caused an uncoupling of phosphorylation from oxidation as evidenced by a reduced P/O ratio. This effect of serotonin was removed by monoamine oxidase blockade. Indication that the effect of serotonin is mediated via its carbonyl derivative was further strengthened by the use of 3-indole-acetaldehyde which gave similar inhibition of phosphorus and oxygen uptake. These findings support the hypothesis that serotonin could impede brain function by inhibition of energy producing reactions.

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Experimental Infection of Chimpanzees with Human Rhinovirus Types 14 and 43* (32875)

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Judging from findings in etiologic studies of upper respiratory illness, rhinoviruses are associated with more "cold-like" illness than any other group of viral agents (1–3). Experimentation on the pathogenesis, prevention, and cure of human rhinovirus infections has been handicapped by the lack of an experimental animal other than man. In 1930, Dochez and his associates (4) found that

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chimpanzees were susceptible to human "colds" transmitted through bacteria-free nasopharyngeal filtrates. In the hope that these "colds" may have been caused by rhinoviruses, chimpanzees were exposed in the present experiments to rhinovirus types 14 and/or type 43. Although the animals did not "catch cold," they did shed these viruses for several days, formed specific neutralizing substances and were apparently not infected when later rechallenged with the same virus.

Materials and Methods. All procedures directly involving animal use were carried out by the author at the Delta Regional Primate Center of Tulane University, Covington, Louisiana using resident chimpanzees and with the collaboration of the Delta staff.

Both rhinoviruses were "H" strains. Type 14, strain NIH 1059, was originally isolated from a marine recruit at Parris Island, S. C., (5) and the virus suspension for infection was supplied by Dr. J. Holper of Abbott Laboratories, North Chicago, Ill. Type 43, strain Wis258E, was isolated from a male graduate student attending the University of Wisconsin (3).

The experimental infections were done in a three-experiment series spanning the year November, 1964–November, 1965, each experiment being a variation on the following. A blood sample was taken from each chimpanzee, and, daily for 2 or 3 days, the animals were examined by a veterinarian or a physician and throat swabs were obtained. After this observation period, the virus was administered intranasally and/or by nebulization. Throat and blood specimens were taken at the intervals shown in the table. Rhinovirus propagation and neutralization techniques have been recently described (3).

Anesthesia was usually necessary in these experiments. Various narcotics, barbiturates and nitrous oxide were used singly or in combination. It was important to use short-acting drugs, as experiments were often performed daily and the animals had to be able to take regular nourishment. All chimpanzees were estimated to be within 2–5 years of age.

Results. Experiment 1, November, 1964. The 500 $TCID_{50}$ of rhinovirus 14 was administered intranasally to each of six chimpanzees. Three of the animals sporadically shed virus in the throat and produced serum antibody with homologous neutralizing titers from 1:64 to 1:256 in around 3 weeks.

Experiment 2, May, 1965. The 10,000 $TCID_{50}$ of rhinovirus 43 was given by nebulization (DeVilbiss no. 40) and intranasal instillation to each of three chimpanzees. Virus was detected in the throat from the first through the eighth day after administration. Antibody titers were 1:4 to 1:8 at 7 days and were 1:256 at 18 days.

Experiment 3, November, 1965. This experiment tested homologous protection against 10,000 $TCID_{50}$ of each virus administered as in experiment 2. Six chimpanzees were given rhinovirus 43; three of the animals had been given this agent in experiment 2 and had serum antibody titers of 1:256. Four different chimpanzees were given rhinovirus 14; two of the animals had been given this virus in experiment 1 and had serum antibody titers of 1:64 (chimp. 315) and 1:256 (chimp. 309). The data from the rhinovirus 14-infected animals are illustrated in Table I. The results of infection with either virus were essentially identical in that the virus was shed regularly in the antibody-free animals and completely inhibited in those with preinfection antibody. Attention is called to chimpanzee 315 which had been infected with this virus in experiment 1; his serum antibody fell from 1:64 to less than 1:6 in the intervening year, and upon this rechallenge exhibited, little, if any, anamnestic reaction. None of the chimpanzees showed signs of clinical illness.

Discussion. The experiments cited here show that after nasopharyngeal administration, two strains of human rhinoviruses can infect chimpanzees. To the writer's knowledge this is the first report of the infection of a nonhuman host with any human rhinovirus. Despite the relative costliness of the chimpanzee and of the difficulty in working with such a powerful primate, it possesses certain advantages over humans as an experimental animal for rhinovirus infections. As examples, promising antiviral agents could be tested for *in vivo* efficacy before putting such drugs through the procedure required to license them for human experimental use; or, similarly, unlicensed vaccines or other virus preparations could be tested for immunogenicity or

TABLE I. Experiment 3, November, 1965: Serum Neutralizing Antibody Responses and Serial Pharyngeal Virus Isolations of Rhinovirus Type 14 Strain NIH 1059 after Nebulization-Intranasal Instillation of 10,000 $TCID_{50}$.

		Days after virus administration												
		−7	−0.1	0	0.2	1	2	4	6	8	10	14	21	28
Chimp. 304	Virus isolates[a]	—	—	+	+	—	+	—	+	+	+	+	+	—
	Antibody titer			<3			<3	<3	<3	<3	<3	<3	<3	90
Chimp. 308	Virus isolates	—	—	+	+	—	+	+	+	+	+	+	—	—
	Antibody titer			<3			<3	<3	<3	<3	<3	181	256	256
Chimp. 309[b]	Virus isolates	—	—	—	—	—	—	—	—	—	—	—	—	—
	Antibody titer			181			181	90	128	128	128	90	90	256
Chimp. 315[b]	Virus isolates	—	—	+	+	—	—	—	+	+	+		—	—
	Antibody titer			<6			<6	<6	<6	<6	45	1444	2048	512

[a] (—) indicates that the throat specimen was passaged once in human embryonic diploid tissue culture and no rhinovirus 14 was isolated; (+) indicates rhinovirus 14 isolation.

[b] Chimpanzees 309 and 315 were previously inoculated with rhinovirus 14.

interference either by injection or by respiratory infection. It should also be possible to carry out the detailed studies on the pathogenesis of rhinovirus infections which are impossible in man.

Summary. In three serial experiments, chimpanzees free of specific neutralizing antibody were infected with rhinovirus types 14 or 43. Although infected animals shed virus from 6 to 21 days and produced high levels of specific antibody, clinical illness was not discernible. Providing serum neutralizing antibody was still present, chimpanzees rechallenged with the same agent shed virus for less than 5 hours. To the author's knowledge this is the first report of successful experimental infection by human rhinoviruses of species other than man.

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A Chemical Method for the Estimation of Brain Sulfhydryl Groups (32876)

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Numerous methods for determining concentrations of sulfhydryl groups (–SH) in tissue homogenates have been developed. In addition to methods measuring total –SH content (1,2); more specific procedures for –SH amino acids (3), glutathione (4,5), total nonprotein —SH (6) and protein–SH (7) have

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