the hemagglutinin moiety are the primary determinant of influenza immunity, this major change in antigen composition largely circumvented existing immunities and initiated an influenza pandemic. Recent evidence from Jerome L. Schulman of Mount Sinai and from Arnold S. Monto and Alan P. Kendal of the University of Michigan, Ann Arbor, suggests, however, that residual antibodies to the neuraminidase antigen of the A_2 strain, present in many people, moderated the severity of the pandemic by providing at least partial immunity to the new variant. A much more severe pandemic occurred, for example, in 1957 when both surface antigens underwent such a gross shift.

The change in antigenic amino acid composition associated with the abrupt emergence of new influenza subtypes is far too large to be explained by conventional concepts of mutation or evolution. A different type of explanation must be found, and that explanation lies in the nature of the viral genome.

Influenza Has a Segmented Genome

The RNA of the influenza virus is found in five to seven discrete pieces, each in its own nucleocapsid, and its total mass is about 4 million daltons. Each of the pieces, suggests George K. Hirst of the New York University Medical School, New York City, is an intact gene that controls at least one characteristic of the virus. The unique genetic plasticity of the influenza virus arises from the ease with which these genes are interchanged among different viral strains.

If a host cell is simultaneously infected by two different subtypes of influenza virus, the genes from these subtypes undergo a random reassortment in the cell to produce not only the two original subtypes, but also one or more hybrid subtypes. Each of these hybrids has a different, but complete, set of genes, and inherits characteristics from each parent. This type of genetic recombination was first observed in influenza viruses, but has subsequently been recognized in reoviruses and certain plant viruses.

It is not absolutely necessary to invoke recombination to explain the minor antigenic mutations of influenza virus; these can be rationalized as merely point mutations in the conventional sense. But even this type of limited antigenic variation has never been recognized with other human viruses. Perhaps, speculates Edwin D. Kilbourne of Mount Sinai, the answer lies in both mutation and recombination.

Recombination within the infected patient could "rescue" noninfective mutations formed during infection because part of the altered RNA from noninfective virions could be incorporated into infective virions—thus creating an extended gene pool in which all mutations would be potentially salvageable, rather than only those that occur in infective virions. Such an explanation is reasonable if it is assumed that the influenza virus is exceedingly susceptible to the evolutionary pressures of homotypic antibodies, so that any mutant that is even slightly changed in either of its external proteins will have a tremendous survival advantage. It is also necessary to postulate that a certain density of infection is critical to survival of the virus, and that this critical density is not adequately maintained solely by the infection of newborn susceptible infants, as it is with measles and poliomyelitis.

Recombination within the infected patient, however, cannot explain the much greater mutations that occur once each decade, for all available evidence indicates that only one influenza subtype can exist in man at any given time. The emergence of a new subtype, such as the Hong Kong strain, is always accompanied by the abrupt disappearance of the antecedent subtype, so there is little chance for the appropriate recombination to occur in man. The most likely explanation, suggests Kilbourne, is that the recombination takes place in animal hosts.

First Isolated from Swine

The first recognized influenza virus was isolated from swine in 1931 by Richard E. Shope, then at the Rockefeller Institute, who postulated from circumstantial evidence that it was a human virus that had descended into swine. More recently, a virus that is antigenically indistinguishable from the Hong Kong subtype has been isolated in swine from Europe and Asia. Influenza viruses have, moreover, been isolated only from domestic animals and birds, further suggesting that the viral strains are human in origin. Most animal and human viruses exhibit almost no cross-infectivity, but Robert B. Couch of the Baylor College of Medicine, Houston, Texas, has overcome this objection by demonstrating both the infection of humans with equine influenza virus and the infection of horses with a human influenza virus.

In contrast to the situation in humans, however, the appearance of apparently new influenza virus strains in animals is not necessarily associated with the disappearance of previously recognized strains. According to Kilbourne, there are currently at least two discrete subtypes of equine influenza virus in circulation, at least eight avian strains of different HA subtype, and at least two subtypes in swine. The hemagglutinin and neuraminidase moieties of some of these subtypes are antigenically very similar to those of several human influenza viruses, both past and present.

Kilbourne thus theorizes that there are no true animal strains of influenza —only human strains that have become adapted to growth in animals. Because of the recombinational ability of the influenza virus, these varied strains serve as an extended pool upon which the human virus can draw in the face of increased evolutionary pressure from rising antibody levels in the population. In the course of their adaptation to animals, however, these strains have lost their ability to infect humans. They can thus return to their primary host only through a combination of events that includes the occurrence of an ecologic niche in man, as the contemporary strain is suppressed by rising antibody levels, and fortuitous genetic recombination to produce a new subtype that is infective in humans and that is not susceptible to existing antibodies. Such new subtypes have generally emerged, and will probably continue to emerge, in Asia, where men and animals continue to dwell in the same buildings.

The remarkable amount of knowledge gained about influenza within the past 10 years has produced some remarkable first steps toward control of man's last great plague. These steps will be considered next week in a succeeding article about the production of influenza vaccines.

—THOMAS H. MAUGH II

Erratum: Several errors occurred in the Research News story "ERTS: Surveying earth's resources from space" (6 Apr. 1973) by Thomas H. Maugh II. In column 3, page 50, the statement, "It thus maps an area of about 6.5 km^2 every day," should read "6.5×10^6 km^2." In Fig. 3, the land masses are identified as Manhattan and Staten Island; actually, the spit at the left of the figure is Sandy Hook, New Jersey, and the barrier beaches further north are Rockaway, Long Beach, and Jones Beach, from left to right. The negative for Fig. 4 was inadvertently flipped over so that the illustration is a mirror image of the actual picture. It has also since been brought to the author's attention that "the previously unsuspected difference in salinity" in the Great Salt Lake described in the caption of Fig. 2 was, in fact, well known before the ERTS picture was taken.