Experimental Studies With the Agent of the Common Cold

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Nasal washings were collected from several cases of common cold infection within 24 hours after the onset of symptoms. The diluent was 2 per cent normal rabbit serum in physiological saline. Each of three such specimens was treated with penicillin sodium (30,000 units for 5 minutes) and then inoculated into the chorioallantoic cavity of 7-day-old incubating chick embryos (0.50 cc./egg). The inoculated embryos were further incubated at 35° C. At 4-day intervals the chorioallantoic fluid was collected from these eggs and pooled from each strain passage. Each strain was passaged blindly at 4-day intervals. Infectivity of the chorioallantoic fluid was checked periodically by inoculating this material into human volunteers[1] by the intranasal route. At no time could visible organisms be cultivated from this material when inoculated into synthetic medium. The results obtained from these three strains were as follows:

Strain I (Haltmar) was negative when chorioallantoic fluid of the second passage was inoculated into two volunteers.

TABLE 1

INTRANASAL INOCULATION OF HUMAN VOLUNTEERS WITH CHICK EMBRYO PROPAGATED COLD AGENT

No	Inoculum	Hours	Symptoms					
			"Stuffy"	Sneezing	Swollen mucosa	Exudate	Headache	Cough
11	MP strain, 2nd passage	24	–	–	+	–	–	–
		48	++	–	++	++MP*	++	–
		72	+++	–	++	++S*	–	–
		96	–	–	–	++P*	–	–
14	"	24	–	–	–	+S	–	–
		48	–	"sniffles"	++	++M	–	–
		72	+++	–	++	++S	–	–
		96	–	–	–	++MP*	–	–
18	MP strain, 3rd passage	24	–	–	–	–	–	–
		48	–	–	–	–	–	–
		72	–	–	–	–	–	–
19	"	24	+	–	+	+S	–	–
		48	–	–	–	–	–	–
		72	–	–	–	–	–	–

* S = serous exudate; M = mucoid exudate; MP = mucopurulent exudate; P = purulent exudate.

Strain II (MP) was infectious for two passages, but very mild or no reactions were induced with the third and later passages when it was inoculated into human volunteers (Table 1).

Strain III (Spill) was able to induce symptoms of the common cold after 9, 11, and 12 series of consecutive passages in the developing chick embryo (Table 2). It should be noted that the later passages of this agent induced much milder symptoms in the inoculated individuals than did the earlier. This might be due, of course, either to a difference in susceptibility of the individuals who were inoculated or to an attenuation of the agent by passage through a series of chick embryos. The clinical diagnosis of cold infection in the human volunteers was based on the development of a congested and swollen nasal mucous membrane, serous exudate, and sneezing. They manifested a feeling of stuffiness in the paranasal sinus areas and of mild malaise. There was no fever and no impairment

TABLE 2

INTRANASAL INOCULATION OF HUMAN VOLUNTEERS WITH CHICK EMBRYO PROPAGATED COLD AGENT

No.	Inoculum	Hours	Symptoms						
			"Stuffy"	Sneezing	Swollen mucosa	Exudate	Headache	Cough	Exercise tolerance
24	Spill strain, 9th passage	24	–	–	–	–	–	–	
		48	+++	–	+++	+S*	–	+	
		72	+++	–	+++	+S	–	+	
25	"	24	+++	Sniffling	+	–	–	–	
		48	+++	–	+++red	+S	–	–	
		72	+	–	red	–	–	+	
26	"	24	–+++	–	+++	–	–	–	
		48	+++	+++	+++	++S	–	–	
		72	++	–	+++	+++MP	–	+	
27	"	24	+++	+++	+++red	++M	–	–	
		48	+++	+++	+++	++MP	–	–	
		72	+++	–	++		–	–	
28	"	24	–	–	–	–	–	–	
		48	++	–	Injected	–	+–	–	Good
		72	–	–	–	–	–	–	Good
29	"	24	+	–	–	–	–	–	
		48	++	–	+++Injected	+M	–	–	Poor
		72	–	+	–	–	–	–	Good
30	Spill strain, 11th passage	24	–	–	+	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
31	"	24	++	Sniffling	+Injected	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
32	Spill strain, 12th passage	24	++	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
35	"	24	–	–	–	+M	–	–	
		48	+++	–	++	Clearing throat	–	–	
		72	–	–	–	–	–	–	
39	Haltmar strain 2nd passage	24	–	–	–	–	–	–	Good
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
40	"	24	+++	–	++Injected	++S	+	+	Fair
		48	–	–	–	–	–	–	
		72	–		–	–	–	–	

[1] We wish to express our appreciation to the staff and inmates of the Sugarland State Farm for their aid and cooperation in this study.

of appetite. The diagnosis was further based on negative hematological changes and negative Hirst tests for influenza A and B.

Six human volunteers were inoculated intranasally with chorioallantoic fluid (Spill strain) of the 9th passage in chick embryos. Five developed symptoms of cold, ranging from severe reactions to transitory, aborted manifestations. Five of these men and five new volunteers were inoculated subcutaneously with two doses of infectious chorioallantoic fluid (Spill strain), 1 cc. at weekly intervals. One week following the second inoculation, they were challenged intranasally with Seitz filtrates of nasal washings from naturally acquired cases of common cold infection. All of the individuals who had been immunized with the chick embryo propagated Spill strain cold agent failed to develop symptoms of cold; and with the same challenge inoculum, the two controls who had not been exposed to the Spill strain cold agent both developed marked symptoms (Table 3).

TABLE 3

CHALLENGE INOCULATION OF IMMUNIZED HUMAN VOLUNTEERS (1cc/week/2 weeks)

No.	Intranasal challenge nasal washings (pool of Connoly, Fly & Thompson)	Hours	Symptoms						
			"Stuffy"	Sneezing	Swollen mucosa	Exudate	Headache	Cough	Exercise tolerance
24	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
28	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
29	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
30	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
31	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
41	Uninoculated control, 1.0 cc.	24	+++	Sniffling	++	++S	"Head tight"	+	Poor
		48	++	+	–	–	–	–	
		72	–	–	–	–	–	–	
32	Pool of Quattlebaum & Jones, 1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
33	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
34	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
35	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
36	1.0 cc.	24	–	–	–	–	–	–	
		48	–	–	–	–	–	–	
		72	–	–	–	–	–	–	
38*	Uninoculated control, 1.0 cc.	24	++	–	++	+++S	–	+	Fair
		48	++++	–	+++red	+++S	–	–	Poor
		72	+	–	++red	–	–	–	Poor

* This case developed an otitis media and ruptured ear drum 3 days later.

Six control volunteers were inoculated intranasally with normal chorioallantoic fluid from 11-day-old incubating chick embryos, and none developed any of the symptoms of cold infection. The same was true of five control volunteers inoculated intranasally with 2 per cent rabbit serum in physiological saline.

Development of Castes in Higher Termites

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Studies on the determination of castes (*5*, *6*) have been confined to the lower families of termites. The higher termites, the Termitidae, seem to offer more favorable opportunities to study the mechanisms which determine the development of the structurally very different castes. They possess a readily distinguishable worker caste, and the colony consists largely of fully differentiated terminal individuals, workers, and soldiers.

The nymphs of the lower families have been shown to be indifferent up to relatively late instars (*5*). Our findings reported here agree with those of Bathellier (*1*) in placing determination of castes in the Termitidae very early in nymphal development.

The lower termites are amenable to laboratory culture, but the literature shows no records of attempts to culture the higher termites except the method for mass culturing of the sterile castes of *Nasutitermes* (=*Entermes*) *exitiosus* Hill, worked out by Holdaway, Day, etc. in Canberra, Australia. A brief report of certain features of the method was presented in 1936 (*4*) by Holdaway and again in 1938 by Day (*2*).

Although the Termitidae are largely tropical, three genera are common in the southwestern United States: *Amitermes*, of which the most common species is *A. wheeleri* (Desneux); *Gnathamitermes*, with the common and widespread species *G. perplexus* Banks; and *Tenuirostritermes*, the most common species of which is *T. tenuirostris* (Desneux). *Tenuirostritermes* is a nasute termite in which the soldiers have only vestiges of mandibles and a long, pointed projection of the head on which opens the cephalic gland.

The writers devoted the spring and summer of 1946 to studies of the last two species in southeastern Arizona, where both are abundant. Using a method reported elsewhere (*7*), we have found that the incipient colonies can readily be cultivated beyond the point necessary to obtain experimental results. Groups from older colonies present greater difficulties, *Gnathamitermes* being less difficult than *Tenuirostritermes*. More detailed reports of field observations and experimental results will be presented elsewhere.

In these Termitidae, living under essentially temperate conditions, reproduction and caste development were found to be restricted to the warmer months.