It at a very early age rarely suffer permanent damage and acquire immunity” (p. 800) [3].

Since the introduction of the WHO vaccination campaign, the situation has changed. If there is reinfection in a country where the wild virus has been removed, the first contact is no longer during infancy but later, during childhood or adolescence. Then these children or adolescents, not being fully protected by vaccination, are likely to become paralyzed. This is the probable explanation for the outbreak in Namibia, where children ≈12 years old developed poliomyelitis, including 3 who had bulbar palsy [4, 5]. It has been confirmed that the source of this outbreak was Angola [6]. A more-severe epidemic occurred in Angola, where there were 1093 cases, including 89 deaths [7].

At present, as a result of the WHO initiative, the wild virus is now confined to a few countries, but naturally acquired immunity has been lost, and the whole of the developing world is now vulnerable to epidemics of poliomyelitis, which could lead to severe paralysis and increased mortality. This has already happened as a result of the spread of the wild virus from northern Nigeria.

In considering the evidence presented here, and given the doubts about the clinical diagnosis of poliomyelitis [8, 9], it would have been more rational to introduce vaccination gradually and only when the infant mortality rate had decreased substantially. Before vaccination was available, Europeans who were living in Casablanca, Kenya, and South Africa had a much higher frequency of developing poliomyelitis than did the indigenous people [9]. Now, individuals in these developing countries with a high standard of living would be at a similar risk of becoming paralyzed, but they could easily be vaccinated.

Not all of the early pioneers concerned with poliomyelitis would have agreed that there was “a clear vision on how to begin the journey to polio eradication” (p. 1343) [1]. Macfarlane Burnet [10], in his classic account of the natural history of poliomyelitis, would not have countenanced the loss of naturally acquired immunity, and he may well have predicted that the present critical situation would occur.

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virus exposure, natural immunity comes at a steep price: ~1 of every 200 initial infections with wild poliovirus results in paralytic poliomyelitis [2]. The misconception that paralytic polio was not a major public health problem in developing countries because infections normally occurred early in life is largely attributable to the previous gross underreporting of cases [3]. Lamine surveys in many developing countries in Asia and Africa in 1976–1980 revealed that <5% of the true number of cases were officially reported [3]. When case estimates were corrected for underreporting, the magnitude of the polio problem in developing countries became apparent. India alone was estimated to have had >200,000 cases of polio during the early 1980s, which accounted for more than one-half of the global total [4]. At that time, the city of Mumbai was reporting >1000 cases per year, >80% of which occurred among children <2 years old [5]. The large majority of these cases occurred in slum areas with intense poliovirus circulation and with very low rates of oral poliovirus vaccine (OPV) coverage, whereas children in immediately adjacent neighborhoods with better living conditions and access to OPV were largely spared.

The sharply divergent risks for paralytic polio between well-immunized populations in developed countries and unimmunized children in developing countries prompted the launch by the World Health Organization (WHO) of polio eradication initiatives, first in the Americas in 1985 and then worldwide in 1988 [6]. The 4-pronged WHO strategy of improved routine vaccine coverage, supplementary large-scale OPV campaigns, targeted outbreak response immunization, and sensitive surveillance for cases of polio has reduced the incidence of polio by >99% since 1988 and prevents at least 400,000 cases/year in developing countries [7] (for updates, see http://www.polioeradication.org). Surveillance for cases of acute flaccid paralysis has been closely integrated with laboratory investigations, such that every wild poliovirus strain isolated from a person with paralytic polio is characterized by genetic sequencing [8]. Special environmental sampling studies, backed by the sequencing of poliovirus isolates, have been implemented in key high-risk areas, to increase surveillance sensitivity [8]. Through this integrated surveillance system, the WHO has a comprehensive, up-to-date view of the worldwide patterns of poliovirus transmission.

Despite these advances, challenges to reaching pockets of underserved children in northern India, southern Afghanistan and adjoining areas of Pakistan, and especially northern Nigeria have given polio a reprieve [7]. Wild poliovirus type 1 has spread from northern Nigeria to 18 countries, from Guinea in the west to Indonesia in the east, and across the border from northern India to Nepal and Bangladesh, and it has been introduced into Angola, the Democratic Republic of Congo, and Namibia in Africa [9]. The ensuing large outbreaks and rapid spread of poliovirus were the result of widening immunity gaps in previously polio-free countries that had failed to sustain high rates of OPV coverage after the eradication of their indigenous wild polioviruses. The current scenario of waning public investment and community participation in immunization after the disappearance of cases of polio was explicitly envisioned by Burnet and White [10] as a serious impediment to global eradication, despite the outstanding success of polio immunization in developed countries. Although developing countries in the Americas, East Asia, and elsewhere have maintained high rates of OPV coverage for many years after the last cases of polio caused by wild poliovirus, serious challenges remain to building routine immunization systems capable of sustaining high rates of vaccine coverage in the poorest countries of Africa and Asia. Now the most direct path to global polio eradication is prompt implementation of high-quality immunization activities in the areas where polio remains endemic while maintaining adequate levels of population immunity elsewhere. Natural population immunity from the recent outbreaks has partially closed the immunity gaps in the last endemic reservoirs, opening a window of opportunity to finally close these critical gaps. Delays in achieving high rates of OPV coverage would allow the gaps in immunity to again widen, prolonging the period of endemicity and presenting a continuing risk of local outbreaks and further dissemination of virus to polio-free countries. Ongoing and future initiatives to control other vaccine-preventable infectious diseases [11] can benefit from the current experience with polio by striving to minimize the period of transition from natural immunity to high levels of vaccine-induced population immunity.

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Influence of High- Efficiency Particulate Air Filtration on Mortality and Fungal Infection: A Rebuttal

To the Editor—The article by Eckmanns et al. [1] on the use of high-efficiency particulate air (HEPA) filtration on fungal infection was of interest to us, because we have been involved in infection prophylaxis for patients with acute leukemia since the 1960s [2]. As effective therapy became available for these patients, it was recognized that infectious complications not only were a major cause of death but also caused delays in the administration and dosage reductions of chemotherapy, thus reducing its efficacy. Protected environment—prophylactic antibiotic (PEPA) programs were developed to attempt to reduce the risk of infection during periods of neutropenia after chemotherapy. These PEPA programs included isolation units with HEPA filtration, strict patient isolation, special water-purification systems, special handling of patient wastes, and food restrictions.

The first type of isolation unit consisted of a bed enclosed within a plastic tent and a HEPA filtration unit. Subsequently, laminar airflow (LAF) rooms were designed in which one entire wall consisted of a HEPA filtration unit. The airflow in these units is laminar in distribution (although not completely), and the number of air exchanges is much higher than that obtained with a simple HEPA unit. The first LAF unit for patient occupancy was installed at our institution in 1968 [2]. The first LAF facility (a 20-bed unit) incorporated into the original design and construction of a hospital was opened here in 1977 and was in continuous operation until 2000 [3]. We have published >40 papers related to PEPA studies, varying from microbiological assessments to chemotherapy dosage escalation studies, and >2000 patients have been treated [4, 5].

Unfortunately, the review conducted by Eckmanns et al. [1] suffers from several methodological flaws. The clinical trials that they examined were designed to evaluate the entire PEPA program and not just air filtration. Most clinical trials of the PEPA program were mainly focused on the outcome of the chemotherapy—specifically whether it increased complete remission rates, the duration of remission, and survival. The focus on infection was whether it occurred and not the infecting organism and site of infection. Hence, most studies of the PEPA program were not designed to evaluate their impact specifically on fungal infections. The authors claim a “bias” because “studies that showed a small effect and no influence of ventilation on fungal infection are missing” (p. 1413), which is an erroneous conclusion for the reason cited above.

The most serious flaw of the analysis by Eckmanns et al. [1] is that the authors used all fungal infections in evaluating the impact of air filtration. Although mold spores are dispersed into the air and are usually respiratory pathogens, air is not the usual mode of transmission of Candida species, which have been the most common cause of fungal infection in these patients. HEPA filtration would not be expected to have a major impact on Candida infections. In an analysis of 102 treatment episodes in protected-environment (PE) units at our institution, 17 patients developed Candida infection, and only 1 developed aspergillosis [6]. Although Candida species can be cultured from various environmental sites, in that study, all of the infected patients had Candida species recovered from body sites before entry that persisted until the time of infection, despite antifungal prophylaxis.

The authors mention as a limitation “that none of the studies was blinded” (p. 1414). They state that “no studies involved the appropriate control subjects, who should have been situated in rooms with air conditioning but without HEPA filters” (p. 1414). Much effort is put forth during the installation of HEPA filters in LAF rooms to ensure that there is a tight seal between components. The HEPA filters cannot be installed and removed at will without damaging these seals. Also, for patients in groups to be comparable except for air filtration would require that all other prophylactic measures be followed in all patients. We recognized the practical impossibility of conducting a blinded study. A statistician with extensive experience in clinical trials was involved in the design and analysis of our studies.

The authors cite one of our studies that they discredited because “it did not contain valid data” (p. 1410), without specifying what was invalid [1, 7]. Presumably, this refers to a comment they made in the following paragraph referring to “a contradiction between the text and a figure” (p. 1410). We have carefully reviewed the article, and we can find no such contradiction.

The authors state that their second study suffered from a “severe methodological flaw in randomization” (p. 1410) [1, 8]. “Patients were only randomized to a PE unit when a unit was available” (p. 1410). The small number of PE units and the economic consequences would not permit us to always have an empty PE unit available. To enter patients in the study only when a PE unit was available would have prolonged the study beyond the period of our grant support. Referral of patients to our institution for therapy was a random event, and patients nearly always required...