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Response: We appreciate the comment by Unterman about our recent report and apologize for not having cited papers by his group (*1*). We note that the model we cited (*2*) also considered the possibility that glucocorticoid-stimulated potential, rather than binding of HNF-3, may be influenced by insulin signaling. In our discussion about the possible mechanisms for the antagonism between the insulin/IGF signaling and HNF-3/*forkhead* proteins, we did not mean to imply that the effects were "direct" or "simple."

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Ending Polio Immunization

In back-to-back Policy Forums on 8 August, A. W. Dove and V. R. Racaniello (p. 779) and H. F. Hull and R. B. Aylward (p. 780) discuss various strategies for the "eventual cessation" of immunization of children against polio, now that the worldwide eradication of the disease is within sight. We, however, would like to add a cautionary point.

If, say, after 5 years of inactivated polio vaccine (IPV) immunization and five further years of nonimmunization, no virus can be detected (even in the susceptible cohorts of nonvaccinated newborns), then intensive surveillance might gradually be ended. It is only at this stage (not likely before the year 2010) that the world could be declared free of poliovirus.

To help this approach, priorities on the research agenda should be (i) to gain insight in enterovirus RNA sequences that determine transmissibility, as well as the possibility that such sequences are obtained by polioviruses, in particular oral polio vaccine (OPV) Sabin strains, through genetic drift or recombination; (ii) to develop serological tests that are able to detect infected persons in populations vaccinated with inactivated polio vaccine; and (iii) to optimize surveillance strategies, sampling theory, and formulation of criteria for certifying countries as poliovirus-free.

We cannot get absolute proof of the absence of "the needle in the haystack" (poliovirus in the world) before we should want to ban immunization. Thus, immediately after ending immunization, a population of susceptible children will develop who necessarily, but much to our unease, will prove the correctness of the assumptions made. Sad disappointments may therefore follow the ban on polio immunization, and we should be prepared to respond rapidly to unpredicted outbreaks with at-the-ready high-quality diagnostics and, above all, large quantities of vaccine (both OPV and IPV).

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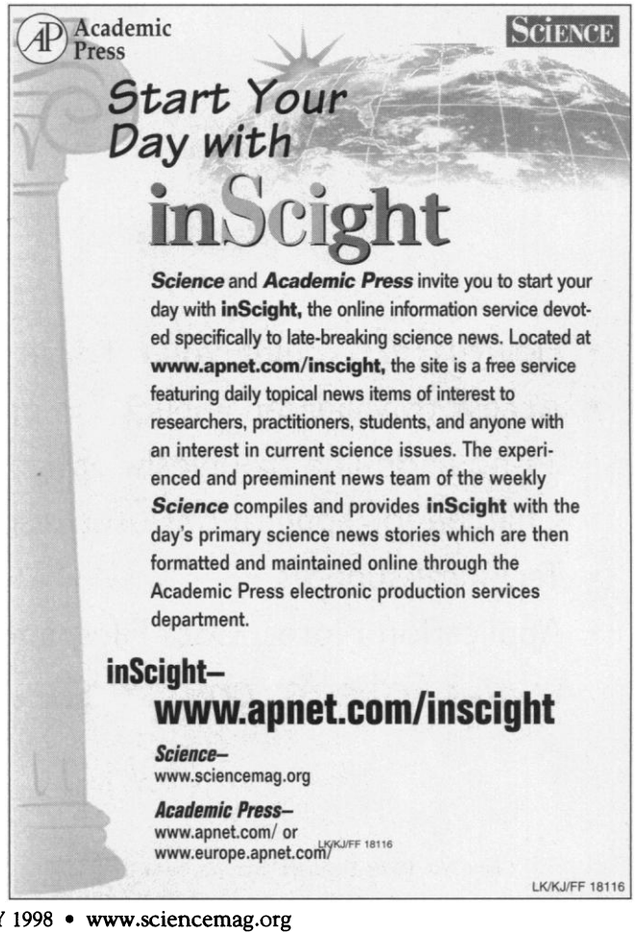

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Response: Kimman *et al.* have provided a useful addition to the debate over polio eradication by outlining specific recommendations for policy changes. We agree that the cessation of vaccination should only occur after an intermediate stage of IPV use, but it is not clear that this strategy alone will make the transition safe, even with improved monitoring.

We agree that large stocks of polio vaccine should be kept on hand if vaccination is stopped, but feel that IPV would be the only viable choice. The use of OPV to control outbreaks in a population that has never been exposed to wild or vaccine polio carries the danger that live vaccine virus may spread outside of the area targeted for control and cause poliomyelitis. Also, the production of vaccine stocks after the end of vaccination presents a serious biohazard, and Kimman *et al.* do not present a plan to ensure the safety of this process. Retooling vaccine production facilities to operate at biosafety level 4 would represent a substantial added cost for the eradication effort.

Kimman *et al.* do not mention the considerable challenge of accounting for worldwide laboratory stocks of neurovirulent, transmissible strains of polio—a challenge made more threatening by the possibility that nations or groups could easily obtain and conceal such stocks for future use as biological weapons if vaccination is stopped.

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Response: The World Health Organization (WHO) welcomes comments during the development of policy on the final phases of polio eradication. The theoretical risk of ongoing circulation of virulent vaccine-derived polioviruses must be balanced against the existing empirical evidence which indicates that vaccine strains do not circulate indefinitely. Recognized gaps in scientific knowledge on this issue are currently being addressed through a number of ongoing studies. Additional studies have been funded and will begin shortly. In March 1998, WHO will hold the next in a series of meetings on the issues raised by Kimman and Dove and their co-authors. This meeting will review the substantial body of existing data and define the additional evidence needed to make a scientific recommendation on stopping polio immunization. Laboratory containment of wild poliovirus stocks/infectious materials and potentially infectious materials was discussed in September 1997. A draft plan of action is being developed for review by the scientific community prior to implementation.

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Letters to the Editor

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