



Biosafety Implications of Polio Eradication

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Introduction

The last case of smallpox occurred in 1978, not in Africa, but in Birmingham, England, transmitted by aerosol from a smallpox laboratory to a person working in a nonlaboratory area of the building (World Health Assembly, 1980). Two persons died: the index smallpox case and the director of the laboratory, who took his own life.

The eradication of polio is now within sight. As with the smallpox virus, the last remaining posteradication reservoirs of wild polioviruses will be in the laboratories of the world. In May 1999, the World Health Assembly (WHA) recognized the consequences of accidental transmission of wild poliovirus from the laboratory to the community and resolved to link Regional certification of polio eradication to progress in laboratory containment (World Health Assembly, 1999).

The first steps toward poliovirus laboratory containment are already underway in the WHO Western Pacific (WPR) and the European (EUR) Regions. The WPR anticipated being certified as polio-free in the year 2000 and the EUR in 2001. Both Regions have begun the process of surveying all laboratories that might possess poliovirus infectious and/or potentially infectious materials and creating agency/institutional, national, and Regional inventories of laboratories that retain such materials.

The American Region (AMR) was the first Region to be certified as polio-free in 1994, before the WHA containment resolution. The AMR now faces the challenge of preparing for high containment by completing the national laboratory surveys and inventories over the next few years, in advance of global certification. The Global Commission for Certification of the Eradi-

cation of Poliomyelitis has advised that destruction or transfer of all wild poliovirus infectious materials to high level containment facilities must be implemented worldwide before global certification of eradication can be achieved. Finding laboratories that may possess wild poliovirus in the developing countries of the Region will be relatively straightforward. Their numbers are few and locations well known. Finding such laboratories in the more developed countries will be more complicated. A large number and wide variety of biomedical control, diagnostic, production, research, and teaching laboratories have worked with known and unknown wild poliovirus infectious materials over the past 60 years. These laboratories may be located in public health, environmental control, and defense agencies; hospitals; universities; and research institutions. Meeting the enormous and complex challenge of wild poliovirus containment requires the full support of nations at all levels of government.

Risk of Wild Poliovirus Escaping from the Laboratory

"Escape from the laboratory" is an unfortunate term, widely used in the media, which conveys the image of a malevolent microorganism flying or crawling from its prison laboratory freezer, intent on wreaking havoc on mankind. This popular, sensationalized image is mentally difficult to overcome. Reality is more mundane. Transmission of wild poliovirus from the laboratory to the community will occur only through human frailty, that is, by someone deliberately or accidentally working with infectious or potentially infectious materials under inappropriate or unsafe conditions.

The World Health Organization (WHO) defines

infectious materials as wild poliovirus isolates, reference strains, research derivatives with wild virus capsid sequences, clinical specimens from confirmed or suspected cases, infected experimental animals, and environmental sewage or water samples known or suspected to be contaminated (World Health Organization, 2000). Potentially infectious materials are defined as throat swabs, feces, and environmental samples collected for any purpose at a time and in a geographical area where polio was known or suspected to be present and maintained under conditions known to preserve the virus.

Poliovirus infections may be acquired through breathing contaminated aerosols or droplets, ingesting contaminated food or water, or placing contaminated objects in the mouth (Melnick, 1996). High doses of poliovirus are more likely to cause infection than low doses, particularly among persons with waning mucosal immunity. Thus, products of the poliovirus laboratory present a much greater risk than clinical materials. Poliovirus grown and manipulated in the laboratory for diagnostic or research purposes may contain 1,000 to 1,000,000 more virus particles than equal volumes of clinical materials. Working in the laboratory was recognized early in the prevaccine polio research era as presenting a much greater hazard than providing clinical care (Wenner & Paul, 1947).

Risks from potentially infectious materials collected from polio endemic regions for studies, for example, in bacteriology, parasitology, or nutrition laboratories, are likely to be very small, but not zero. The rationale for including potentially infectious materials on the list for containment stems from the high rate of subclinical to clinical (100 - 1,000 to 1) poliovirus infections (Melnick, 1996). During the polio high season in endemic countries, many children will be infected but not ill. Thus, some of the throat or stool specimens collected for other purposes may unknowingly contain wild poliovirus. Contaminated specimens in most collections will be random, and poliovirus content low. Risks further decrease if procedures in such laboratories involve heating or chemical treatment that may inactivate the virus. Risks increase when contaminated specimens are inoculated into cells or experimental

animals in which unsuspected wild polioviruses may also replicate.

Transmission of poliovirus from the laboratory to persons outside the laboratory through contaminated sewage effluents, solid wastes, or spent unfiltered air is theoretically possible, but difficult to document against a background of high level immunity in the population. Also, there is no direct evidence of the infection of others through contaminated skin or the clothing of laboratory workers. More readily documented has been disease among laboratory workers.

Twelve laboratory-acquired cases of poliomyelitis were reported from 1941 through 1976, all with potential for virus transmission to the community (World Health Organization, 2000). That no cases of polio among laboratory workers have been reported since 1976 testifies to the effectiveness of attenuated oral polio vaccine (OPV) and inactivated polio vaccine (IPV) and major improvements in laboratory techniques, equipment, and facilities. For many years, working with wild poliovirus has raised little concern about laboratory safety because of the strong protection against the disease provided by near universal immunization of laboratory workers and the population at large.

Unknown, however, is the occurrence of poliovirus infections among laboratory workers in the absence of disease. The effectiveness of polio vaccines in preventing laboratory-associated poliomyelitis does not necessarily extend to prevention of subclinical infections (Sutter, Cochi, & Melnick, 1999). Virus shedding in saliva and stools from unrecognized subclinical infections represents a serious potential for polio transmission to the community.

Silent transmission from the laboratory to the community can occur. Van Loon and coworkers reported the recovery of a wild poliovirus from an 18-month-old son of a worker in an IPV production facility (Mulders et al., 1997). The father had been exposed to an accidental spill of preinactivated virus a few weeks before the virus was recovered from the child. The mechanism of virus transmission from the father to the child was undetermined. The authors also describe a separate incident of the isolation of a common laboratory reference strain of unknown origin from a 3-year-old child.

Consequences of Transmitting Wild Polioviruses from the Laboratory to the Community

The purpose of wild poliovirus containment is to protect the community. The immunized laboratory worker is not at risk of disease. Neither is the community at significant risk of transmission as long as high levels of polio immunization are maintained worldwide (preeradication). After virus eradication (posteradication phase), the potential for erosion of immunization levels increases with time. Inadvertent transmission and spread of the virus during this phase is likely to be interrupted, but at considerable financial and programmatic costs. Once OPV immunization stops (postimmunization phase), the public health consequences of virus transmission from the laboratory to the community assumes greater proportions with each

new unimmunized annual birth cohort. Eventually a susceptible population will emerge which includes adolescents and adults who are at highest risk for the most severe consequences of infection, paralysis, and death. The potential for such an unprecedented pandemic dictates the need for increasingly stringent attention to containment in the years following cessation of immunization.

Stopping OPV Immunization

If the consequences of transmission are so great, why stop OPV immunization? For several reasons: First, continuing immunization in the absence of disease is difficult to justify and even more difficult to maintain. Second, nearly all vaccine or drug interventions carry some risks. The current Sabin OPV is associated with a risk of about one case of vaccine associated paralytic poliomyelitis (VAPP) per 2.4 million first doses of vac-

Figure 1

Requirements for Laboratories Having or Working with Polioviruses

		Eradication phase		
		Pre-eradication	Post-global eradication	Post-OPV immunization
		Wild virus circulating	No wild virus circulating for at least one year	OPV stopped
All laboratories	OPV vaccine/vaccine-derived virus	BSL*-2/polio	BSL-2/polio	BSL-3/polio
	Wild virus	BSL-2/polio	BSL-3/polio	BSL-4
Special circumstances	Public health and clinical (diagnostic tests only)	BSL-2/polio	BSL-2/polio†	BSL-2/polio**
	Vaccine production	OPV	BSL-2/polio	BSL-2/polio†
IPV		BSL-2/polio	BSL-3/polio	BSL-4‡
<p>* Biosafety level (see Box 9) † No live wild virus controls used in diagnostic or reference tests. ‡ Maximum containment in vaccine production facilities will be addressed on a facility-by-facility basis. ** No live virus controls used in diagnostic tests.</p>				

cine (Sutter, Cochi, & Melnick, 1999). VAPP was of little consequence when paralytic polio in the United States reached as much as 20,000 cases annually. But in the absence of epidemic polio for more than 20 years, the 4 to 8 VAPP cases each year became increasingly unacceptable. In the year 2000, the United States joined Canada and many Western European countries in recommending only IPV in its routine immunization schedule.

OPV continues to be essential for eradication in polio endemic countries because of its cost, ease of administration, and superior immunizing qualities. With each passing year after polio eradication, VAPP in developing countries will be more readily recognized and difficult to defend. Just as vaccine policy evolved away from OPV in the United States, the developing countries should expect no less. The appropriate strategy for stopping OPV immunization worldwide is the subject of current research. Whether stopping will be a synchronized regional or worldwide effort, with or without replacement by IPV for a limited time, is yet to be decided. The probability is high that OPV immunization will stop globally when it can be assured that wild poliovirus has been eradicated, that no OPV derived viruses are freely circulating, and wild polioviruses are contained in the laboratory (World Health Organization, 1998).

No laboratory is asked to destroy programmatically important viruses at this time, only that laboratories retaining wild poliovirus infectious and potentially infectious materials are listed on national inventories and meet the progressively stringent containment standards. Similarly, the identification of potentially infectious specimens need not culminate in the destruction of valuable research materials, but appropriate action should be initiated to complete studies on the materials, test for polioviruses, treat to inactivate polioviruses, or prepare for containment.

Action to be taken over the next few years in the Americas is a prerequisite for global certification of eradication. It includes national surveys of all biomedical laboratories, urging destruction of all unneeded wild poliovirus infectious materials, and the creation of national inventories of laboratories/agencies/institutions retaining such materials. This will be a major challenge for all nations, but particularly for those with large research institutions. Generic guidelines have been pre-

pared by WHO to assist Regions and nations in conducting surveys and preparing inventories. The scheme is hierarchical (Figure 2). Key to its success is the full cooperation and support of national governments, agencies/institutions, and the laboratories under their jurisdiction. At each of these levels, the role of the biosafety community is crucial.

Conclusions

There are those who maintain that it will be easier to eradicate wild poliovirus in nature than in the laboratories of the world. The former can be verified. The latter cannot.

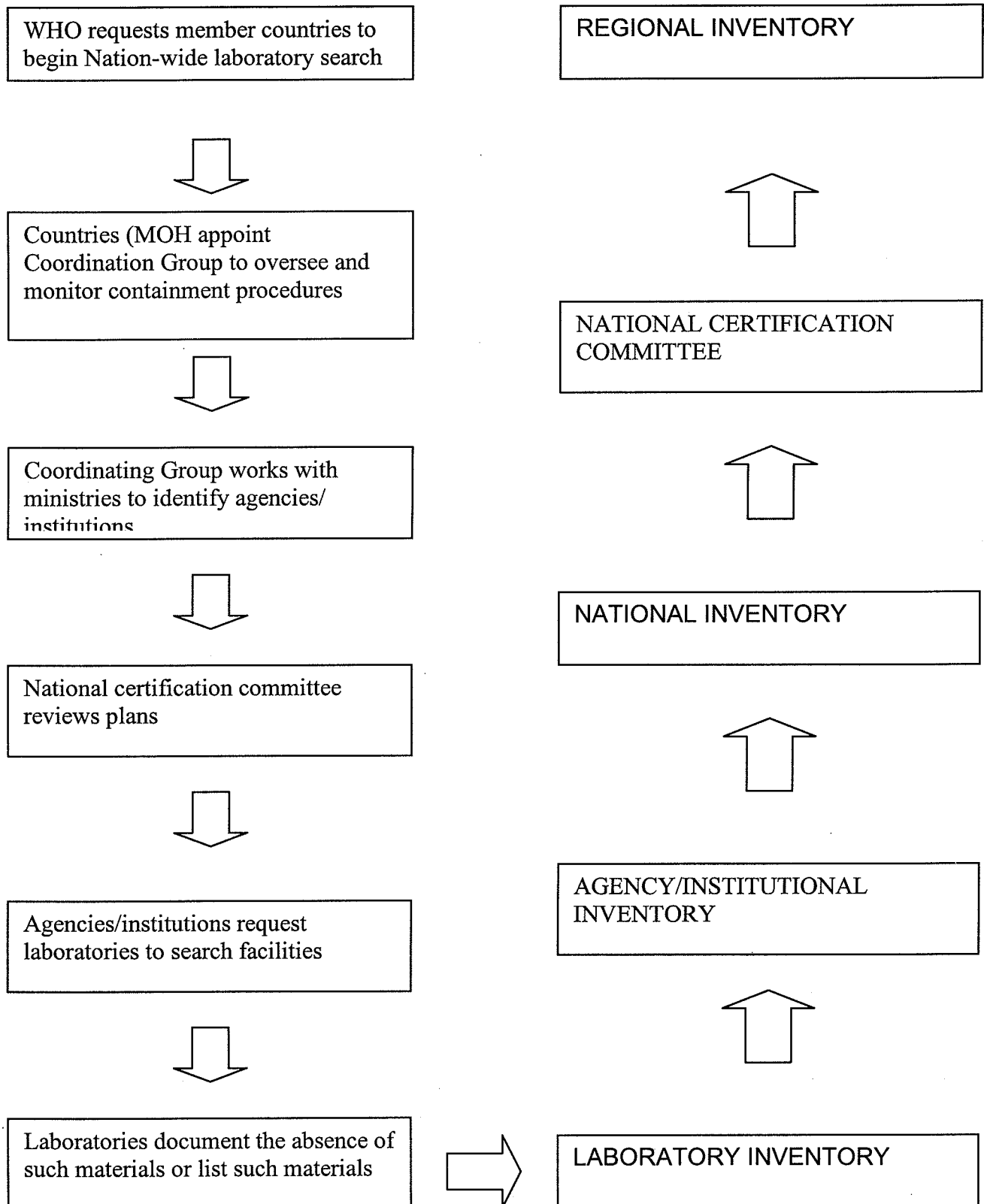
However, time is on our side. The step-wise process of national sensitization to the challenge begins now with the national survey and inventory of laboratories retaining wild poliovirus infectious and potentially infectious materials. Containment comes to the forefront again in 2 to 3 years when the wild virus in nature has been eradicated and the same laboratories are requested to implement high containment. The third opportunity to review compliance will occur in 5 to 10 years when decisions will be made on how and when to stop OPV immunization. Adequate evidence of wild polioviruses being present in a limited number of laboratories and under maximum containment will be key to that decision.

Attrition among the laboratories retaining wild polioviruses is expected with each containment phase. Moving from good laboratory practices to high containment represents a major investment in facilities, maintenance, and personnel, and an increasing national responsibility for safety. Moving from high to maximum containment represents still another major step in national investment and responsibility. At some point, nations and institutions will have to weigh the high costs of containment against the value of retaining a virus of no diagnostic or public health value.

As with smallpox, global surveillance for wild polioviruses will continue through the WHO Poliovirus Laboratory Network for many years after eradication. A polio vaccine stockpile and rapid response emergency plan will provide further insurance against the initial uncertainties of laboratory containment, bioterrorism, and reemerging virus. The polio eradication effort grew out of an unprecedented spirit of support among all na-

Figure 2

Developing the Global Inventory of Wild Poliovirus Infectious and/or Potentially Infectious Materials



tions, public and private organizations, and people at all levels all over the world. There is every reason to assume that this spirit of collaboration will continue and within a few years the risk of transmission of wild poliovirus from the laboratory to the community will no longer exist.

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