

the absorption of cholesterol. However, when only the specimens obtained 11 hours or more after the feedings are considered this apparent discrepancy disappears. For the control group the average chyle cholesterol then becomes 120 mg.; for the normal dogs given cream and cholesterol, 206 mg.; and for the iodized animals, 193 mg.

*Conclusion.* Potassium iodide does not prevent the absorption of cholesterol from the gastro-intestinal tract of dogs.

### 8467 P

#### Vaccination of Human Subjects with Virus of Human Influenza.

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The immunization of ferrets and mice<sup>1, 2</sup> with human influenza virus has been reported. When injected into these animals by the subcutaneous or the intraperitoneal routes the virus elicits no evidence of infection, but the animals so treated develop circulating antibodies against the virus and become actively resistant to the infectious agent introduced by the intranasal route. More recently it has been possible to demonstrate the same effects with virus grown outside the animal body in tissue culture medium.<sup>3, 4</sup>

The successful cultivation of the virus in artificial medium immediately eliminated many of the undesirable features, such as the possibility of bacterial contaminants, extraneous viruses, etc., which constantly attend the use of virus from infected animals for studies in human individuals. After preliminary tests upon 3 human subjects which demonstrated that the artificially cultivated virus injected subcutaneously produced no serious reactions, a group of adult human volunteers was selected to determine the immunizing capacity of culture virus.

From among the subjects available, those individuals were selected whose serum beforehand exhibited the least protective power against the human influenza virus, as measured by its capacity to protect white mice against a high concentration (10% suspension)

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<sup>1</sup> Francis, T., Jr., and Magill, T. P., *J. Exp. Med.*, 1935, **62**, 505.

<sup>2</sup> Smith, W., Andrewes, C. H., and Laidlaw, P. P., *Brit. J. Exp. Path.*, 1935, **16**, 291.

<sup>3</sup> Francis, T., Jr., and Magill, T. P., *Science*, 1935, **82**, 353.

<sup>4</sup> Magill, T. P., and Francis, T., Jr., *J. Exp. Med.*, in press.

of mouse passage virus. From each individual a sample of serum was obtained immediately before the first injection of virus and again before each subsequent inoculation. To each of 10 individuals 3 doses of culture virus, 0.5 cc., 1.0 cc., and 1.0 cc., respectively, were given subcutaneously at weekly intervals. After 2 to 3 weeks another dose of 2.0 cc. of culture virus was given to each individual by the same route, and approximately 10 days later the final sample of serum was obtained. In one group of 4 individuals, doses of 1.0 cc., 1.0 cc., and 2.0 cc., respectively, were given at weekly intervals.

The only reactions observed were mild local erythematous areas, sometimes slightly tender, at the site of injection. The erythema was usually first apparent in 18 to 24 hours after inoculation, and subsided in another 24 hours. No constitutional or significant febrile reactions, no respiratory symptoms or evidence of infection were noted.

The sera collected at intervals in the course of vaccination were then tested by mouse protection tests for their capacity to neutralize a 10% suspension of mouse passage virus. All tests of the serum of a single individual were made at one time; in fact, the sera of 4 or more individuals were always included in the same experiment. Control tests were run simultaneously with a serum which was known to protect mice completely and with another serum which was known to have no protective action. The development of circulating antibodies against the virus was then determined by comparing the neutralizing capacity of the serum after vaccination with that of the serum before the injections were begun. Furthermore, the titer of protective substances in the sera of different individuals could be compared by relating the results to those obtained with the control sera.

Table I presents the results of tests made with the serum of each subject taken before vaccination was begun and after the final inoculation. The results show that while the antibody response varied among the different individuals, in all, except possibly subject H. S., a sharp increase in the protective capacity of the serum occurred. In 4 instances the serum before vaccination exhibited no neutralizing action against the virus, in the dosage employed, while subsequent to the course of inoculations, the serum of the same individuals exerted essentially complete neutralization. In those subjects whose sera afforded partial protection to mice before vaccination, an increased protective capacity of the serum after vaccination was also noted.

The questions of persistence of antibodies following vaccination

TABLE I.  
The Development of Antibodies in Human Subjects Following Vaccination with Human Influenza Virus in 1935.

Subject	Serum No.	Date	Date of Test	Tested Against PR8 Strain Mouse Passage Virus			
				Severity of Pulmonary Lesions in Mouse			
				No. 1	No. 2	No. 3	No. 4
L.A.	1.	10/19	12/12	++++*	++++*	++++*	++++*
	6.	12/4	"	+	0	±	0
D.T.	1.	10/19	"	++++*	++++*	++++*	+++
	6.	12/4	"	0	0	0	+
W.M.	1.	10/26	"	+++	+++	++	+++
	5.	12/4	"	0	0	+	0
A.T.	1.	11/2	"	+++	+++	+++	±
	5.	12/11	"	0	0	0	0
F.R.	1.	10/26	"	+++	+++	++	+++
	5.	12/4	"	0	0	0	0
S.O.	1.	10/19	"	++	+++	+++	+++
	6.	12/4	"	+	0	+	0
M.R.	1.	10/26	"	++	++	+++	++
	5.	12/4	"	0	±	0	+
W.H.	1.	10/19	"	+	++	+	+
	6.	12/4	"	0	0	0	0
H.S.	1.	10/26	"	++	0	+	+
	5.	12/4	"	0	0	+	0
T.F.	1.	9/16	11/14	++++*	++++*	++++*	—
	4.	11/7	11/14	0	0	0	—
E.Mc.	1.	10/31	12/4	++++*	++++*	++++*	++++
	4.	11/23	"	0	0	0	+
D.D.	1.	10/31	"	++++*	+++	+++	+++
	4.	11/23	"	0	0	0	0
E.M.	1.	10/31	"	++	++	++	+++
	3.	11/14	"	0	0	0	0
F.F.	1.	10/31	"	++++*	++++*	++++*	++*
	4.	11/23	"	++	+	++	++
R.D.	Neg. Control	"	"	++++*	++++*	++++*	++++*
		12/12	"	++++*	++++*	++++*	++++*
SS.	Pos. Control	12/4	12/12	0	0	0	0
		12/12	"	0	0	+	0

O = No pulmonary lesions.

± to ++++ = Degree of pulmonary involvement.

\* = Mouse died.

with the living virus and the significance of these antibodies in relation to immunity to the natural disease must await further study for their solution. Nevertheless, the present results show clearly that the subcutaneous inoculation of artificially cultivated, active human influenza virus into human individuals elicits the production of specific protective substances, without causing any unfavorable reactions in the recipient.