged outbreak of human monkeypox occurred in the Democratic Republic of the Congo: it has been postulated that lack of vaccination and an epizootic allowed multiple virus transmission events to humans across the species barrier.

In the 1980s about 75% of reported cases were attributable to contact with affected animals; in recent outbreaks it appears that a larger number of cases were attributable to person-to-person contact. The longest chain of person-to-person transmission was 7 reported serial cases, but serial transmission usually did not extend beyond secondary. Epidemiological data suggests a secondary attack rate of about 8%. Most cases have occurred either singly or in clusters in small remote villages, usually in tropical rainforest where the population has multiple contacts with several types of wild animals. Ecological studies in the 1980s point to squirrels (*Funisciurus* and *Heliosciurus*), abundant among the oil palms surrounding the villages, as a significant local reservoir host. Maintenance of an animal reservoir and animal contact is required to sustain the disease among humans. Thus, human infection may be controllable by education to limit contact with infected cases and potentially infected animals. A recent outbreak of human monkeypox in the USA, thought to be related to importation and sale of exotic animals from western Africa as pets, resulted in over 70 cases, mainly among children and animal handlers.

Monkeypox virus is a species of the genus *Orthopoxvirus*, with biological properties and a genome map distinct from variola virus. There is no evidence that monkeypox will become a public health threat outside of enzootic areas. Cross-protective vaccination against smallpox is not recommended by WHO. A WHO Technical Advisory Committee on

monkeypox has recently recommended continued studies, in particular, intensified prospective surveillance and ecological studies.

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