

### **A Study of Acute Infection of the Respiratory Tract in the Ape.**

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During an investigation of the type of acute infections of the human upper respiratory tract usually grouped under the term "Common Cold", we have considered the possibility of finding an animal susceptible to infections of this nature. Such animal diseases as distemper in dogs and snuffles in rabbits, though having a certain resemblance to the human disease, seemed in all probability to be too dissimilar from an etiological standpoint to be of immediate value. Our search led us to consider the advisability of employing the anthropoid ape for the purpose. On questioning curators of zoological collections and others having to do with the importation and study of the higher apes, it quickly became obvious that those animals not only frequently suffered from "Common Colds", but that the source of infection was a human being similarly afflicted. The description of the condition bears a striking resemblance to the human disease and not infrequently it is followed by a secondary pneumonia of severe character.

Having assured ourselves of the probable susceptibility of these animals to the condition under investigation, the decision was made to collect a small colony of anthropoids and to study in them the spontaneous occurrence of upper respiratory infection and the nature of the experimentally produced disease. The animals were obtained from dealers, had been exposed to intimate human contact for from 3 months to a year, and some were known to have suffered from acute upper respiratory infection of the type described. Young animals of about 3 years of age and under 30 pounds weight were chosen because of the ease with which they could be handled. The animals were at all times protected from frequent human contact and during the period of experimental observation were under strict quarantine, all attendants employing surgical aseptic technic of sterile hood, mask, gown, and rubber gloves.

The first undertaking was a study of the upper respiratory flora during periods of normal health. This was found to resemble, in respect to organisms present, that of the human upper respiratory tract to a surprising degree. The organisms more or less continuously present are shown in the following table:

TABLE I.  
Comparison of percentage incidence of bacteria in noses and throats of normal simians and humans.<sup>1</sup>

		Organisms												
		Gram-negative cocci	Streptococcus non-hemolytic	Bacillus "X"	<i>B. Pfeifferi</i>	Diphtheroids	Large Gram-positive cocci	<i>Staphylococcus albus</i>	<i>Streptococcus hemolytic</i>	<i>Staphylococcus aureus</i>	Pneumococcus	<i>B. coli</i>	Strepto-Bacillus	Total Cultures
Nose	Monkey	17	60	0.6	13	21	8	95	1.2	26	1.2	4	15	169
	Man	1	7	0	0	79	0	92	0.4	36	0.	0	0	265
Throat	Monkey	99	99	21	92	11	5	31	45.	9	0.6	13	0	159
	Man	99	99	49	47	45	45	40	17.	14	2.0	0	0	265

<sup>1</sup> Shibley, Hanger, and Dochez, *J. Exp. Med.*, 1926, xliii, 415.

During the period of observation a number of the animals, while not under quarantine, have contracted upper respiratory infections presumably from chance human contacts. The following symptomatology was the one generally observed: the first sign of upper respiratory infection was a discharge of mucus from both nostrils accompanied by occasional attacks of sneezing. During the act of sneezing considerable amounts of mucus were blown from the nostrils. Somewhat later the nares became obstructed and the breathing audible. In from 3 to 5 days a cough frequently developed, lasting sometimes as long as 2 weeks. In some instances the mucus discharge became purulent and continued from one or the other nostril for as long as 3 weeks. There was some lassitude and loss of appetite and occasionally diarrhea. The temperature was seldom elevated and then only to an insignificant degree. In 3 animals the attack was complicated by bronchopneumonia with marked prostration, loss of appetite, and fever. One of these animals died and the lungs showed pneumonic lesions of somewhat unusual character.

One of the striking features of the picture is the marked increase in numbers and spread in area involved by the potentially pathogenic bacteria already present in the upper respiratory tract.

One of the objects of this investigation has been to determine whether it is possible to communicate to anthropoids by means of a filterable agent a respiratory infection comparable to the human

cold. For this purpose single animals were chosen at a time when they had been free from respiratory symptoms for at least 6 weeks. They were placed in a special room in individual cages and strict quarantine maintained by the technic described. They were kept under observation for from 1 to 2 weeks to test the efficiency of the isolation. No animal under such conditions acquired a spontaneous respiratory infection. A daily study of the bacteriology of the upper respiratory tract was conducted.

As a source of the infectious agent, human beings were chosen with typical manifestations of a common cold of at least moderate severity. Nasopharyngeal washings were obtained within the first 24 hours of symptoms. This material was rapidly passed through a Berkefeld filter V. Both the unfiltered and the filtered washings were carefully studied bacteriologically. To test for the presence of herpes virus, intra-cerebral inoculations into rabbits were made with the filtrate. Usually within an hour from the time the washing took place, from 1 to 2 cc. were instilled into each nostril of the experi-

		Inoculation														
		Oct.							November							
		30	31	6	12	13	14	15	16	17	18	19	20	21	28	
General	Well	+	+	+	+	+									+	
	Mucus in nose							+	+	+	+	+	+	+	+	
	Running nose							+	+	+	+	+	+	+	+	
	Sneezing															
	Coughing															
	Red Throat								+	+						
	Appetite impaired								+							
	Diarrhea															
Cultures	Nasopharynx															
	Gram neg. cocci	●	●	●	●	●	●	●	●	●	●	●	●	●	○	
	non-hemol. strep	○	○	○	○	○	○	○	○	○	○	○	○	○	○	
	B. Pfeifferi	■	■	■	○	+	■	■	■	■	■	■	■	■	■	
	hemol. strep	■	+					■							+	
	pneumococcus							○	■						●	
	Nose															
	Gram neg. cocci							+	■	■				+	+	○
	non-hemol. strep		○	+	+	■	■							+	+	○
	B. Pfeifferi										○					
	Diphtheroids		■	■	●	○	○	○								■
	Staph. aureus	●	●	●	○	○	■	■						○	+	■
pneumococcus								●	●	●			●	●	●	
Staph. aureus															●	

FIG. 1.

Chart showing development of symptoms in experimental animal following inoculation with filtered nasal washings obtained from an early cold in a human. The bacterial flora in the nose and throat before, during and after, is shown. Solid circle indicates organisms present in greatest numbers, blank circle the next most numerous, and plus signs indicate the remaining ones.

mental animal. A second instillation of the same material was made 6 hours later. At first plain broth and heated filtrate controls were carried out, but were later discontinued as inadequate. A different type of control is planned at a period when human colds are not prevalent.

Of the first 7 animals inoculated intra-nasally according to the technic described above, 3 contracted upper respiratory infections similar in their manifestations to the spontaneous infections of the simian and to the "common cold" in human beings. In 2 experiments the symptomatology was ambiguous and in 2 no symptoms developed.

The experiment charted below is a typical example of the phenomena observed. The incubation period of the experimental infection was about 36 hours. The symptomatology and alteration of the bacteriological flora of the upper respiratory tract are shown in the chart. In the experiment charted, a healthy chimpanzee kept in close contact with the experimental animal, contracted, presumably by contact, a spontaneous cold on the fourth day of the experimental infection.

The nature of the active filterable agent is as yet unknown. In one positive experiment the filtrate contained herpes virus, and from the filtrate in all positive experiments a Gram negative anaerobic bacillus of the type described by Olitsky and Gates was cultivated.

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### Oral Immunization Experiments with Disrupted, Dissolved and Avirulent Pneumococci. Time of Appearance of Immunity.\*

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Earlier experiments<sup>1</sup> have demonstrated that when dead pneumococci are fed to white rats, the animals become immune to an injection of virulent germs of the same type. The present report deals with the observations made when mechanically disrupted, bile dissolved and avirulent organisms are fed. It also includes a report of experiments in which rats were fed the pneumococcus grown in

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\* The author wishes to express his thanks to Mrs. K. L. Harriman for her kindness in providing financial support for the work. He is also indebted to Dr. Wm. H. Park and Dr. Wm. G. Lyle for aid, advice and facilities.

<sup>1</sup> Ross, Victor, *J. Lab. and Clin. Med.*, 1927, xii, 566.