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Dear Dr. Lederberg,

Your approach to the threat of pandemic disease is much broader than that which I followed in the enclosed papers. I chose to focus on the effect of population homogeneity on adaptation by infectious agents, rather than adaptation to the world's population as a whole.

The evidence is thin and I put this out as a hypothesis in the hope that more evidence, pro or con, might be mustered. It has now been presented orally in a number of forums, with no convincingly negative data elicited in rebuttle. The hypothesis derived from the inverse relationship between polymorphism at the MHC and susceptiblity to epidemic disease in New World and Old World populations. The best hard evidence comes from the work of Garenne and Aaby on the dependence of measles mortality on genetic relatedness between primary and secondary patients (JID 161:1088,1990). A weakness here is that closely related people may transfer larger innocula, but there is data indicating the effect of innoculum size is minor. I also consider supportive that fact that EBV takes on a different antigenic structure in a population (New Guinea lowlanders with high A11 freq.) that is particularly responsive, immunologically, to the usual form (deCampos-Lima et al Science 260:98,1993). The chief alternative explanation of high New World mortality has been that these people are genetically more susceptible, but we find almost no evidence of this in extensive studies with standard (vaccine) infections that have no opportunity to adapt.

The idea that viruses might take on host HLA proteins and thus hide from new hosts that carry the same alleles, opens up an alternative mechanism for dependence of virulence on population homogeneity and I thank you for drawing it to my attention. I gather this phenomenon is known only in HIV, but it would seem possible with other enveloped viruses. I shall particularly bear it in mind vis-a-vis HTLV-II which attains extraordinary prevalence rates in some of our populations (AIDS Res Hum Retrov 10:1165,1994).

Thank you for your suggestions,

Francis L. Black

cc: Cosby 4/95