

ABO Blood Groups and Viral Diseases*†

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INTRODUCTION

The role of ABO blood groups in differential susceptibility to various diseases has long been a subject of investigation and debate(1). The genetic factors involved in resistance against virus infections have been reviewed by Allison(2). In the past few years three reports by English writers have claimed to show a higher susceptibility of persons of blood group O to influenza than other blood groups. In 1962 McDonald and Zuckerman analyzed the distribution of blood groups among 2000 serologically confirmed respiratory illnesses in Royal Air Force personnel from 1956 to 1961 as compared to their distribution in a control group of about 50,000 RAF recruits whose blood groups were known(3). A statistically significant excess of Group O patients was found among those with illness due to A2 influenza but not among those with illnesses due to influenza A1 or B or to Coxsackie A21. An opposite trend was seen for certain adenovirus infections. In 1968 Potter and Schild(4) tested the prevalence of antibody to the A2/Singapore strain of influenza in the sera of 515 persons of different ages collected from 1961 to 1963. A higher prevalence of this antibody in persons of group O blood was observed in all age groups but in only two age groups, age 16 to 20 and over 30-years-old, was this relationship significant by the X^2 test. In a third study by Tyrell, Sparrow, and Bear published in 1968(5) the role of ABO sus-

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ceptibility was determined in volunteers experimentally inoculated with influenza, rhinoviruses, or coxsackie A21. The occurrence of influenza infections, particularly group B, as judged by virus isolation and/or antibody rise was higher in volunteers of blood group O than in those of group A. No differences for the other viruses were reported. On the other hand, the occurrence of *clinical* illness among those with virologically proved influenza infections was higher in group A than in group O. These three studies stimulated us to examine the possible relationship of ABO blood groups to viral and *M. pneumoniae* infections in prospective seroepidemiologic analyses of four groups of adults as well as the prevalence of viral antibodies in these and other populations. The viruses studied include influenza A and B, parainfluenza 1-3, Epstein-Barr (EB), rubella, measles, mumps, and arboviruses.

MATERIALS AND METHODS

This paper was based on analyses of results of current and past seroepidemiological surveys carried out by the WHO Serum Reference Bank. Appropriate reference to the detailed reports of these studies will be made.

Laboratory tests. The hemagglutination-inhibition test was carried out by microtiter methods for myxoviruses and rubella virus according to the general methods of Sever(6) as modified by the National Center for Disease Control. Sera were inactivated at 56°/30 min. For influenza tests sera were pretreated with potassium periodate/trypsin, or with RDE, and for parainfluenza were absorbed by guinea pig kidney RBC. For rubella the dextran pretreatment and method of Liebhaber was used(7). All paired sera showing four-fold or greater rises were confirmed by a repeat test. EBV antibody was measured by the indirect immunofluorescence test described by Henle *et al.*(8). Neutralization tests for adenovirus 3, 4, and 7 were carried out in tube cultures of human embryonic kidney using about 100 TCD₅₀ of each virus. Blood grouping was performed on red cells at the time the blood samples were obtained from military recruits and West Point Cadets, and were later tested using serum from the other populations studied.

Statistical and computer methods. The blood groups, antibody results, epidemiological data, and clinical information where available were punched onto IBM cards. A program was written for the IBM 7094-7040 DCS computer which analyzed and printed out antibody results according to blood groups. A chi-square test was used to measure statistical significance based on differences between blood groups of those with and without antibody. A probability value of .05 was regarded as significant. Tabular data is available on request for each of the analyses made but only a limited number have been published to conserve journal space.

Population groups. For prospective studies four groups of young male adults were bled at the start and end of a defined experience and questionnaires taken (Table 1). Since most infections (four-fold or greater antibody rises) occurred at the end of 3 months basic training in the Argentine recruits and after the first

year in the field in the Peace Corps volunteers only these periods were analyzed for AEO association. Clinical data was available only for Yale freshman; for this purpose health records were color tagged for special clinical analysis at the start of the study and blood samples were often obtained at the time of illness. Detailed etiologic and epidemiologic analysis of each of the groups studied will be or has been published separately. The results of serum tests of other samples from Colombian recruits in 1966(9) and Argentine recruits in 1965 and 1966(10) were available as well as results from Brazil recruits in 1964(11) and U.S. recruits in 1962(12). These collections represented nationwide recruit surveys carried out by the WHO Serum Reference Bank at Yale University. We are most indebted to the authors of these papers for use of these data for analysis by ABO blood groups.

RESULTS

Respiratory Viruses

The incidence of viral respiratory infections in four groups of young adult males as measured by a four-fold or greater serologic rise in antibody titer between bleedings is presented in Table 2.

Influenza infection. The observed number of influenza A2/Taiwan infections in each ABO blood group among 132 Argentine recruits for A2 influenza was not significantly different from the expected number had there been no ABO effect(12). This was based on a 75.0% infection rate occurring during a 3-month-period in recruit camps where the amount of exposure was probably similar and simultaneous. No significant difference between group A and O was seen when calculated separately. Data for the Colombian recruits during 23 months of military service based on a 39.6% infection rate revealed more group A and less group O infections than expected but the difference was significant only when blood groups B and AB were excluded from the analyses ($p < .05$)(14). Peace Corps Volunteers in their first 15 months of overseas duty in Colombia had an A2 influenza serologic infection rate of 11.9 based on four-fold or greater rises occurring in 177 paired sera taken 15 months apart. The distribution of infection among all four blood groups showed more AB and B infections and less A than expected. However, analysis of A vs O showed no statistical difference between these two. In each of these 3 populations the infection strain was not a new one

TABLE 1
GROUPS STUDIED FOR RESPIRATORY VIRUSES

Group	Type of Experience	Time of Bleeding
Argentine Army Recruits	Recruit training rest of military service	0, 3, and 9 months
Colombian Army Recruits	Military service	0 and 23 months
Peace Corps Volunteers	Overseas duty in Colombia, S.A.	0, 15, and 22 months
Yale University Freshman	During first academic year	0 and 9 months

to the groups at the time of the study so that preexisting antibody to a related strain was present in most sera. A total of only 62 persons completely lacked antibody at the start of observation, a number which was too small for statistical analysis. However, the 75% prevalence of antibody in sera taken at the start of the observation period of these 650 military recruits and Peace Corps Volunteers showed no significant ABO differences. Another subsample of about 600 Argentine and Colombian military recruits was similarly tested and analyzed. Again, no significant relation of A2 influenza antibody prevalence to ABO blood types was found.

The fourth group studied prospectively, Yale College freshman, represented an ideal group for ABO/influenza analysis for several reasons: 1) They were exposed for the first time to a new influenza antigen (A2/Hongkong) to which they had neither prior experience nor prior antibody; 2) There was an attack rate of nearly 50%; and 3) Clinical data were available. The results are given in Table 3. Clinical and laboratory data have been previously published(15). The infection rate measured by serologic conversion showed no significant difference among the four blood groups nor when group A and O were compared separately. To approximate the data of McDonald and Zuckerman(3) an analysis

TABLE 2
INCIDENCE OF SEROLOGICALLY CONFIRMED RESPIRATORY INFECTIONS
IN FOUR YOUNG ADULT GROUPS

Antigenic Group	Population Group and Period of Observation							
	Arg. Recruits (over 3 months)		Col. Recruits (over 23 months)		Col. PCV ^a (over 15 months)		Yale Freshman (over 9 months)	
	No. tested	Percent positive	No. tested	Percent positive	No. tested	Percent positive	No. tested	Percent positive
Influenza								
A2	132	75.0	341	39.6	177	11.9	276	42.8
B/M	132	0.8	341	13.8	177	0.6	Not tested	
B/GL	132	2.3	341	12.9	177	1.1	276	1.8
Parainfluenza								
1	132	0.8	341	4.7	177	0.0	276	0.4
2	132	1.5	341	3.2	176	1.1	276	1.1
3	132	3.0	340	15.3	177	1.1	276	1.1
Adenovirus (over 9 mo.) ^b								
3	127	7.9						
4	127	0.0						
7	127	12.6						
<i>M. pneumoniae</i>	127	17.3	176	17.0	143	16.1	211	0.9

Note:

Positive: A four-fold or greater rise in titer between paired serum samples. The HI test was used except for the metabolic inhibition for *M. pneumoniae* and the neutralization test for adenoviruses 3, 4, and 7 in Arg. recruits.

^a Peace Corps volunteers working in Colombia.

^b No adenovirus infections were found in the first three months of recruit training.

was made of just the serologically confirmed clinical cases. In contrast to their results with a higher incidence among group O we found no significant ABO differences (Table 3). In addition the frequency of clinical illness among those with serologic evidence of A2 infection was analyzed by blood groups. A clinical attack rate of 47.5% was equally distributed among the blood groups. Finally, all groups were combined and analyzed. This represented 926 young adults followed prospectively for evidence of infection over 9 months to 2 years. The analysis again revealed neither ABO nor A vs. O differences (Table 4).

Other myxovirus infections. Except for influenza B and parainfluenza 3 infections in Colombian military recruits (C.M.R.), the *incidence* of seroconversion for influenza B and parainfluenza viruses in the four young adult populations was too low for meaningful analysis (Table 2). In addition, the presence of pre-existing antibody and the known occurrence of reinfection for the parainfluenza viruses complicated the interpretation. Analysis of the C.M.R. group for the *incidence* of influenza B and parainfluenza three infections revealed no statistical difference among the blood types.

The prevalence of antibodies to influenza B and the parainfluenza viruses in the four populations also revealed no statistical difference in persons of one blood type over another.

TABLE 3
DISTRIBUTION OF SEROLOGIC AND CLINICALLY CONFIRMED A2/HONGKONG INFLUENZA INFECTIONS IN 276 SUSCEPTIBLE YALE UNIVERSITY FRESHMAN DURING AN EPIDEMIC PERIOD^{a b}

Blood Group	Total No.	Serologic evidence of infection				Clinical illness serologically Confirmed as due to A2/Hongkong			
		Infected		Not infected		Ill		Not ill	
		Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
A	110	54	47.0	56	63.0	25	22.3	85	87.7
O	114	44	48.7	70	65.3	23	23.1	91	90.9
B	29	14	12.4	15	16.6	6	5.9	23	23.1
AB	23	6	9.8	17	13.2	2	4.7	21	18.3
	<u>276</u>	<u>118</u>		<u>158</u>		<u>56</u>		<u>220</u>	

^a Serologic infection rate = 42.75%. $X^2 = 5.58$. Not significant at 5% level.

^b Illness rate = 20.3%. $X^2 = 2.32$. Not significant at 5% level.

TABLE 4
SUMMARY OF INFLUENZA A₂ INFECTIONS IN ARGENTINE MILITARY RECRUITS, COLOMBIAN MILITARY RECRUITS, COLOMBIAN PEACE CORPS VOLUNTEERS, AND YALE FRESHMAN^a

Blood Group	Total No.	Infected		Not infected	
		Obs.	Exp.	Obs.	Exp.
A	313	134	126.08	179	186.92
O	478	185	192.54	293	285.46
B	89	36	35.85	53	53.15
AB	46	18	18.53	28	27.47
	<u>926</u>	<u>373</u>		<u>553</u>	

^a Attack Rate = $373/926 = 40.28\%$. $X^2 = 1.35$. Not significant at 5% level.

Adenoviruses. Adenovirus antibody to types 3 and 7 were determined by an HI test in Colombia recruits and Peace Corps personnel(14). The seroconversion rate and the prevalence rate were too low as measured by this test to make a meaningful analysis. Neutralization tests for types 3, 4, and 7 were performed on sera from 127 Argentine recruits taken at the time of induction into service, after 3 months when basic training was completed, and at 9 months at the time of discharge(13). The total seroconversion rate per 100 over this period was 7.9 for type 3, 0 for type 4, and 12.6 for type 7 adenovirus (Table 2). No significantly greater number of infections occurred in any one ABO group than would have been expected by chance alone.

The prevalence of type 3 and 7 antibodies was as expected in ABO blood groups but type 4 showed a significantly higher number of persons of blood type AB with antibody than was expected. When just A and O blood types were compared, there was no statistical difference.

Mycoplasma pneumoniae. The metabolic inhibition (MI) test and/or the tetrazolium reduction inhibition test (TRI) which detect long lasting antibody were carried out on several populations as summarized in Table 2. Incidence data was studied in all four groups but as only 2 of 211 Yale students showed serologic evidence of infection, they were excluded from analysis. The distribution of 446 infections in the other three groups revealed no difference among ABO blood types when analyzed separately or when the data were combined. Analysis of individual groups for prevalence of antibody to *M. pneumonia* also showed no ABO differences.

EBV. The presence or absence of antibody to EB virus as measured by the indirect immunofluorescence test(8) has been a reliable indicator of susceptibility and immunity to infectious mononucleosis(16-18). The incidence of EB virus infection over the freshman year among 160 Yale University students on whom blood types were available and whose serum lacked EBV antibody on entry was 11.9%(18). Analysis by ABO blood group showed no tendency for significantly more infections in one type than another confirming an earlier observation(19).

The largest group we have studied for prevalence of EBV antibody is an ongoing survey of a cadet class at the (West Point) United States Military Academy, U.S. Army(20). No relation to ABO group was observed in 1375 cadets tested.

Rubella. On entry into Yale 75% of 251 students possessed HI antibody to rubella at a titer of 1:8 or more(15). The occurrence of antibody prevalence by blood groups showed no significant difference between observed and expected values. During the academic year sera from 49 freshman students showed a four-fold or greater rise in titer, 22 with clinical rubella and 27 without. In order to eliminate the effect of prior immunity, the ABO analysis was limited to the 63 students who lacked antibody at the start and who subsequently experienced a 64% infection rate. Because the numbers were small the B and AB groups were combined. No significant variation of observed-expected was seen.

Measles. Only prevalence data were available. This was recorded in the computer records of the WHO Serum Bank from tests done by Dr. Frank L. Black on military recruits in Brazil(11). A prevalence rate of 95.0% was found for HI

antibody to measles in 1425 recruits. The distribution of antibody was as expected according to ABO groups.

Mumps. Hemagglutination-inhibition antibody tests were done on 1191 Brazilian military recruits by Dr. Frank L. Black(11) and the results were on record in the WHO Serum Reference Bank. A prevalence rate of 69.2% was reported. No predilection was seen by ABO blood groups. No serial samples were available for incidence rates.

Poliomyelitis. A large number of neutralization tests have been carried out for polio 1, 2, and 3 antibody in recruit populations. The prevalence of antibody in 2500 Brazilian recruits on whom blood group data was available was 89.7% for type 1, 78.1% for type 2, and 78.9% for type 3(11). However, an uncertain number of these recruits had received poliomyelitis vaccination making the data questionable. A similar problem of polio vaccination existed in the other groups studied so that further analysis was abandoned.

Arboviruses. Quite low prevalence rates have been found by Dr. J. Casals in HI tests on Argentine and Colombian recruits(9,10). Of 527 Argentine and Colombian soldiers tested only 3.6% had group A antibody, and 27.7% had group B antibody. No ABO differences were found when chi square tests were done. Incidence data was not available.

DISCUSSION

There are many methodological problems besetting the proper evaluation of ABO blood groups and susceptibility to disease. Ideally the criteria for a good study of infectious disease might include: 1) a prospective survey so that incidence can be determined; 2) prior knowledge of the blood groups of the persons at risk to infection; 3) a similar exposure of all ABO blood groups to the infectious agent; 4) a means of determining both infection rates and clinical illness rates in the population under study; 5) the elimination of prior immunity as a factor; 6) an attack rate high enough and a study group big enough to permit statistically significant analysis; 7) a short period to exclude changing immunity status in the population during the study; 8) data on age, sex, ethnic origin, and other possible factors. For prevalence data the antibody measured should be lifelong, reflect immunity to reinfection, and eliminate possible cross-reacting antigens. The material available from a number of surveys carried out by the WHO Serum Reference Bank at Yale University met many of these criteria. However, disadvantages of these collections are that they represent largely young adults whereas children might be the ideal population of study in order to focus on the *first* contact with the infectious agent, and secondly, that clinical data was available only for the Yale college group.

The results of prospective analyses of 4 groups of young adults for a number of respiratory viruses and *M. pneumoniae* have failed to indicate a consistent differential ABO blood group susceptibility to *infection* as measured by significant antibody rises in paired sera. These include influenza A2 and B/Maryland,

parainfluenza 1-3. For some of these viruses the infection rates were rather low to give meaningful incidence data. This was not true of A2 influenza, however, for which the attack rates ranged from 13 to 75%. In 3 of the groups analyzed the A2/Asian or Taiwan strains were involved and many of the individuals already possessed antibody to the same or a related A2 strain at the start of the observation period. In Colombian recruits no significant ABO difference in A2 infection was found when all four blood groups were analyzed but in a comparison of just A vs. O, a significantly higher rate in group A was found ($p < .05$). In Peace Corps Volunteers more AB and B infections occurred and less A but analysis of just A vs. O showed no difference. Neither of these results are in accord with McDonald and Zuckerman data in which more A2 infections in group O were found(3). However, in these three population groups as well as in their study the existence of antibody to the infecting strain in many individuals at the start of the study complicated the analysis of subsequent infection rates. There were too few lacking antibody in our series for statistical treatment. In contrast to this the Hongkong influenza outbreak represented an entirely new antigenic experience for the Yale students studied and one in which prior immunity played no role. Analysis of this group showed no differences by ABO blood groups in the rate of A2/Hongkong infection, or in the rate of serologically confirmed clinical illness, or in the number of infected persons who showed clinical symptoms.

The large scale study of ABO blood groups in RAF recruits with clinically confirmed A2 infections poses some of the problems of retrospective analysis(3). As the ABO distribution among the groups from whom the clinical cases were actually drawn was not known, they reversed the usual procedure and determined the distribution of ABO groups among proved cases as compared to ABO distribution among a large group of entering RAF recruits. Variations in ABO distribution from one part of the country to another were noted but were presumably not enough to account for the differences found. Furthermore their analysis was limited to *clinical* cases, not total infection rates, in a population whose initial antibody status was not known and which must have changed during the 4-year observation period. These methodological problems make interpretation very difficult. The study of Potter and Schild(4) actually involved *prevalence* of influenza antibody rather than incidence as stated in the title. A statistically higher prevalence of A2/Singapore antibody was found in group O blood types among only two of seven age groups. These groups were age 16-20 and over 30-years-old which is surprising as younger age groups would seem the most likely to reveal true differences if they existed. In their combined group of 515 persons tested no significant differences by ABO group were present. The use of volunteers as reported by Tyrell *et al.*(5) would seem to be an excellent approach to the problem because the number of each blood group at risk, the antibody status at the start of the study, the degree of exposure, and the means of recognizing infection and illness can all be defined. However, the number of subjects that can be studied is often too small to be meaningful statistically. In their study 199 volunteers were inoculated with influenza viruses but they excluded from analysis all volunteers with antibody titers of 1:96 or more presumably in an

effort to eliminate persons who were supposedly immune. However, no evidence to substantiate this assumption of immunity is presented. In our studies only those with HI titers of 1:10 or under seem fully susceptible and those at 1:40 or higher fully protected(14). Their test group thus contained an unknown mix of immunes and susceptibles. After inoculation with influenza B/Eng./65, 75% of 40 group O volunteers became infected compared to 44% in 27 group A volunteers ($p < 0.01$). However, in those infected, more group A than group O became clinically ill, in contrast to results of McDonald and Zuckerman who found more group O RAF recruits in those clinically ill with proved A2 infection(3). No evidence of higher infection and/or illness rates in group O volunteers among the 50 volunteers receiving influenza A2 strain was presented by Tyrell *et al.*(15) which was the influenza strain studied by McDonald and Zuckerman(3).

While this manuscript was in preparation Cuadrado and Davenport(21) reported the prevalence of influenza antibodies among 1500 military recruits according to their blood group. They used the swine, PR8, FM1, and Asian (A2/Ann Arbor/60) strains of influenza virus in HI antibody tests on microtiter plates for 1500 sera from Argentine, Brazil, and Colombia military recruits. These represented selected samples obtained from the WHO Serum Reference Bank at Yale, some of which have also been included in the present paper. They also employed ABO blood group data from our records. They reported a higher prevalence of antibody to the FM and Asian strain of influenza strains in recruits of blood group O and B as opposed to blood group A. This was statistically significant for each group of recruits. Their results with the A2 influenza strain are in contrast to our own inability to find such differences in many of the same sera, in other sera from the same recruit groups, and in prospective analysis of incidence in these and other young adults. We have reexamined our data and our analyses without finding an adequate explanation. The differences in the A2/Asian strains used¹ and the methods employed for removal of nonspecific inhibitors would not seem likely explanations. However, the latter may have played a role because our higher antibody prevalence rate might represent incomplete removal of inhibitors. If so, an ABO relationship might be obscured. We are skeptical of this explanation because our prevalence rates of 90% or so agrees closely with worldwide surveys of Taylor-Robinson *et al.*, who tested 161 sera from 15 countries with A2/Pakistan/57 and found 86% positive at 1:8 or more(22). Cuadrado and Davenport's average prevalence rate for A2/Asian, A2/Ann Arbor/60, of 65% seems unusually low.

In the final analysis the impact of influenza on genetic selection in a population would depend on its influence on mortality patterns and not on infection rates or morbidity patterns. While both infection and clinical illness are necessary preludes to death from influenza, it does not follow that a genetic selection necessarily must operate at these levels during initial infection. It could also exert its effect on the ratio of deaths to clinical cases. Because of the low mortality from influenza today the examination of this question would require a

¹ They used AS/Ann Arbor/60 and we used A2/Taiwan and A2/Japan in antibody prevalence tests on these recruits.

nationwide study of mortality during an influenza outbreak with retrospective attempts to ascertain the blood group in the fatal cases and in a control group.

Analyses were also made in the current study for antibodies to several other respiratory pathogens in these populations: influenza B (Maryland and Great Lakes strains), parainfluenza 1-3, adenovirus types 3 and 7, and *M. pneumoniae*. Again, no consistent ABO blood type differences were observed for either the prevalence of antibody at the start of the observation period or subsequent occurrence of infection during the period. The relatively low attack rates for some of these agents provided less statistically impressive results than with influenza A2 infections.

Prospective analysis of inapparent and apparent infections with EB virus and rubella virus in Yale students lacking specific antibody have also failed to show a statistical difference according to ABO blood types. The prevalence of EBV and rubella antibodies in sera taken at the start of the observation period also showed no ABO differences.

The prevalence of antibodies to measles(12), mumps(12), and to certain arboviruses(9,10), in several military recruit populations was also compared to ABO blood group distribution as recorded in the computer programs of the WHO Serum Reference Bank. No evidence of ABO selection could be demonstrated. The mumps and measles HI antibodies are long lasting, related to immunity, and usually represent infections occurring in childhood. If selective ABO susceptibility existed, it should, therefore, be reflected by these analyses. The data on poliomyelitis, however was complicated by previous polio immunization in an uncertain number of recruits and that for arboviruses by the low prevalence of infection and the broad cross-reactivity of group B antibody in hemagglutination inhibition test.

The extensive analyses reported here that fail to reveal any consistent statistical relation between ABO blood groups and viral infections may seem to complicate rather than clarify the question. This is especially so since the influenza results are in disagreement with two English studies(3,5) and a recent American study(21). We are willing to rest our case on the prospective studies in which susceptibility and immunity can be controlled and the infection rate in the entire group can be measured. In such situations a susceptible person of one ABO blood type was not at higher risk to infection than a person of another blood type to any of the pathogens tested. While we feel that inherited characteristics may well alter the immune response to infection and the frequency and type of clinical illness, the ABO blood groups do not reflect these genetic influences for the antigens tested.

SUMMARY

1. A prospective analysis of influenza A2 infections (serologic rises) as related to the ABO blood groups was made in four groups of young adults who had attack rates ranging from 13 to 75% during the observation period. No

consistent significant difference of observed to expected attack rates among persons of different ABO blood types could be demonstrated: one study group showed more A and another more AB and B infections than expected. The prevalence of influenza antibodies on entry was similar among ABO blood groups. In one group (Yale students) an A2/Hongkong outbreak occurred for which prior antibody and immunity did not exist at the time of exposure so that all were susceptible to infection. In this group 42% developed specific antibody and 20.3% clinical illness without regard to ABO blood groupings. Analysis of the frequency of clinical illness among those with serologic evidence of infection in this group also showed no ABO preferences.

2. The prevalence of antibody to influenza B and parainfluenza viruses at the start of the observation period and the subsequent rise in antibody following exposure could not be related to the blood group of the individual. The prevalence rates ranged from 40 to 90% and subsequent infection rates ranged 1 up to 23% for these viruses.
3. In 127 Argentine recruits infections with type 3 and 7 adenoviruses bore no relation to ABO blood types nor did the prevalence of these antibodies. The prevalence of type 4 adenovirus antibody was significantly higher in persons of group AB but no significant A vs. O blood group difference was seen.
4. The incidence of *M. pneumoniae* infections in three study groups with significant attack rates was unrelated to ABO blood types as was the prevalence of antibody in these populations.
5. The occurrence of clinical and subclinical infections with rubella and EB viruses in prospective surveys of susceptible Yale freshman students during the first academic year showed no significant variation over the expected incidence among persons of different ABO blood groups. Serologic evidence of infection was found in 64% of students susceptible to rubella and in 13% susceptible to EB infection over the 9-month period. The prevalence of EBV antibody was unrelated to ABO blood groups in tests made on 1375 West Point Cadets.
6. The observed prevalence rates of antibody to measles, mumps, and group A and B arboviruses among young adults of different ABO blood types did not differ statistically from the expected rates.
7. The accumulated evidence presented fails to substantiate a higher susceptibility of persons of one ABO blood type over another to any of the viruses studied.

Additional tables supporting one or more of the analyses made are available on request when ordering reprints.

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