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SPECIAL ARTICLE

Human poxvirus infection after the eradication of smallpox

There occurred during the planning and publication of this review: the twentieth anniversary of the start of the intensified WHO Smallpox Eradication Campaign and the tenth anniversary of the last endemic case of smallpox; debate about the fate of smallpox virus and possibly its irrevocable destruction; claims that mass smallpox vaccination campaigns may have helped the spread of AIDS in Africa; publication of the definitive account of *Smallpox and its Eradication* (Fenner *et al.* 1988), and the closure of the WHO Smallpox Eradication Unit (SEU). It is therefore perhaps an appropriate moment to assess the current status of human poxvirus infections and their epidemiology; this review concentrates on those viruses antigenically related to smallpox (i.e. orthopoxviruses).

SMALLPOX

The intensified Eradication Campaign started in 1967, and the case detected near Mogadishu in October 1977 was, in one sense, the culmination of a tremendous global effort. In another it was just the start because at the time it was not known that this would be the last endemic case.

Certification of eradication

The key to eradication was aggressive surveillance – containment activity, and eradication was confirmed by extension of these surveillance techniques. *Smallpox and its Eradication* provides detail on all certification exercises (Fenner *et al.* 1988), but certification in India, the last and most important stronghold of variola major was particularly impressive. The National certification exercises were reviewed by independent international commissions and in 1980 the WHO General Assembly accepted the proposal that smallpox had been eradicated (WHO, 1980). The evidence collected should have convinced even the most sceptical but the SEU continued to investigate rumours of smallpox (e.g. Arita & Gromyko, 1982) although no cases were detected. Finally the SEU, which had co-ordinated work on other orthopoxvirus infections particularly monkeypox (see below), closed down on 31 December 1987.

An animal reservoir for smallpox discounted

Although epidemiological data supported the view that smallpox virus had no animal reservoir two sets of laboratory data cast doubt on this and the issue was not resolved until after eradication.

The first doubt was raised by the isolation of 'whitepox' viruses, so-called because they produced white pocks on the chick chorioallantois. Two strains were isolated in Holland from the kidneys of Asiatic monkeys (Gispen & Brand-Saathof, 1972), and four in Moscow from wild animals caught in Zaire

(Marennikova, Shelukhina & Shenkman, 1976). Phenotypic and later DNA analysis failed to separate them from smallpox virus (Dumbell & Archard, 1980; Esposito & Knight, 1985). However, detailed studies of the Dutch strains, including examination of how they were isolated, showed that they represent contamination with an Indian strain of smallpox virus being studied in the laboratory at the same time (Dumbell & Kapsenberg, 1982). The other whitepox strains were also isolated in a smallpox laboratory and it is probable that they are also contaminants (Fenner *et al.* 1988).

The second doubt was caused by the isolation from monkeypox virus strains of 'mutants' which were indistinguishable from smallpox virus (Marennikova *et al.* 1979). This was particularly ominous because monkeypox virus was known to be established in an unknown West African reservoir and to cause human infection with an appreciable mortality (see below). However, the results could not be repeated in other laboratories (Dumbell & Archard, 1980; Esposito, Nakano & Obijeski, 1985). Further, detailed analysis of the DNA of smallpox and monkeypox virus, true white pock mutants of monkeypox and the 'mutants' isolated in Moscow showed the clear separation of monkeypox and smallpox viruses, and again suggested contamination as the most likely explanation for the results (Esposito, Nakano & Obijeski, 1985; Fenner *et al.* 1988).

The future of smallpox virus

With the eradication of naturally-occurring smallpox, possible sources of infection are deliberate release of virus for military purposes, entombed smallpox victims, or accidental escape of virus from a laboratory. Smallpox would be an inefficient biological weapon, but United States and Soviet Military personnel are still vaccinated (Capps, Vermund & Johnsen, 1986; Sidel, 1986; Halsey & Henderson, 1987 and below).

The possibility that archaeologists and demolition workers may be at risk from entombed smallpox victims has been raised (Zuckermann, 1984). However, although smallpox virus has been recognized by electron microscopy in 16th and 19th century smallpox victims, the virus was non-viable (Fornarcieri & Marchetti, 1986; News Item, 1985). The risks to the individuals involved must be very small, and the general public health risk even smaller but the possibility that virus might survive in victims preserved in perma-frost has been emphasized (Lewin, 1985). This limited risk must be assessed when such work is undertaken and the possibility of vaccination discussed (see below).

What was, one hopes, the world's last case of smallpox occurred as a result of a laboratory accident in Birmingham UK, in 1978 (HMSO, 1980). This followed a similar incident in London in 1973 (HMSO, 1974), and in part led to improvements in laboratory containment and a reduction in the number of laboratories handling smallpox virus. By 1984 only the two WHO reference laboratories in Atlanta and Moscow held smallpox virus. The WHO Committee on Orthopoxviruses recommended that smallpox virus stocks should be destroyed (WHO, 1986) and this might yet occur in the near future. Arguments for and against must be at least partly subjective. Those opposing retention point to the potential dangers and the fact that retention is unnecessary now that genome fragments of smallpox virus strains have been cloned into bacterial plasmids

Table 1. *Cases of human monkeypox 1970–87*

	Year								
Cases	70–79	80	81	82*	83	84	85	86	87
Zaire	43	3	6	39	56	86	62	NA†	NA
Total	54	3	7	39	56	92	62	59‡	32‡

* Surveillance activity increased.
† NA, Data not available.
‡ Data incomplete.

(WHO, 1986; Dumbell, 1987). Those favouring retention believe the dangers are exaggerated, and point to the safety with which vaccinated individuals could handle the virus in secure facilities, and the fact that destruction denies future scientists the opportunity to study the whole virus (Baxby, 1987).

MONKEYPOX

Between 1958 and 1968 the orthopoxvirus called monkeypox virus caused 10 outbreaks in captive monkeys, primarily Asiatic (Arita *et al.* 1972). Particular attention was paid to the virus after 1970 when post-eradication surveillance detected human cases of monkeypox in West Africa (Foster *et al.* 1972; Ladnyi, Ziegler & Kima, 1972). To date over 400 human cases have been investigated, most of them from Zaire (Table 1) (Arita *et al.* 1985; Jezek *et al.* 1986*b*; 1987).

Human infection

The clinical features of human monkeypox are essentially those of ordinary or modified smallpox with the exception that lymphadenopathy and 'cropping' of lesions is more pronounced in the former (Arita *et al.* 1985; Jezek *et al.* 1987). A low (3%) proportion of sub-clinical infections occurs in unvaccinated contacts, whereas sub-clinical smallpox in the unvaccinated was extremely rare (Jezek *et al.* 1986*b*).

Infection is more common in children and the unvaccinated; a recent survey of 282 cases showed that 262 (93%) were in children < 15 years old; of these 247 (94%) were in unvaccinated children, (Jezek *et al.* 1987). No deaths occurred among vaccinated patients or among children > 10 years old; the crude fatality rate in 250 unvaccinated patients was 11%, but 15% in children 0–4 years (Jezek *et al.* 1987).

Human monkeypox is less communicable than smallpox; the attack rate among unvaccinated contacts is 12% compared to $> 37\%$ for smallpox (Jezek *et al.* 1986*b*. Person-to-person transmission is uncommon and human transmission beyond four generations has not been recorded (Jezek *et al.* 1986*a*). Many instances have been recorded of failure to transmit infection to unvaccinated close contacts (Jezek *et al.* 1986*b*).

The reservoir of monkeypox virus

Monkeypox virus was so called because it was first detected in monkeys and was assumed to circulate naturally in wild monkeys. Although most outbreaks

occurred in captive Asiatic monkeys, human infections occurred in West Africa and so the natural reservoir must be sought there.

Due to the close serological relationships between orthopoxviruses and the possibility that other, perhaps unknown, orthopoxviruses may circulate in Africa mere detection of orthopoxvirus antibody is inconclusive evidence of monkeypox infection. A monkeypox-specific antigen has been identified and antibody to it can be detected by suitable absorption tests (Hutchinson *et al.* 1977). Initial general surveys were unsuccessful but recent surveys in Zaire have proved most fruitful. In considering potential reservoirs and sources of infection account was taken of the range of wild animals used for food and their ecological distribution, and that most human cases occurred in young children who stayed close to their homes. Although monkeys are eaten and a chimpanzee is believed to have transmitted infection to a child (Mutombo, Arita & Jezek, 1983), monkeys are not found very close to villages, virus has not been isolated from native monkeys and only a very small number of monkeys has been found to have monkeypox-specific antibody (Arita *et al.* 1985).

From 1984 attention was focused on the 'agricultural' area immediately surrounding villages where human cases had occurred, and where squirrels and terrestrial rodents predominate. A breakthrough was made in July 1985 when monkeypox virus was isolated from a wild squirrel (*Funisciurus anerythrus*). The virus was isolated by two WHO collaborating laboratories and the animal had monkeypox-specific antibody, which eliminates the possibility of contamination (Khodakevich, Jezek & Kinzanzka, 1986). A more extensive survey in January–February 1986 failed to isolate virus from any animal specimen but detected monkeypox-specific antibody in 79/320 (25%) *Funisciurus anerythrus*, and 6/27 (16%) samples from another squirrel species *Heliosciurus rufobrachium*; no monkeypox-specific antibody was detected in samples from 233 terrestrial rodents (Khodakevich *et al.* 1987). The failure to isolate virus was a disappointment but from what is known about poxvirus reservoirs and the role of antibody surveys in their detection (Baxby, 1977*a*) the conclusion that squirrels are an important reservoir of monkeypox, at least in part of Zaire, is sound (Khodakevich *et al.* 1987).

The future

Attention has focused on human monkeypox in certain regions of Zaire and the extent of human infection in other areas of the tropical rain forest where occasional cases have been reported is not known. Nor is it known whether other hosts and reservoirs may be involved outside the extensively studied area. Monkeys and squirrels are used as food but it is not known precisely how infection is transmitted. Most cases have occurred in unvaccinated children but it is interesting that cases have recently been reported in those previously vaccinated; this indicates that immunity is waning (Khodakevich *et al.* 1987). Only time will tell whether human monkeypox will become a more serious problem in Africa (Lancet, 1987).

The possibility of monkeypox should perhaps be considered in those returning from the endemic area. The cropping of lesions resembles varicella but electron microscopy of skin lesions should provide rapid differential diagnosis. In view of

the poor communicability of monkeypox and the ease with which outbreaks of smallpox could be controlled in poorly-vaccinated communities (HMSO, 1980; Fenner *et al.* 1988), human monkeypox should be not considered as a general public health risk.

Although attention has occasionally been drawn to similarities between smallpox and monkeypox viruses, they are quite distinct and stable (Dumbell & Archard, 1980; Esposito & Knight, 1985; Esposito, Nakano & Obijeski, 1985). There is no reason to suppose that changes will occur in monkeypox, or any other orthopoxvirus, which may have serious implications for future human populations.

SMALLPOX VACCINATION

The dramatic reduction in the numbers of smallpox cases led many countries to stop routine vaccination before eradication, and all looked forward to the final end of vaccination and vaccination complications. Ironically recent developments could mean perhaps greater usage of smallpox vaccine than ever.

At this stage continued use of smallpox vaccine can be discussed from three viewpoints: (1) for the purpose for which it was intended, i.e. to prevent smallpox, and by logical extension to prevent monkeypox where indicated; (2) its originally unintended and perhaps illogical use to prevent human infection by other orthopoxviruses; (3) as an infectious vector for foreign genes.

Vaccination to prevent smallpox and monkeypox

All countries have now stopped routine civilian vaccination but some, particularly the United States and the Soviet Union, still vaccinate military personnel. In consequence occasional complications in vaccinees and their contacts are still reported (e.g. CDC, 1985; Redfield *et al.* 1987). Any decision to stop such vaccination is inextricably linked with political decisions to renounce the use of smallpox as a biological weapon, and with problems of verification (Capps, Vermund & Johnsen 1986; Sidel, 1986).

As discussed above the vaccination of archaeologists and demolition workers has been proposed (Zuckermann, 1984). Here the risk of smallpox is very small and any decision on vaccination should be made on an individual basis after appropriate counselling.

The vaccination of those working with monkeypox is a prudent precaution required by most regulatory bodies; no cases have been reported in those studying the virus.

Vaccination to prevent other orthopoxvirus infections

At present in the UK the Joint Committee on Vaccination and Immunization recommends vaccination for those working with cowpox and vaccinia. The Advisory Committee on Dangerous Pathogens, whose regulations are not enforceable, and the Advisory Committee on Genetic Manipulation whose regulations are enforceable, also require it for those working with these viruses.

The rationale of deliberately using smallpox vaccination to prevent accidental infection with vaccinia and cowpox viruses is, in this writer's opinion, sufficiently

unsound to make statutory requirement or even over-zealous recommendation for vaccination highly questionable.

Britain abandoned routine vaccination in 1971 and, with increasing interest in recombinant vaccinia, primary vaccination of increasing numbers will be required. Primary vaccination accepts rigors, vomiting, bed rest, and absence from work as part of the normal course (Christie, 1980); in addition a minor complication rate of *c.* 8% can be expected (Symposium, 1977). Although human cowpox can be severe (Baxby, 1977*b*) and accidental vaccinia at an awkward site could be inconvenient, one has to balance the risk between an accidental infection should one occur, and at least the guaranteed 'normal' morbidity of primary vaccination plus the potential risk of a complication. The degree of protection will be limited and has not been assessed properly; revaccination studies have produced 'primary' responses in 10% of those properly vaccinated 6 months earlier (Symposium, 1977), and vaccination could not be expected to protect against e.g. accidental ocular infection.

Those required to defend the requirement for a primary vaccination which caused a complication, or which failed to prevent a subsequent accidental infection are in an unenviable position. This reaches its (il)logical conclusion with the enforceable requirement for primary vaccination with wild-type vaccine to prevent possible accidental infection with attenuated recombinant vaccinia strains (Buller *et al.* 1985).

This requirement for vaccination is currently being re-assessed and may well be relaxed. There is no public health risk from accidental cowpox or vaccinia providing simple precautions are taken. The risks to the individual from vaccination and accidental infection should be assessed carefully and the decision to accept vaccination or not should be left to the individual concerned after proper counselling. Refusal of vaccination should not necessarily exclude someone from work with cowpox or vaccinia viruses. Gloves, eye protection and careful technique are the only precautions available to those who have not had herpes simplex infection but are working with the virus; an unvaccinated individual working with cowpox and vaccinia is in no worse position.

Recombinant vaccinia vaccines

A major breakthrough with wide implications was the demonstration by two groups that foreign genes could be inserted into the genome of infectious vaccinia (Panicali & Paoletti, 1982; Mackett, Smith & Moss, 1982). The vaccinia genome has 'spare capacity' of at least 25000 base pairs (Smith & Moss, 1983) and this allows multiple copies of one gene, or a number of different genes to be inserted (Paoletti *et al.* 1985).

The list of genes inserted is extensive; it includes genes from human viruses e.g. hepatitis B (Smith, Mackett and Moss, 1983), and HIV (Chakrabarti *et al.* 1985; Hu, Kosowski & Dalrymple, 1985), animal viruses e.g. vesicular stomatitis (Mackett *et al.* 1985), plant viruses e.g. tobacco etch virus (Dougherty, Franke & Hruby, 1986), protozoa e.g. *Plasmodium* (Smith *et al.* 1984) and pharmacologically important products e.g. neuropeptides (Hruby & Thomas, 1987). In some cases, where the foreign genes have been inserted into and inactivated the vaccinia thymidine kinase gene, a degree of attenuation has been achieved (Buller *et al.*

These development open up the possibility of using the well-established practice of smallpox vaccine production and delivery to facilitate large scale production of recombinant vaccines and important biopharmaceuticals, (Quinnan, 1985; Brown, Schild & Ada, 1986; Hruby & Thomas, 1987). Before this can be put into practice more information is required about the genetic stability of, and immune response to, these recombinants. Ecological factors also need to be assessed, in particular the possibility that the recombinants may establish in animal populations or interact with viruses already established there (Baxby *et al* 1986). In this respect it is of interest that vaccinia, generally thought to be a laboratory virus with no natural reservoir, may have become established in India as 'buffalopox' (Baxby *et al.* 1986; unpublished; Dr Z. Jezek and Dr K. R. Dumbell, personal communications).

Vaccination and AIDS

A case of complicated vaccinia occurred in a military recruit who quickly developed clinical AIDS (Redfield *et al.* 1987). It was suggested that the vaccination had triggered the development of AIDS and that immunization programmes, particularly involving future use of recombinant vaccinia should be re-assessed, particularly in countries with a substantial incidence of sub-clinical AIDS (Redfield *et al.* 1987). A simultaneous review argued that vaccination programmes and other infections had not precipitated AIDS and that WHO recommendations on vaccination of HIV-positive individuals did not require revision (Halsey & Henderson, 1987). However, the idea that vaccination could trigger AIDS was extended to include the suggestion that the spread of HIV in Africa had been accelerated by mass smallpox vaccination (News Item, 1987*a*). It is doubtful whether the morbidity caused by vaccination campaigns in Africa added significantly to the general debilitation already caused by endemic infections and poor nutrition, and any spread of HIV via improperly sterilized vaccination needles must have had a very minor impact. Claims that vaccination might have helped to spread HIV infection were assessed by WHO and knowledgeable individuals and dismissed (News Item, 1987*b*).

COWPOX

The rarity of bovine cowpox, that most human cases have no link with cattle, and concurrent studies on the epidemiology of monkeypox and 'cowpox-like' viruses from Europe (see below) prompted a re-assessment of the epidemiology of cowpox (Baxby, 1977*b*). The conclusion that cowpox virus is not enzootic in cattle and probably circulates in a wildlife reservoir is generally accepted (Lancet 1986; Fenner *et al.* 1988).

Orthopoxvirus antibody has been detected in small numbers of voles and fieldmice in Britain (Kaplan *et al.* 1980). Because cowpox virus is the only orthopoxvirus indigenous to Britain, with the exception of ectromelia which has not reliably been detected in wildlife, the presumption that cowpox virus circulates in these rodents is a reasonable one. However, the precise animal reservoir(s) and full range of hosts still require detection.

Feline cowpox

Cowpox was diagnosed in captive cheetahs in British zoos in 1977 (Baxby *et al.* 1982), and the first case was detected in a domestic cat in 1978 (Thomsett, Baxby & Denham, 1978). Since then information has been collected on over 90 cases of cowpox in domestic cats, and details of many cases have been published (e.g. Gaskell *et al.* 1983; Martland, Poulton & Done, 1985; Bennett *et al.* 1986; Gaskell, Baxby & Bennett 1988; Baxby, 1988).

Infection is usually generalized but only limited cat-to-cat spread has occurred. Serological surveys have found little evidence of cowpox antibody in cats, so the cat should be considered as an indicator rather than a reservoir host (Bennett *et al.* 1986). Nevertheless the general picture of feline cowpox, with primary lesions which apparently occur as a result of bites, and the natural habits of cats are consistent with acquisition of infection from a wildlife reservoir (Bennett *et al.* 1986; Baxby, 1988). Further studies are needed on the epidemiology and significance of feline cowpox.

Human cowpox

Human cowpox is reported rarely (Baxby, 1977*b*, 1988; Lancet, 1986). However, because of interest in the infection it is likely that most diagnosed cases are reported (Lancet, 1986). It is of interest that cases of human cowpox contracted from, or least closely associated with, feline cowpox are now being reported (Willemse & Egberink, 1985; Pether *et al.* 1986; Lancet, 1986; Casemore *et al.* 1987). Human cowpox can be relatively severe especially in children (Baxby, 1977*b*) and veterinarians and cat owners should be aware of the risk of infection. The identification of a host for cowpox virus that is in intimate contact with humans is interesting in that human cowpox is reported relatively rarely. This suggests that trivial cases are being missed in which case the severe cases reported form a very small proportion, or that cowpox virus is of relatively low human infectivity (Lancet, 1986; Baxby 1988). Human cases occur in which no contact with cats or cattle is admitted and indirect infection via e.g. barbed wire, brambles has been suggested (Lancet 1986).

Cowpox-like viruses

Although cowpox virus is indigenous to Continental Europe the position there is complicated by the existence of 'cowpox-like' viruses (Baxby *et al.* 1979). These were isolated initially from captive exotic species such as large felines and elephants (Marennikova *et al.* 1977; Baxby & Ghaboosi, 1977). Further studies showed that the viruses circulate in Russian rodents (Marennikova *et al.* 1978). These viruses are very closely-related to cowpox and care is needed in differentiating them (Baxby *et al.* 1979; Pilaski, Rosen & Darai, 1986). The taxonomic position of these viruses requires clarification. Depending on results of DNA analysis not yet complete they will possibly be regarded as variants or sub-species of cowpox virus. In any event this close relationship will complicate searches in Europe for the hosts and reservoirs of these viruses and cowpox virus itself.

OTHER POXVIRUS INFECTIONS

This review has concentrated on those poxviruses which are human pathogens and antigenically related to smallpox (i.e. orthopoxviruses). Recent progress in the epidemiology of other poxvirus infections is briefly reviewed below.

Molluscum contagiosum

Attention has been drawn to the increasing tendency for molluscum contagiosum to present as a sexually-transmitted disease (Brown, Nalley & Kraus, 1981; Oriel, 1987). The infection also seems to be more common, or least more commonly reported; in the USA genital cases have increased tenfold between 1966 and 1983 (Becker *et al.* 1986), and in England cases have quadrupled between 1971 and 1985 (Oriel, 1987). The possibility that this relatively trivial infection may act as a marker for more serious conditions has been raised (Oriel, 1987).

The virus has still not been cultivated, but molecular studies on DNA from virions in clinical material have shown that at least two types of molluscum virus are in circulation (Porter *et al.* 1987) and extension of these studies may prove of clinical and epidemiological importance.

Tanapox

Little attention has been paid to this relatively trivial African zoonosis which has a non-human primate reservoir. However, the opportunity was taken during monkeypox surveillance activities in Zaire to collect data on Tanapox during 1979–83 (Jezek *et al.* 1985). A total of 357 cases were investigated of which 264 were confirmed by laboratory studies. Multiple lesions were rare; 78% had only one lesion, and very few had more than three. The lesions were usually found on exposed areas of the torso, but surprisingly rarely on the head. Case-to-case spread was extremely uncommon and the relative importance of direct infection from monkeys or insect transmission was not resolved. In view of the relative severity and poor prognosis of human monkeypox, the accurate diagnosis of these two poxvirus infections which occur in the same area is important (Jezek *et al.* 1985).

Parapoxvirus infections

The economic importance of parapoxvirus infections, particularly in sheep, and even in developed countries, continues to be emphasized (Robinson, 1983). However, human infections are relatively trivial and in most cases go unreported and uninvestigated (Baxby, 1988). Recent analysis of the DNA of various strains has lent some support to the traditional view that ovine (orf) and bovine (paravaccinia, pseudocowpox) strains are distinct (Gassman, Wyler & Wittek, 1985). However, such differences are very slight and probably do not justify the taxonomic separation of the species.

Camelpox and capripoxvirus infections

In the post-eradication era it was perhaps inevitable that WHO paid particular attention to monkeypox and other zoonotic orthopoxviruses (Arita & Gromyko, 1982; Fenner *et al.* 1988). However, now that smallpox has been eradicated

camelpox, which is not known to cause human infection, is probably the most important orthopoxvirus infection although unfortunately it has received relatively little attention (Baxby, 1988). Outbreaks can have serious consequences in nomadic communities dependent on the camel (Kriz, 1982; Davies *et al.* 1985). Although limited serological surveys have shown the extent of camelpox in Kenya (Davies *et al.* 1985), clinical surveys have been compromised by the failure to appreciate fully that pox in camels can also be caused by a parapoxvirus (Roslyakov, 1972; Kriz, 1982). More information is required on the epidemiology and relative importance of these two virus infections.

The sheep- and goat-pox – lumpy skin disease complex caused by capripoxviruses is now the most important of all poxvirus infections although again, not known to cause human infection (Baxby, 1988). The infections are widespread in Africa and the Indian sub-continent and cause great hardship to communities dependent on the host species. Recent work has greatly clarified the interrelationships of these viruses and provided potentially valuable means for their control.

The traditional view was that these viruses were host specific and that African and Indian virus strains were different (Singh, Pandey & Srivastava, 1979; Kitching, 1983). However, cross-infection experiments using strains from widely different countries, and from different species do not support this view (Kitching & Taylor, 1985). Further analysis of viral DNA shows the very close relationship of the capripoxviruses, and the current view is that sheeppox, goatpox and lumpy skin disease virus strains should be regarded as one capripoxvirus species (Kitching & Taylor, 1985; Black Hammond & Kitching, 1986). Appreciation of the close immunological relationships of the viruses and the fact that they are not host-specific has led to the development of a 'universal' capripoxvirus vaccine. This live attenuated vaccine, usable in cattle, sheep and goats, and effective against different virus strains has shown great initial promise, and is now undergoing further trials (Davies & Mbugwa, 1985; Kitching, Hammond & Taylor, 1987).

CONCLUSIONS

The last ten years have seen confirmation that smallpox has been eradicated, an increase in our knowledge of human poxvirus infections and their epidemiology, and posed questions still to be answered. In a wider context the successful eradication programme has led to consideration of what other infections could be eradicated (Symposium, 1982), and recent work on vaccinia virus opens up the prospect of its extended use as a vaccine vector and source of important biopharmaceuticals.

DERRICK BAXBY,
University Department of
Medical Microbiology,
Royal Liverpool Hospital,
Prescot Street,
Liverpool L7 8XW
UK

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