Serologic Studies of Acute Respiratory Infections in Military Personnel[1,2]

ALFRED S. EVANS

*WHO Serum Reference Bank,
Department of Epidemiology and Public Health,
Yale University School of Medicine,
New Haven, Connecticut 06510*

The advantages, disadvantages, and uses of serological epidemiology are discussed in relation to acute respiratory infections in military personnel. The prevalence of antibody reflects both current and past experience with respiratory agents and is a measure of susceptibility. Incidence data calculated by testing two serial serum samples, on entry and discharge from the service, has indicated high influenza and *Mycoplasma pneumoniae* rates in South American recruits and low rates of adenovirus and parainfluenza infections. Serologic analysis of reinfection rates showed high protection against influenza infections at HI antibody levels of over 1:40, against adenovirus infections at neutralizing titers of 1:5, and against *M. pneumoniae* infections at TRI antibody levels over 1:8. Antibody responses persisting at least 7 mo following immunization were demonstrated in 70% of 428 vaccinated young adults for A_2 antigen and 20% for influenza B antigen. No relation of ABO blood groups to respiratory infection was found. The lack of myxovirus infections in four Polaris submarines is presented.

Most data on the incidence of acute respiratory infections in military personnel are based on reporting systems that record *cases* of disease which are hospitalized or seen in outpatient clinics. Information derived from these sources are presented in the other articles of this symposium.

This paper will discuss the advantages and disadvantages of serological epidemiology in acute respiratory infections of military personnel and presents the results of various studies illustrating the uses of this technique. The examples will be drawn from our own published and unpublished work carried out under the sponsorship of the Commission on Viral Infections of the Armed Forces Epidemiological Board[3] or in association with the Naval Submarine Medical Laboratory, Groton, Conn.

DEFINITION

Serological epidemiology can be defined as the systematic testing of blood samples from a defined population for antibodies to various microbiological agents. A book (1) and two WHO Expert Committee Reports (2, 3) deal with the methodology.

TABLE 1

Advantages of Serological Surveys

1. Indicates cumulative prevalence rates of current and past infections
2. Reflects both clinical and subclinical infections and epidemics
3. Can measure the incidence of infection in two sera spaced in time
4. Relates infection rates and protection to preexisting antibody levels
5. In immunization programs measures
   a. Need for immunization
   b. Percentage of seroconversion following immunization
   c. Quantity and quality of antibody produced
   d. Duration of antibody and protection
   e. Reinfection rates.

ADVANTAGES AND DISADVANTAGES

The major advantages of serological surveys over case-reporting methods are listed in Table 1. The most important of these are (1) the ability to determine both current and past experiences of a group with various microbial agents (cumulative prevalence) and (2) the measurement of both clinical and subclinical infections. The majority of the respiratory agents infecting military personnel result in a large number of inapparent or very mild illnesses which would be missed by the case-reporting system. Data systems based on the *reporting* of disease are notoriously inadequate; similarly, problems may arise in the collection and analysis of out-patient or even hospitalization admission or discharge records. It may also be difficult to define the appropriate denominator in calculating rates for a mobile recruit population. Serologic techniques avoid some of these problems and do not depend on historical or clinical information.

The disadvantages are the necessity and cost of obtaining a blood sample from a representative segment of the population and the work involved in performance of antibody tests. This author would emphasize that the benefits far outweigh the disadvantages in most situations.

PREVALENCE

The presence of antibody on entrance into military service reflects the prior experience of the recruits with the antigens employed in the test and indicates the level of susceptibility. The hemagglutination-inhibition (HI) antibody measured in surveys for influenza virus is long-lasting so that a pattern of cumulative prevalence is revealed by the test. These correlated closely with protection against infection and disease. Persons who have no HI antibody at the lowest dilution tested, usually 1:10, can be regarded as susceptible to infection and those with titers over 1:40 as immune. For the adenoviruses, antigen-specific neutralization tests should be used although antibody to some types can be measured by a hemagglutination-inhibition test. For *Mycoplasma pneumoniae* either the tetrazolium-inhibition reduction (TRI) or the metabolic-inhibition tests are good epidemiologic tools to indicate suscepti-bility and immunity.

The prevalence of antibody to a variety of respiratory antigens is summarized in Table 2 for Argentine (4, 5) and Colombian recruits (6, 7) on entry into the service as compared to U.S. Peace Corps Volunteers (7) in Colombia using sera taken before leaving the U.S. for duty in South America. Most persons in all three groups possessed antibody to current influenza A strains. However, the low level of 18% prevalence to A_2/Hong Kong/68 in Argentine recruits bled in that same year indi-

TABLE 2
Antibody Status of Argentine and Colombian Recruits and Peace Corps Volunteers
in Colombia at Time of Entry into the Service

Virus group	Test used level[a] pos.	Antigen used	Argentine recruits			Colombian recruits			Peace Corps in Colombia		
			Year bled	No. tested	Percent positive	Year bled	No. tested	Percent positive	Year bled	No. tested	Percent positive
Infl. A	HI	A2/Jap/	65/66	328	92	66A	296	91			
	(1:10)	A2/Tai/64	68	143	88	66B	346	88	64	208	36
		A2/HK/68	68	143	18						
Infl. B	HI	B/GL/54	65/66	328	64	66A	296	75			
	(1:10)	B/Md/59	65/66	328	49	66A	142	83			
		B/GL/54	68	143	92						
		B/Md/59	68	143	45	66B	346	67	64	208	41
Para 1	HI	Type 1	65/66	328	64	66A	285	80			
	(1:10–20) 1:20		68	143	60	66B	346	85	64	208	33
Para 2	HI	Type 2	65/66	328	84	66A	288	74			
	(1:10–20)		68	143	35	66B	346	86	64	208	25
Para 3	HI	Type 3	65/66	328	33	66A	288	99			
	(1:10–20)		68	143	99	66B	346	94	64	208	80
Adeno	Neut. (or HI)[a]	Type 3	68	140	28	66B	346	0	64	201	31
		Type 4	68	140	21	Not tested			Not tested		
	1:5	Type 7	68	140	8	66B	346	16	64	201	21
M. pneu.	TRI (1:1)		68	138	66	66B	176	50	64	111	49

[a]HI tests used for adenovirus 3 and 7 in Colombia Recruits and Peace Corps Volunteers. HI = Hemagglutination-inhibition. NEUT. = Neutralization test. TRI = Tetrazolium-reduction-inhibition test.

cated that the epidemic had not yet reached there and vaccination would have been desirable; similarly antibody to A_2/Tai/64 was present in only 36% of Peace Corps Volunteers bled in that year.

Antibody prevalence levels to influenza B/GL/1959 were generally below 50% in all three populations tested, again indicating the need for this vaccine.

Parainfluenza vaccines are not available but with a few exceptions antibody prevalence rates were high.

Adenovirus vaccine for types 4 and 7 is available and in use in the U.S. Armed Forces because of the high infection rates to these strains during recruit training. These are discussed in another paper in this symposium (8). The low antibody prevalence rates to adenovirus types 4 and 7 in the populations tested as well as to type 3 indicate a high level of susceptibility in South American recruits and in the U.S. Peace Corps group at the time when they entered service.

Antibody to *M. pneumoniae* as measured by the TRI or metabolic-inhibition tests was present in only about half of the three groups tested, again indicating a large group of susceptibles. The potential morbidity from these patterns of susceptibility will depend on the activity of the agent in the group and on the degree of exposure. These are discussed below.

INCIDENCE

The incidence of *infection* can be measured in a population between two points in time by comparing antibody titers taken from the same persons at the start and at the end of this period. Infection is indicated either by the appearance of antibody in

TABLE 3
Overall Incidence Rates

| | Percentage showing antibody rise | | | | | | | |
| | Argentine recruits | | | Colombia recruits | | Colombia Peace Corps | | |
Antigen	No. tested	First 3 mo	Next 9 mo	No. tested	First 23 mo	No. tested	First 15 mo	Next 7 mo
Influenza A	142	72.5	0.7	346	39.0	205/41	10.7	2.4
B	142		0	346	13.6	205/41	2.0	2.4
Parainfluenza 1	142	1.7	3.5	346	4.9	205/41	0	0
2		1.7	00	346	2.9	205/41	2.0	0
3		2.6	7.0	346	15.0	205/41	2.0	2.4
Adeno 3	135	0.7	7.9	346	0	197	0	NT[a]
4	140	0.0	0.7					
7	139	0.7	8.4	346	6.3	197	0	NT
M. pneumoniae	138	18.1	12.3	176	17.0	111	22.3	NT

[a]NT = not tested.

the second sera when absent from the first or by the demonstration of a fourfold or greater rise in antibody titer. Table 3 summarizes the infection rate of Argentine recruits during 9 mo of service (5) Colombian recruits during 22 mo of service (7), and of Peace Corps Volunteers serving 2 yr in Columbia, S.A. (7). Very high infection rates to influenza A were seen in Argentine Recruits during the basic training period involving almost three-fourths of the population; influenza B was essentially absent. In 346 Colombian military recruits the infection rate for influenza A_2 was 39% over 22 mo, for influenza B was 13.6%, and for parainfluenza viruses was 22.8%, mostly due to type 3. In total, 75.4% had a myxovirus infection during military service (7). In 201 Colombian Peace Corps volunteers 16.6% had myxovirus infections in the first 15 mo; in 41 of these volunteers followed over 7 mo 7.3% had a myxovirus infection (7). The much higher infection rate in recruits as compared to the Peace Corps group was shown to be due both to higher susceptibility and to higher exposure.

Adenovirus infections which were so common in U.S. recruits during basic training prior to the use of type 4 and 7 vaccine (8) produced few infections in 135 Argentine recruits tested at the start and end of their basic training by neutralization tests. Only 9 infections to type 3 (0.7%) and 9 to type 7 (0.7%) were demonstrated in 135 recruits during basic training; no serologic evidence of infection to type 4 was seen in 140 recruits tested. There was evidence of adenovirus infections in the subsequent 9 mo involving 7.9% with type 3 and 8.4% with type 4; only 10 type 4 infections (0.7%) were found.

In the Columbian group, tests for adenovirus antibody were made by hemagglutination-inhibition tests. Very low infection rates were observed: in 346 recruits tested none showed serologic evidence to type 3 adenovirus and only 6.3% to type 7; in 197 Peace Corps volunteers none had evidence of infection by either type. Type 4 antibody was not tested because of technical difficulties.

Infections with *M. pneumoniae* which are important in U.S. recruits (9) also proved to be important in South American recruits both during basic training and subsequently. In Argentine recruits 18.1% experienced infections during the first three mo and 12.3% in the next 9 mo; in Colombian recruits 17% were infected over 23 mo. *Mycoplasma pneumoniae* was the most important cause of respiratory infection in the Peace Corps group with 22.3 showing antibody rises over the first 15 mo.

TABLE 4
Infection Rates in Persons Lacking Antibody

Type	Argentine recruits		Colombian recruits		Peace Corps Volunteers	
	Number of susceptibles[a]	Rate/100	Number of susceptibles[a]	Rate/100	Number of susceptibles[a]	Rate/100
Influenza A	16	100	125	64.0	25	40
B	16	18.7	205	19.0	68	7.3
Adenovirus 3	100	12.0	331	0	139	0
4	110	0.9				
7	128	10.1	277	7.2	158	0.6
M. pneumoniae	44	45.4	97	30.9	57	46.2

[a]Lacking antibody in lowest dilution tested.

INCIDENCE IN SUSCEPTIBLES

The data presented above are based on the overall infection rates without considering the initial antibody status of the groups. Serological techniques also permit calculation of incidence rates in susceptibles, i.e., those lacking antibody. Under such conditions the resulting rate probably reflects the intensity of exposure. Table 4 presents an analysis of the data in this way. In susceptible recruits influenza A had rates of 40–100%, adenovirus type 7 of 0.6–10%, and M. pneumoniae of 31–45%. Knowledge of the infection rates and of the antibody prevalence rates of new recruits would provide a basis for estimating the number of infections that might occur. Unfortunately, this does not indicate the number who might become clinically ill. This type of information must be obtained from case reports and clinical surveillance. One analysis of this type was done in Yale University students during their freshman year at a period when influenza was epidemic (10). On entry, tests were made on 281 students of whom only 8.9% had preexisting antibody at low levels to the infecting strain. Of 273 paired sera obtained at the start and end of the year 45.2% showed serologic evidence of infection; of those infected 59% had clinical symptoms of respiratory disease. Similar data have been reported by Davis et al. (11). Given infection rates of 50–100% for epidemic influenza in a recruit setting and a clinical illness rate of about 60%, some 30–60% of the population can be expected to become clinically ill during basic training. Such estimates provide unequivocal testimony to the need for routine immunization of recruit populations against influenza using the most recent viral antigens in the vaccine. In a comprehensive summary of this practice in U.S. recruits over many years a vaccine effectiveness of 70–90% has usually been found (12).

REINFECTION

The occurrence of reinfection can be determined by prospective serologic surveys of naturally infected or vaccinated subjects. Table 5 summarizes analyses of this type and includes, for comparison, the attack rate in those lacking antibody. It can be seen that the risk of reinfection decreases sharply with increasing levels of preexisting antibody. For influenza A very low reinfection rates were observed at antibody levels over 1:40 and for influenza B at levels over 1:10. Such antibody levels would be desirable to attain in immunization programs. While levels of nasal secretory antibody are undoubtedly of importance in protection against natural infection, the levels measured in tests for humoral antibody are also correlated with protection and are simpler to perform.

The relation of antibody levels to reinfection to M. pneumoniae as determined by

TABLE 5

Relation of Infection Rates in Recruits to Prior Antibody Levels[a]

Test	Prior antibody level	Infection rates			
		Influenza A		Influenza B	
		No. tested	Rate	No. tested	Rate
HI	<1:10	166	63.8	205	19.0
	1:10	206	40.8	86	9.3
	1:20	143	32.9	25	0
	1:40	99	20.2	20	0
	>1:40	82	6.0	10	0

Test	Prior antibody level	M. pneumoniae	
		No. tested	Infection rate
TRI	<1:2	44	45.4
	1:2	27	25.9
	1:4	43	32.6
	1:8	16	6.2
	>1:8	28	0

[a]This table incorporates data from both Argentine (5) and Colombia (7) military recruits.

the tetrazolium reduction-inhibition test revealed a decreasing infection rate with increasing antibody level and no infections over a titer of 1:8. Monto *et al.* (13) reported reinfection rates of 22.0% in the presence of preexisting complement-fixing antibody but did not record the levels. Steinbert *et al.* (14) have found that the rate of *M. pneumoniae* infection in Marine recruits correlated well with the level of preexisting growth inhibition antibody; when infection occurred in seropositive individuals its severity was inversely related to the level of preexisting antibody.

IMMUNIZATION PROGRAMS

The use of serological surveys in defining the need for immunization programs has already been mentioned. Other uses are listed in Table 1 and the serologic evaluation of response to adenovirus vaccines will be discussed in the paper by Top (8). An example of HI antibody responses to influenza vaccine in 428 cadets at the U.S. Military Academy is presented in Table 6 as measured in sera taken on entry into the Academy in July 1969, and approximately 1 yr later, in June 1970 (15). Influenza vaccine consisting of A_2/HK, A_2/Ann Arbor and B/Mass antigens had been given in two doses of 0.5 each November 1969, 7 mo prior to the second bleeding. The tests used cannot differentiate between a response to immunization and a response to

TABLE 6

H.I. Antibody Responses to Homologous Antigens 9 mo after Influenza Immunization in 428 Cadets at the U.S. Military Academy in Relation to Preexisting Antibody Levels

Test antigen	Preexisting antibody titers							
	<10	10	20	40	80	160	≥320	Totals
A2/Hong Kong								
No. tested	176	68	52	59	45	17	11	428
Percent with antibody rise[a]	69.8	51.4	55.7	25.4	8.8	5.8	9.9	48.5
B/Mass.								
No. tested	36	65	87	123	62	38	17	428
Percent with antibody rise[a]	83.3	53.8	22.9	10.5	3.2	0	0	20.3

[a]Fourfold or greater rise in hemagglutination-inhibition (HI) antibody titer.

natural infection between the two bleedings but no known outbreak of influenza had occurred and there was a low rate of respiratory admissions to the hospital. Furthermore, many cadets developed antibodies to both A and B antigens and a double natural infection would be unlikely. It is therefore probable that the responses found were vaccine-induced and not naturally acquired. Fifty-eight percent of the cadets already had prior antibody to the A_2/Hong Kong antigen contained in the vaccine at the time of administration; of 176 lacking antibody 69.8% developed antibody levels which were still present 7 mo later. In those with prior antibody at levels of 1:10 or higher a fourfold rise in titer occurred in 51.4% and the frequency of this response diminished with increasing titers of preexisting antibody. Similar results were seen with influenza B antigen; of 36 lacking antibody at the time of immunization 83.3% had demonstrable antibody 7 mo later; again a decreasing frequency of response was observed with increasing levels of preexisting antibody. Overall, 48.5% of the 428 cadets developed antibody rises that persisted 7 mo against the homologous influenza A antigen following immunization and 20.3% developed persisting antibody rises to influenza B. The reason for the poorer response to B antigen is not known but may reflect the smaller antigenic mass of influenza B contained in the vaccine.

INFECTION IN A CLOSED ECOLOGIC SETTING

A prospective analysis of infection and illness rates for influenza and parainfluenza viruses has been made in four Polaris submarine crews to determine the risk of infection in a closed ecologic setting and the degree of spread in crew members isolated for 2 mo on an undersea mission (16). Three serial serum samples have been tested from over 500 crew members. The first sample was collected prior to departure from the U.S. to an overseas base, a second just prior to the mission after 3 wk on shore there in a "refitting operation," and the third at the end of an 8 wk underwater exercise. Antibody prevalence rates were very high at the start: 90.8% had HI antibody to A_2Hong Kong, 78.8% to A_2England, and 96.4 to B/GL or B/Mass. Similar high antibody prevalence rates were seen for the three parainfluenza viruses, ranging from 73.9 to 99.4%. This high level of prior protection may explain the low rates of subsequent infection during the observation period: antibody rises to A_2/Hong Kong occurred in only 2.4%, to A_2/England in 4.2%, and to B strains in only 1.9% of the crew members. The total parinfluenza rate was 4.0%. Minor respiratory illnesses, not identified serologically, were common during the "refit period" in the community abroad but disappeared while on the mission. These observations should not result in underestimating the possible spread of an infectious agent under these circumstances if the population is a susceptible one. Indeed, one outbreak of *M. pneumoniae* with a 50% attack rate has been reported in a Polaris submarine (17).

RISK FACTORS IN RELATION TO INFECTION

Prospective serological surveys permit measurement of the risk of infection in relation to various attributes of the host or of the environment. In a military setting this might include calculation of respiratory infection rates in different types of barracks, or under different training schedules, or according to the size of the recruit unit, or in relation to the number of new recruits mixed in with the old. Host factors might include age, prior immunity, and genetic characteristics. One host factor we have measured prospectively in recruits in relation to susceptibility to viral infec-

tions is that of ABO blood groups. We undertook this study because a previous English investigation had suggested an ABO relationship (18). They carried out a retrospective analyses of 2000 Royal Air Force recruits with serologically confirmed respiratory infections in whom they compared the distribution of ABO blood groups with that of about 50,000 recruits whose blood group had been recorded on induction. They reported a statistically significant excess of Group A individuals in those with A_2 infections over controls but not with A, B, or Coxsackie infections. This type of retrospective analysis may have hidden biases and cannot measure the actual risk of infection according to blood group. We decided to conduct a prospective study. This was based on the incidence rate of serologically confined respiratory infections in recruits, Peace Corps volunteers, and Yale freshman according to their ABO blood type. The infection rate was calculated on a fourfold or greater rise in titer in two sera from the same persons spaced in time (19). In 926 young adults followed in this way 40.3% had evidence of influenza A_2 infections but no significant difference in the incidence of infection was seen in persons of different ABO blood groups. Similarly, no significant differences were encounted by blood groups when the incidence of influenza B, parainfluenza 1–3, adenovirus, and *M. pneumoniae* infections were analyzed. Thus we were unable to confirm by prospective analysis the retrospective observations of the English group which had reported a higher frequency of clinical influenza in persons of blood group O (18).

DISCUSSION

In this paper the advantages, disadvantages, and uses of seroepidemiological surveys of acute respiratory infections in military personnel have been presented using examples from our own published and unpublished work. The application of this method to supplement other sources of morbidity data is strongly recommended. It can provide answers to some questions not measurable by case reporting techniques. These advantages include the identification of susceptibles, the calculation of the total infection rate (clinical and subclinical), the response to vaccines, and the effect of various host and environmental factors on the incidence of infection. We have also applied the technique to investigations of acute respiratory infections in civilian groups (10), to community health surveys (20), and to a variety of prevalence and incidence studies of EB virus and infectious mononucleosis in both civilian (21–23) and military personnel (24–26).

REFERENCES

1. Evans, A. S., Influenza and other respiratory infections. *In* "Serological Epidemiology" (J. R. Paul and C. White, Eds.), pp. 69–81. Academic Press, New York and London, 1973.
2. WHO Technical Report Series, No. 454, Multipurpose serological surveys and WHO Serum Reference Banks, Geneva, 1970.
3. WHO Technical Report Series, No. 181, Immunological and Haematological surveys, Geneva, 1958.
4. Evans, A. S., Casals, J., Opton, E. M., Borman, E. K., Levine, L., and Cuadrado, R., A nationwide serum survey of Argentinian military recruits, 1965–1966. I. Description of sample and antibody patterns with arboviruses, polioviruses, respiratory viruses, tetanus, and treponematosis, *Amer. J. Epid.* **93**, 111–121 (1971).
5. Evans, A. S., Cenabre, L., Wanat, J., Richards, V., Niederman, J. C., and Actis, A., Acute respiratory infections in different ecologic settings. I. Argentine military recruits. *Amer. Rev. Resp. Dis.* **108**, 1311–1319 (1973).
6. Evans, A. S., Casals, J., Opton, E. M., Borman, E. K., Levine, L., and Cuadrado, R. R., A nationwide serum survey of Colombian military recruits, 1966. I. Description of sample and antibody patterns with arboviruses, polioviruses, respiratory viruses, tetanus, and treponematosis. *Amer. J. Epidemiol.* **90**, 292–303 (1969).

7. Evans, A. S., Jeffrey, C. and Niederman, J. C.: The risk of acute respiratory infections in two groups of young adults in Colombia, South America. *Amer. J. Epidemiol.* **93,** 463-471 (1971).

8. Top, F. S., Jr., Adenoviruses. *Yale J. Biol. Med.* **48,** 000 (1975).

9. Forsyth, B. R., Bloom, H. H., Johnson, K. M., and Chanock, R. M., Etiology of primary atypical pneumonia in a military population. *JAMA* **191,** 364-368 (1965).

10. Evans, A. S., Niederman, J. C., and Sawyer, R. N., Prospective studies of a group of Yale University freshman. II. Occurrence of acute respiratory infections and rubella. *J. Inf. Dis.* **123,** 271-278 (1971).

11. Davis, L. E., Caldwell, G. G., Lynch, R. E., Bailey, R. E., and Chin, T. D. Y., Hong Kong influenza: the epidemiologic features of a high school family study analyzed and compared with a similar study during the 1957 Asian influenza epidemic. *Amer. J. Epid.* **92,** 240-247 (1970).

12. WHO Technical Report Series, No. 408, Respiratory Viruses, Geneva, 1969.

13. Monto, A. S., Byran, E. R., and Rhodes, L. M., The Tecumseh study of respiratory illness. VII. Further observations on the occurrence of respiratory syncytial virus and mycoplasma pneumoniae infections. *Amer. J. Epid.* **100,** 458-468 (1974).

14. Steinberg, P. R., White, R. J., Field, S. L., Gutekunst, R. R., Chanock, R. M., and Senterfit, L. B., Ecology of *Mycoplasma Pneumoniae* infections in Marine recruits at Parris Island, South Carolina. *Amer. J. Epid.* **89,** 62-72 (1969).

15. Evans, A. S. and Wanat, J., Unpublished studies carried out in the WHO Serum Reference Bank, Yale University.

16. Sphar, R. L., and Evans, A. S., Seroepidemiological studies of Polaris submarine crews. I. Acute respiratory infections. *Military Med.* (in press).

17. Sawyer, R., and Somerville, R. G., An outbreak of *Mycoplasma pneumoniae* infection in a nuclear submarine. *JAMA* **195,** 958 (1966).

18. McDonald, J. D. and Zuckerman, A. J., ABO blood groups and acute respiratory disease. *Brit. Med. J.* **1,** 89-90 (1962).

19. Evans, A. S., Shepard, K. A., and Richards, V. A., ABO blood groups and viral diseases. *Yale J. Biol. Med.* **45,** 81-92 (1972).

20. Evans, A. S., Cox, F., Nankervis, G., Opton, E., Shope, R., Wells, A. V., and West, B., A health and seroepidemiological survey of a community in Barbados. *Int. J. Epid.* **3,** 167-175 (1974).

21. Evans, A. S., Niederman, J. C., and McCollum, R. W., Seroepidemiological studies of infectious mononucleosis with EB virus. *N. Engl. J. Med.* **279,** 1121-1127 (1968).

22. Niederman, J. C., Evans, A. S., Subrahmanyan, L. and McCollum, R. W., Prevalence, incidence, and persistence of EB virus in young adults. *N. Engl. J. Med.* **282,** 361-365 (1970).

23. Sawyer, R. N., Evans, A. S., Niederman, J. C., and McCollum, R. W., Prospective studies of a group of Yale University freshman. I. Occurrence of infectious mononucleosis, *N. Engl. J. Med.* **123,** 263-270 (1971).

24. Evans, A. S., Infectious mononucleosis in the Armed Forces. *Military Med.* **135,** 300-304 (1970).

25. Hallee, T. J., Evans, A. S., Niederman, J. C., Brooks, C. M., and Voegtly, J. H., Infectious mononucleosis at the United States Military Academy. A prospective study of a single class over four years. *Yale J. Biol. Med.* **47,** 182-195 (1974).

26. Storrie, M. C., Sawyer, R. N., Sphar, R. L., and Evans, A. S., Seroepidemiological studies of Polaris submarine crews. II. Infectious mononucleosis, *Military Med.* (in press).