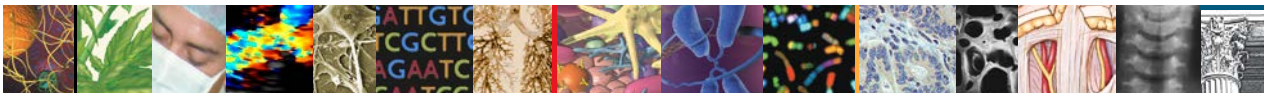

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Perspective

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Lessons from a Public Health Emergency — Importation of Wild Poliovirus to Israel

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Last year, Israel's polio-free status was seriously challenged. On May 28, 2013, a sample obtained during routine supplementary environmental surveillance at a sewage-treatment plant in the South district tested positive for wild poliovirus type 1.[1] Additional analyses retrospectively confirmed that the virus had already been present in February 2013 in samples from sewage-treatment plants near the capital of the South district. The virus found in these samples was closely related to polioviruses that have been circulating in polio-endemic Pakistan since 2012 and to the poliovirus that had been isolated from sewage samples in neighboring Egypt in December 2012.[2]

This public health emergency posed two major challenges for decision makers in Israel. The first one concerned the sustainability and interpretation of our supplementary environmental surveillance. Since the last poliomyelitis outbreak in Israel in 1988,[1] the country has developed the capacity in our environmental laboratories to detect pathogens such as polioviruses in very low quantities within large volumes of sewage, and we have fully deployed this high-sensitivity detection on a national scale. This system routinely covered approximately 30 to 40% of the population in a representative fashion,[2] and it was substantially intensified beginning in June 2013, shortly after the detection of the wild poliovirus importation. The number of sewage sites being sampled increased from a range of 8 to 10 per month to 80 per month at the height of the effort, to keep up with poliovirus activity.[2] The coverage of the sampling was thereby expanded to include as much as 80% of Israel's population, and the sampling frequency was increased from monthly to weekly.

This dramatically enhanced environmental surveillance, which has continued in 2014, has demonstrated the gradual clearance of the imported wild poliovirus since September 2013. Samples at all sampling sites outside the epicenter sites in southern Israel began testing negative quite rapidly, and later, the wild poliovirus gradually disappeared from the epicenter sites themselves — findings that indicated the fading out of human-to-human transmission of the virus and its excretion in feces. The latest surveillance data (from August 14, 2014) confirm the consistently negative results for all tested sites in Israel.

Since Israel's enhanced national environmental surveillance was functioning properly in real time, we had a substantial early-warning period that allowed decision makers to implement tailor-made, evidence-based public health interventions. It is unclear, however, whether such environmental surveillance is ripe for full deployment at a national scale in other regions of the world. Not only would the tool we used be difficult to sustain financially in many countries,[3] it has also not yet been scientifically shown to provide convincing correlations between positive surveillance samples and actual polio transmission in humans, nor have its methods (e.g., sample collection, laboratory analysis, and interpretation of results) been standardized by the international scientific community.

We would therefore support a recommendation that environmental parameters be added to the clinical definition of a polio-infected country, as long as such a measure would be comparable in sensitivity to the long-standing gold-standard criteria used for polio eradication worldwide, which involves the detection of clinical poliomyelitis cases. Such an addition would have to include valid, internationally accepted, standard definitions for detection of poliovirus circulation, as well as a consensus definition of poliovirus clearance.

The countries in which poliovirus is currently endemic (Pakistan, Nigeria, and Afghanistan) have not deployed such highly sensitive surveillance,[4] nor have some currently polio-free European countries that have environmental surveillance capabilities. In most countries, these capabilities are still limited in terms of population coverage and representativeness — they cover the population only partially and do not necessarily prioritize subpopulations according to the risk of polio transmission, which is higher in recently displaced and mobile populations than in more settled ones. Moreover, surveillance in many countries has not been deployed nationally to a truly representative population scale.

Israel's second challenge in addressing the poliovirus situation was deciding whether to use oral polio vaccine (OPV) in a population that had high coverage with inactivated polio vaccine (IPV). From the time the event began, it was understood that since the immunoprotection of children born after 2004 is based solely on high coverage with IPV, a large cohort of children was susceptible, in terms of intestinal immunity, to the silent transmission of wild poliovirus at the time of its initial importation early in 2013 and during the period of its sustained transmission in the summer of 2013.

Nevertheless, rapid implementation of multiple successive rounds of national supplementary OPV immunization activities, which is suggested in the global recommendations for clinical poliomyelitis outbreaks, was considered unjustified, given both Israel's high rate of protective IPV coverage (an average of 95% in recent years, as verified by recent national serologic surveys revealing that 98.2 to 100% of people have protective titers) and the country's sensitive, and now intensified, environmental surveillance. Public health policymakers therefore decided to use bivalent OPV (bOPV) in a single continuous national supplementary immunization activity.

Implementation of this public health measure began in August 2013. One dose of bOPV is now recommended for all children in Israel, including migrants, who were born after January 1, 2005, have received at least one dose of IPV in the past, are not currently immunocompromised, and do not live with an immunocompromised person. In the epicenter of wild poliovirus transmission in southern Israel, 90% coverage was achieved soon after implementation began, and by the end of 2013, national bOPV coverage among all vaccine-eligible candidates approached 80%. Since January 1, 2014, all children born after July 1, 2013, are candidates for two supplementary doses of bOPV, at the ages of 6 months and 18 months, in addition to the five-dose IPV routine childhood schedule.[1] This sustainable interim policy is expected to continue as long as poliomyelitis cases are detected in the region (for example, in Syria).

In designing a vaccination strategy, Israel faced a dilemma: conform to the global guidelines for management of a poliomyelitis outbreak or rely on its advanced environmental surveillance capacity to follow the road not taken. Other countries may also encounter this contemporary and critical challenge of choosing between automatically triggered multidose OPV use and an informed, evidence-based decision-making process; in Israel's case the latter option was made possible by our ultrasensitive early-warning system. We believe that Israel is now even safer for residents and travelers in terms of poliovirus transmission, given the intensified national environmental surveillance, combined with the continuously high routine

childhood IPV coverage and the interim bOPV supplementation.

We believe that the reasonable policy that was pursued in response to the detection of wild poliovirus has led to broad professional and political commitment to the public health response, as well as consistent resource allocation for implementing it.[1,5] Such national consensus should allow our public health record to remain intact: since 1988, no case of paralytic polio nor any wild-poliovirus–associated disease has been diagnosed in Israel.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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Medical Marijuana, Physicians, and State Law

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As Massachusetts prepares to implement its new medical-marijuana law, agents of the federal Drug Enforcement Administration (DEA) have reportedly visited at least seven Massachusetts physicians at their homes or offices and told them they must either give up their DEA registration or sever formal ties with proposed medical-marijuana dispensaries. These encounters were meant to intimidate the physicians and to discourage them from taking an active role in medical-marijuana dispensaries, and they have apparently succeeded. But there are differences between state and federal law, between talking to patients and selling drugs, and between acting as a physician and acting as a marijuana entrepreneur. With medical-marijuana laws poised to come into effect in a majority of states, it seems worthwhile to put medical marijuana in historical and legal context.

Americans strongly support making marijuana accessible to sick people who might benefit from its use, with 86% believing that physicians should be able to recommend marijuana to their seriously ill patients. The DEA has been consistent in its campaign to discourage physicians from discussing marijuana with their patients, probably because the agency sees such discussions as legitimizing the use of a drug that it still apparently believes, in disregard of the evidence, was reasonably designated a Schedule I drug — a drug with no medical use and a high potential for abuse.

In 1997, the editor-in-chief of the *Journal* argued that the federal drug laws that prohibited physicians from helping their suffering patients by suggesting that marijuana may be beneficial to them was "misguided, heavy-handed, and inhumane."[1] The editorial was responding to California's first-in-the-nation broad medical-marijuana law and DEA agents' subsequent threats to revoke the DEA registrations of California physicians who suggested that a patient might benefit from marijuana as permitted by the new law.[2] California has now been joined by more than 20 additional states in permitting patients to possess marijuana on the advice of their physician (see table). There has, however, been no change in federal law — which still prohibits possession and sale of marijuana — and little change in the DEA's tactics.

State law cannot change federal law, and in late 1996 the Department of Health and Human Services, the U.S. attorney general, and the DEA announced their intention to continue to enforce federal drug laws in California regardless of California's new law. Attorney General Janet Reno put it this way: "Federal law still applies . . . . U.S. attorneys . . . will continue to review cases for prosecution and DEA officials will review cases as they have to determine whether to revoke the registration of any physician who recommends or prescribes so-called Schedule I controlled substances."[2]