

Search for Illness Due to Adenovirus Type 4 Among College Dormitory Freshmen.* (25028)

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Illness due to adenovirus type 4 has been described in military (1,2,3) but not in civilian populations (4). As part of continuing interest in epidemiology of this disease, the present study was designed to search for infection with adenovirus type 4 in groups of college freshmen living in dormitories. This was considered a logical population to explore because it resembled in certain aspects the military recruit population in which illness due to adenovirus type 4 had been characteristically described (1). Both included a large number of young adults from a variety of geographical locations, living in close personal contact, newly exposed to one another, and engaged in similar activities.

Methods. Freshmen dormitory students from Case Inst. of Technology (men) and from Adelbert (men) and Mather (women) Colleges of Western Reserve Univ. donated blood specimens during first week in dormitories and again at end of first school year, 1955-56. One hundred and two students voluntarily complied. In addition, acute and convalescent phase serum samples were collected from 24 freshmen with respiratory tract infections at U.S. Military and Naval Academies during academic years 1955-56 and 1956-57. Serum specimens were stored at -20°C , and pairs of sera from each student were subsequently analyzed for changes in titer of complement-fixing antibodies against an antigen prepared from adenovirus type 4. Pairs of sera that revealed increase in titer

during interval of study were reexamined for presence of neutralizing antibodies against adenovirus types 1, 2, 3, 4, 5, 6, and 7. The methods used have been described (2,5,6).

Results. Pairs of serum specimens were available from the 102 students, the time span between individual pairs being $7\frac{1}{2}$ months in 99 students and 3 months in 3 students. The 102 students comprised 25% of the freshman dormitory population and 11% of total freshman class in the 2 schools. Pairs of sera samples were available from 24 students from U.S. Naval and Military Academies. Occurrence of increase in titer of complement-fixing antibodies was sought. The results are summarized in Table I. An increase in titer was noted in specimens of 3 students, 2 from Adelbert College, Western Reserve Univ. and 1 from Case. None of the 3 showed increase in titer of serum neutralizing antibodies against adenovirus types 1, 2, 3, 4, 5, 6, and 7. None of the paired serum samples from the Service Academies demonstrated significant rises of complement-fixing antibody. The sera of one individual from Service Academies showed a 1-tube rise in complement-fixing antibody and a 3-tube rise in neutralizing antibody to type 7 adenovirus, but no antibody rise to type 4 adenovirus.

Discussion. On the basis of epidemiologic studies during World War II the Commission on Acute Respiratory Diseases described a febrile respiratory illness among military recruits (1). The illness became known as "acute respiratory disease (ARD)." More recently, the etiology of the disease was ascribed principally to adenovirus type 4, although adenovirus type 7 was shown to be a cause, and adenovirus types 3 and 14 possible causes of such illness (2,3,7,8). With development of methods for detection of serum antibodies, additional tools became available for

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TABLE I. Complement-Fixation Titers against Adenovirus Type 4 in Dormitory Freshmen of Case Inst. of Technology (1955-56), Western Reserve Univ. (1955-56), and U. S. Military and Naval Academies (1955-56, 1956-57).

Institution	No. of dormitory freshmen	No. tested	Complement-fixation titer		
			Increase	No increase	Anticomplementary
Case Institute (men)	264	74	1	69	4
WRU					
Adelbert (men)	63	13	2	11	0
Mather (women)	74	15	0	14	1
Service academies		24	0	24	0
Totals		126	3	118	5

the hitherto unsuccessful search for presence of the disease among civilians(9,10,11).

The antibody analyses in the present study revealed no instance of infection due to adenovirus type 4 in 102 dormitory freshmen during the school year 1955-56, nor in 24 students from U.S. Military and Naval Academies, who experienced respiratory infections during academic years 1955-56 and 1956-57. A significant rise in type 7 adenovirus neutralizing antibody was demonstrated in the paired sera of one student from the Naval Academy: a 1-tube rise in complement-fixing antibody was demonstrated in sera from this individual. It is believed that the sample of students in our study was adequate to indicate the minor role of infections due to adenoviruses in freshman dormitory population. It is of interest that paired sera from an additional 29 students from the Naval Academy, all from upperclassmen, also failed to show a rise in complement-fixing antibody.

Absence of increases in neutralizing antibody titers against adenovirus types 1-7 in sera of the 3 students with increases in complement-fixing antibody titers signified that the agent responsible for the increase in titers was immunologically different from but related to adenovirus types 1-7. This may be explained by previously reported observation that complement-fixing antibody against viruses of adenovirus group is group-specific, while neutralizing antibody is strain-specific (11,12,13,14).

Summary. A search was made for presence of infection due to adenovirus type 4 in dormitory freshmen of Case Inst. of Technology, Western Reserve Univ., and U.S. Military and Naval Academies. Antibody

analyses revealed no instance of such infection in 126 students. Three students had rises in serum titers of complement-fixing antibodies against adenovirus type 4; however, none of the 3 had rises in serum titers of neutralizing antibodies against adenovirus types 1, 2, 3, 4, 5, 6, and 7. One student from the Naval Academy who had only a 1-tube rise in complement-fixing antibody developed a significant rise in neutralizing antibody against type 7 adenovirus.

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High Activity of Potent Analgesics on Conditioned Rat Tranquilizer Test. (25029)

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Inhibition of conditioned avoidance-escape response in rats has been widely used as one of the pharmacological tests for tranquilizing agents of reserpine and chlorpromazine types (1,2). Furthermore, it has been reported that blocking of this conditioned response is also produced by morphine(1). To investigate the possible correlation between analgesic potency and inhibition of this conditioned response with compounds related to morphine, we have now compared 3 analgesics and 2 well known tranquilizers on this test. The 2 tranquilizers used were chlorpromazine hydrochloride (Thorazine Hydrochloride ampuls, 25 mg/cc) and perphenazine (Trilafon ampuls, 5 mg/cc). The 3 analgesics were the following: Codeine Phosphate, U.S.P., a moderately potent analgesic; Morphine Sulfate, U.S.P., a highly potent analgesic; and *l*-14-hydroxydihydromorphinone hydrochloride (HDM hydrochloride, Numorphan Hydrochloride), a new and very highly potent analgesic. The latter has been reported 12 to 18 times as active as morphine sulfate by injection in mouse analgesia studies(3,4) and 8 to 10 times as active in clinical studies(3,5,6,7).

Methods. The apparatus and method for conditioned avoidance-escape response were essentially those described by Cook and Weidley(1). Rats were conditioned to jump onto a wooden pole at the sound of a buzzer to avoid a mild electric shock from metal rod floor. If the conditioned response to buzzer was blocked, the electric shock was then turned on to make the rat jump to the pole by unconditioned response. This procedure

demonstrated that blocking was specifically of the conditioned response and was not attributable to general depression or motor weakness. Female albino rats of CF strain (Carworth Farms), weighing 120-220 g, were used. In a confirmatory experiment full-grown female albino rats of a different strain (Supplee-Wistar), weighing 200-300 g, were used. Analgesic activity was determined by the mouse hot-plate method(8) in CF-1 male mice (Carworth Farms), weighing 20-28 g. The ED₅₀ values were calculated graphically(9).

Results. In the first experiment on conditioned response, the 5 drugs were administered subcutaneously to CF rats, 40 rats being used for each drug. The 3 analgesics all demonstrated blocking activity on this test, although of varying degrees (Table I). The very highly potent analgesic HDM was even slightly more active than perphenazine, one of the most potent tranquilizers in clinical use. HDM was about 1.6 times as potent as perphenazine on this test, calculated as base. Essentially similar results were obtained when the 2 compounds were compared again in older rats of the Supplee-Wistar strain, although the

TABLE I. Inhibition of Conditioned Response, by Subcutaneous Injection.

Drug	ED ₅₀ ± S.E.,* mg/kg	Potency
Chlorpromazine	7.0 ± .7	1.0
Perphenazine	.42 ± .05	17
Codeine	.49 ± .7	.14
Morphine	7.4 ± .8	.95
HDM	.26 ± .01	27

* Calculated as base.