

*Summary.* Four generations of vitamin E-low rats were observed as to growth and reproductive behavior. In the female there was a delay in maturity in each successive generation. Growth was also affected.

The males in each generation were sterile but fertility was maintained in the fourth generation by the prophylactic administration of wheat germ oil.

Coarse, sparse, yellowish fur and dystrophy that appear in rats maintained on vitamin E-low diets appeared progressively earlier in each successive generation.

### 11615

#### **A Virus from Cases of Influenza-like Upper-respiratory Infection.**

THOMAS P. MAGILL. (Introduced by Joseph C. Hinsey.)

*From the Department of Bacteriology and Immunology, Cornell University Medical College, New York City.*

During the past few years at least two groups of investigators<sup>1,2</sup> have reported cases of upper-respiratory infection of unknown etiology, that resembled true "epidemic influenza" in clinical respects but which differed in that the convalescent serums failed to show any increase in capacity to neutralize standard strains of the influenza virus. Two similar cases of influenza-like infection occurred among the workers in this laboratory in February, 1940. The serums obtained from these cases 4 weeks after the infection and those obtained either at the time of or 3 weeks before the onset of illness were tested against the PR8 strain of the virus of epidemic influenza. Neither of the convalescent serums showed any detectable increase in capacity to neutralize the usual 1000 lethal doses of the virus; and neither of them fixed complement in tests against antigens prepared in the usual manner<sup>3</sup> from mouse lung suspensions. This apparent lack of development of antibodies reactive against this standard strain of influenza virus seemed to indicate that the influenza-like infection of neither of the cases had been due to the virus of epidemic influenza.

---

<sup>1</sup> Reimann, H. A., and Stokes, J., Jr., *Tr. Assn. Am. Physn.*, 1939, **54**, 123.

<sup>2</sup> Stuart-Harris, C. H., Smith, W., and Andrewes, C. H., *Lancet*, 1940, **1**, 205.

<sup>3</sup> Francis, T., Jr., Magill, T. P., Rickard, E. R., and Beck, M. D., *Am. J. Pub. Health*, 1937, **27**, 1141.

TABLE I.  
Neutralization Tests of Serums from 2 Cases of Influenza-like Infection Against the PR8 Strain of Influenza Virus and Against the TM Virus.

Serum		PR8 strain versus different dilutions of serum					TM virus versus different dilutions of serum				
		1-10	1-25	1-50	1-100	1-250	1-2	1-8	1-32	1-128	1-512
TM	Time after onset										
	Less than 12 hr	0	0	+	++	D	++	++	D	D	D
		0	0	++	+++	D	++	++	++	D	D
4 wk		0	0	++	+++	D	0	0	0	+	++
		0	+	++	+++	+++	0	0	0	+	+++
		0	++	++	+++	+++	0	0	0	++	+++
EJ	3 wk before	0	0	++	+++	D	+	++	D	D	D
		0	0	++	+++	+++	++	++	D	D	D
		0	0	0	++	+++	++	++	++	++	++
4 wk		0	0	+	++	D	0	0	+	++	D
		0	0	++	+++	D	0	0	+	++	D
		0	0	0	++	D	0	+	++	++	++

0—Mouse showed no pulmonary consolidation.

+, ++, +++, ++++—Degrees of pulmonary consolidation in mice that survived.

D—Mouse died; extensive consolidation of lung.

The throat washings from both patients when inoculated intranasally in ferrets under ether anesthesia evoked a fever of the type considered characteristic of influenza. The infectious agent from one of the cases was transmitted serially in ferrets, but even after 10 passages the lungs of infected animals showed no consolidation. The infection was transmitted by intranasal inoculation from ferrets to Swiss mice; in that species blue-gray areas of pulmonary consolidation were produced on the first passage. After 9 passages the virus increased sufficiently in virulence to kill some of the mice but although it has now been passed over 20 times it has not yet acquired the capacity of regularly killing all of the mice that are inoculated. The virus nature of this infectious agent is indicated by the fact that it passes through Berkefeld filters which retain ordinary bacteria and by the fact that it maintains its virulence for mice after storage for at least one month in 50% glycerol. In order to avoid circumlocution the term *TM* virus will be applied to this infectious agent.

Neutralization tests were made with the *TM* virus against the serums obtained from the 2 cases. The procedure was the same as that ordinarily employed;<sup>3</sup> however, the 10% suspensions of infected mouse lung that were used as antigen contained only about 10 infectious doses per 0.025 cc and did not regularly kill mice. For purposes of comparison a new series of neutralization tests against the PR8 strain of virus were made in which the test amount of virus was reduced from the usual 1000, to less than 10 lethal doses. The results of these experiments are summarized in Table I.

The data (Table I) show that even when tested against less than 10 lethal doses the convalescent serums of neither of the patients had any detectable increase in capacity to neutralize the PR8 strain of influenza virus. In contrast, the serums from both of the patients showed a significant increase in capacity to neutralize the *TM* virus. That virus had been isolated from case *TM* at the time of onset of infection and can be assumed to have been the etiologic agent of that case and probably also of case *EJ*. Thus, the results in Table I present an example in which the convalescent serums of patients who had recently recovered from an influenza-like infection showed an increase in capacity to neutralize the particular virus homologous to their infection but did not show an increase in capacity to neutralize a standard strain of the virus of epidemic influenza. The question of whether or not the *TM* virus is a strain of the virus of epidemic influenza that differs in antigenic properties from the PR8 strain or is an entirely unrelated virus has not been determined.