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Hilleman M R & Werner J H. Recovery of new agent from patients with acute respiratory illness. *Proc. Soc. Exp. Biol. Med.* 85:183-8, 1954.
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A new viral agent was recovered from a military recruit with primary atypical pneumonia (PAP). This patient, together with other patients with acute respiratory disease and PAP, developed complement-fixing and neutralizing antibodies against the virus showing its etiologic significance. Demonstration of antibody in the general population indicated widespread prevalence of the agent. [The *SCI*® indicates that this paper has been cited in over 240 publications since 1955.]

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While at what is now called the Walter Reed Army Institute of Research in Washington, DC, I was engaged in studies of acute respiratory illnesses, particularly influenza, with a view toward control of pandemic disease. I'd located an influenza outbreak at Fort Leonard Wood, Missouri, in 1953 and took a team out to harvest throat washings from a very large number of cases for studies of influenza virus in its natural state in humans. On return, laboratory tests showed that the cases were not influenza; the epidemic had changed from influenza to acute respiratory disease (ARD) and primary atypical pneumonia (PAP), etiology unknown.

This was a huge embarrassment, and it was necessary to take action to retrieve something of value after having made such a "blooper." Jacqueline Werner and I tried to isolate the responsible agent by application of Enders's newly rejuvenated tissue-explant technology. We prepared explant cultures of tracheal epithelium from a patient who had expired at Walter Reed Army Hospital and inoculated them with throat washings from patients in the epidemic. On the first try, we isolated viruses we then called RI viruses but that are now called adenoviruses. Later, we found them to be related to "latent" agents, called APC viruses, that Robert Huebner was getting out of tonsils and adenoids but that were unassociated with disease. Luckily, J. Syverton's technology for mass preparation of HeLa cells in culture came along at that time and provided us with a reliable and practical system for virus propagation and measurement. The findings with a single virus strain, RI-67, which was recovered from one of the clinical specimens, were recorded in this publication.

Things moved very quickly. In the short span of three years, we were able to develop routine diagnostic technology for adenovirus infection and to describe the clinical illnesses of PAP and ARD on an agent-specific basis. We described the epidemiology of these diseases in detail, showed the existence of numerous viral serotypes, and developed and proved the high-level protective efficacy of a killed adenovirus vaccine that we made using RI-67 virus grown in cultures of monkey kidney.

These were exciting times, working with a new family of viruses that were soon found to cause widespread respiratory illnesses in children and, for certain of the serotypes, to display oncogenicity in animals, if not in humans. The paper has been highly cited because it represents a major breakthrough in viral etiologic discovery and in viral oncogenicity as well. It opened a door to understanding a prime cause for epidemic respiratory illnesses, not only in military recruits, but in the general population also. Additionally, it provided a prime model for the study and understanding of the induction of cancer by viruses as well as the molecular genetics of oncogenesis by DNA viruses. I received a number of awards and recognitions at the time, the most outstanding being the Armed Forces Distinguished Civilian Service Award given in 1957 by "Engine Charlie" Wilson, then Secretary of Defense. Werner von Braun received the same award at the same time for his rocket research. I suppose this basic work, together with other research I did in continuing years, contributed to my receipt of the Albert Lasker Medical Research Award in 1983 and my election to the National Academy of Sciences. Additional references relating to the adenovirus work are cited in the bibliography.[1-6]

1. **Hilleman M R, Warfield M S, Anderson S A & Werner J H.** Adenovirus (RI-APC-ARD) vaccine for prevention of acute respiratory illness. 1. Vaccine development. *J. Amer. Med. Assn.* 163:4-9, 1957.
2. **Stallones R A, Hilleman M R, Gauld R L, Warfield M S & Anderson S A.** Adenovirus (RI-APC-ARD) vaccine for prevention of acute respiratory illness. 2. Field evaluation. *J. Amer. Med. Assn.* 163:9-15, 1957.
3. **Hilleman M R, Gauld R L, Butler R L, Stallones R A, Hedberg C L, Warfield M S & Anderson S A.** Appraisal of occurrence of adenovirus-caused respiratory illness in military populations. *Amer. J. Hyg.* 66:29-41, 1957.
4. **Hilleman M R.** Adenovirus vaccine: development, field evaluation, and appraisal of the need for vaccination in military and civilian populations. *AMA Arch. Intern. Med.* 101:47-53, 1958.
5. **Hilleman M R, Greenberg J H, Warfield M S, Anderson S A & Glabere R R.** Second field evaluation of bivalent types 4 and 7 adenovirus vaccine for prevention of acute respiratory disease in military recruits. *AMA Arch. Intern. Med.* 102:428-36, 1958.
6. **Larson V M, Girardi A J, Hilleman M R & Zwickey R E.** Studies of oncogenicity of adenovirus type 7 viruses. *Proc. Soc. Exp. Biol. Med.* 118:15-24, 1965.

