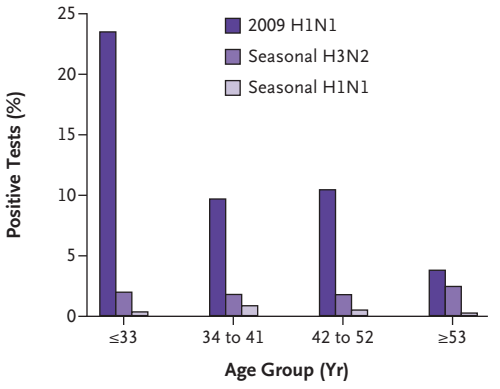

Figure 1. Age-Related Probability of Seasonal Influenza A and 2009 H1N1 Influenza in 11,560 Tested Patients.

Patients who were born after 1957 (i.e., ≤53 years of age) have an increased risk of infection with the 2009 pandemic influenza A (H1N1) virus. The results of testing show no significant relationship between age group and the risk of infection with seasonal influenza A viruses (either H3N2 or H1N1).

number of infections was not simply a reflection of decreased testing in this group. The mechanism for this association is unclear but is compatible with the reported age-related increase in the prevalence of neutralizing antibody titers against the 2009 H1N1 virus[3] and may reflect some immunity to infection as a result of exposure to similar viruses in early life. Maximally effective host immune responses to influenza may be generated by early-life infections.[4] These findings are consistent with the high frequency of outbreaks of 2009 H1N1 influenza in schools[5] and the decreased frequency of outbreaks in long-term care facilities that have been associated with this pandemic virus to date.

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Pathological Changes Associated with the 2009 H1N1 Virus

TO THE EDITOR: Between April 23, 2009, and May 15, 2009, we performed 15 autopsies on deceased patients in whom probable influenza had been diagnosed either clinically or macroscopically. Small samples of lung tissue were obtained and taken for analysis to the Institute of Epidemiological Diagnosis and Reference in Mexico City. Five infections with the 2009 pandemic influenza A (H1N1) virus were confirmed with the use of a real-time reverse-transcriptase–polymerase-chain-reaction assay, after it was determined that these patients were seronegative for influenza B virus, respiratory syncytial virus, parainfluenza virus (types 1, 2, and 3), and adenovirus.[1] From these five patients, organ samples were collected, fixed in 10% formalin, embedded in paraffin, and stained with hematoxylin and eosin. In the remaining 10 patients in whom the 2009 H1N1 virus was not detected, histopathological analyses identified bacterial pneumonia.

All five patients with diagnosed 2009 H1N1 influenza had been residents of Mexico City. Four of them were young adults (ages 22, 26, 28, and 37 years) who were hospitalized with the presump-

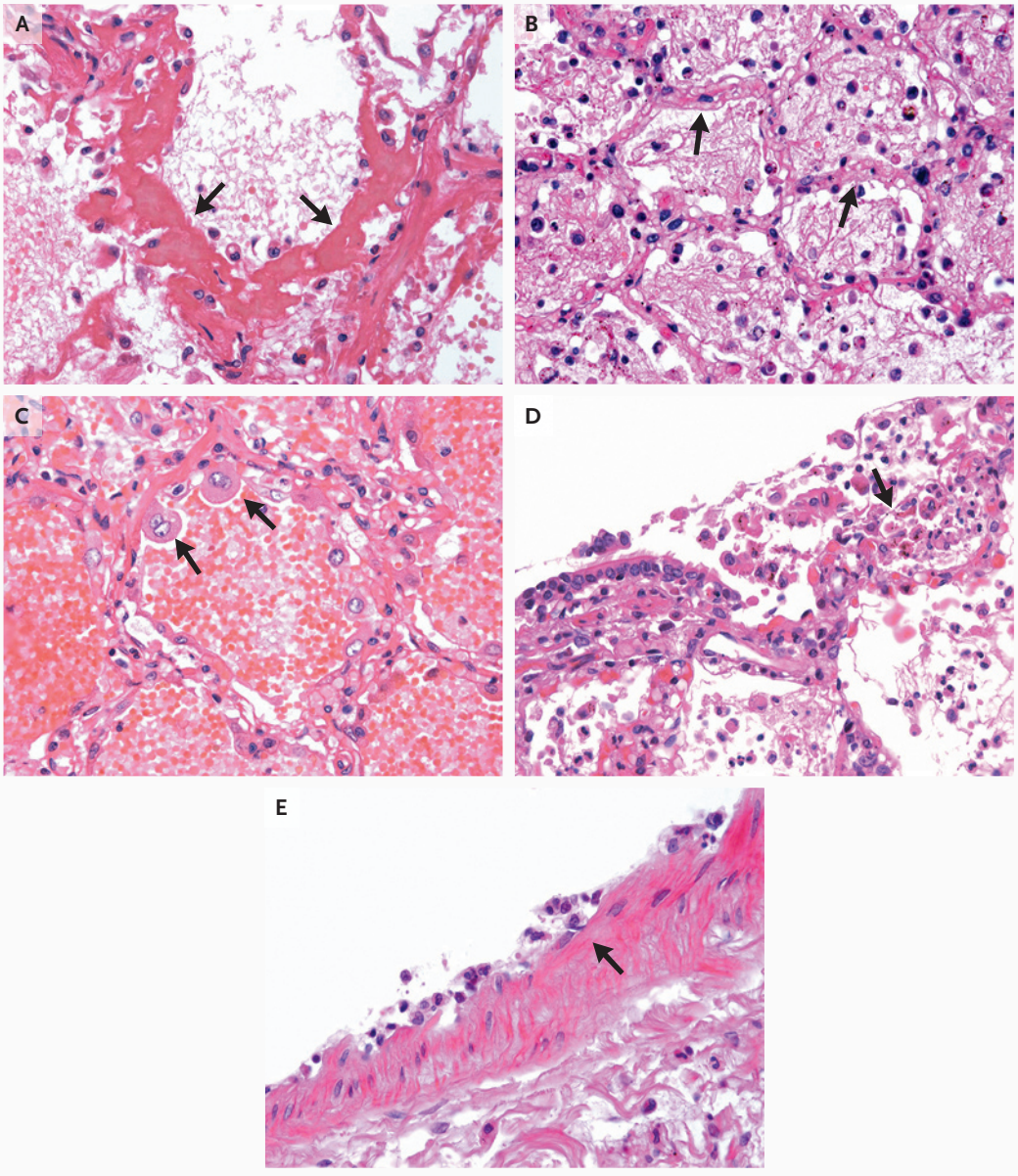

Figure 1. Micrographs of Lung Tissue from Five Patients with Fatal 2009 H1N1 Influenza.

Panel A shows hyaline membranes (arrows). Panel B shows a thickened alveolar septum associated with predominant edema (arrows). Panel C shows hyperplasia of type II pneumocytes (arrows). Panel D shows an inflamed, necrotized bronchiole wall with partial loss of the coating epithelium (arrow). Panel E shows inflammatory infiltrate in the intima of the wall of a medium-caliber blood vessel, below and between the endothelial cells (endotheliitis) (arrow).

tive diagnosis of influenza. These patients were initially treated with antibiotics for bacterial pneumonia. The fifth patient was an 83-year-old woman with a diagnosis of cerebral hemorrhage, who had no clinical signs of influenza but showed characteristics of hemorrhagic pneumonia on macroscopic evaluation. The patients had died 7 to 13 days after the onset of influenza symptoms.

On autopsy for all five patients, the right and left lungs had increased in weight (650 to 1200 g for each lung; normal, 450 g) and had a solid consistency (see Fig. 1 in the Supplementary Appen-

dix, available with the full text of this letter at NEJM.org). In four patients, zones of edema, hemorrhage, or necrosis were observed in the upper respiratory tract on the internal surface of the larynx and trachea, as reported in previous cases of seasonal influenza.[2,3] All five patients showed evidence of pulmonary damage and signs of acute interstitial lesions, as noted in patients with avian influenza A (H5N1) virus infection.[3,4]

In four patients, we observed hyaline membranes, alveolar septal edema, hyperplasia of type II pneumocytes, fibrin thrombus in the vascular lumen, and necrosis of the bronchiolar walls; three patients had inflammatory infiltrate below the endothelium and partial loss and adherence of the endothelium in the medium- and small-caliber intrapulmonary blood vessels (Fig. 1). These histologic changes are characteristics of influenza though not pathognomonic. In three patients, we observed pneumonia foci with intraalveolar exudates without evidence of bacterial colonies; however, nearly all the patients had received antibiotic treatment. In two patients, we observed erythrophagocytosis and phagocytosis of inflammatory cells in the liver, spleen, and bone marrow, which is similar to observations in lethal cases of infection with the avian influenza A (H5N1) virus[2] (Fig. 2 and 3 in the Supplementary Appendix). One patient had focal centrilobular necrosis of the liver and hemorrhagic necrosis of the adrenal gland cortex, and acute tubular necrosis was observed in another patient.

The cause of death in one patient was parenchymal cerebral hemorrhage. Histologic evaluation of the lungs showed only septal edema and extensive hemorrhage with scarce fibrin thrombi. The interstitial lesion was incipient, and hemorrhage was the predominant characteristic. These observations may represent an early stage of an acute pulmonary lesion that had not yet transitioned from the exudative phase to the proliferative phase.

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