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Relationship between Infectious Diseases and Human Blood Type

S. A. Berger^{1*}, N. A. Young², S. C. Edberg²

During the past eight decades, a large number of studies have examined the possible relationship between blood type and infection. Many publications reflect uncritical attempts to mathematically link unstratified or random data. The interaction of pathogen and erythrocyte membrane may reflect antigenic similarity, adhesion through specific receptors, or modulation of antibody response. Anthropological surveys suggest that the geographic and racial distribution of human blood groups reflects susceptibility of populations with specific blood types to the plague, cholera, smallpox, malaria and other infectious diseases.

Carl Landsteiner's discovery of blood group antigens contributed to the revolution which swept bacteriology at the turn of the century (1). New pathogens and disease mechanisms were being identified at a rapid rate, and the interaction of host and pathogen was finally visible to the eye of science. As microbes were found to enter, lyse, engulf, attach to or kill virtually all human substances, it was inevitable that some interaction would be found to occur with the newly discovered blood group antigens. For eight decades, a vast number of studies have examined the relationship of human blood groups to disease. Studies on the relationship of blood groups to infectious disease deal with essentially four aspects of this relationship: the antigenic relatedness of microbe and red cell membrane; adhesion of microbes to cells which express blood group substances; modulation of the antibody response related to blood group; and anthropological and geographic considerations.

Many studies on blood group and disease are of the case-control variety and exhibit errors of data stratification, pooling of results, sampling bias and definition of disease or blood type (2–4). Thus, longevity, fracture of the femur and temperament have been statistically linked to certain blood types (3). The difficulties inherent in assessing the literature are illustrated by the widely conflicting conclusions of studies on the relationship between hepatitis B antigen carriage and blood type: an association has been claimed for types A, O, AB and for no blood type (5–8). Similarly, investigators have found that blood group O is either associated with, or protects against,

pulmonary tuberculosis (9–12). In at least 27 studies conflicting conclusions are drawn on a possible association in leprosy (13).

Results of a variety of studies concerned with the relationship of infection to human blood type are summarized in Table 1. Several studies represent retrospective evaluations of large pools of miscellaneous data. Thus, one investigator classified the blood groups and diseases of 8,177 inpatients, suggesting blood group specificity in tuberculosis, brucellosis, typhoid, bartonellosis, septicemia, hepatitis, echinococcosis and many additional infectious or non-infectious ailments (14). Since studies varied considerably in techniques and conclusions, a critical analysis of each disease examined is not possible. This review was therefore executed in order to outline the controversies and mechanisms involved in the association between blood group and infectious diseases, and to present a comprehensive source reference.

Antigenic Relatedness of Microbes and Red Cell Membrane

The ABH and Lewis blood group antigens are not limited to erythrocytes, but are found in secretions and cell membranes throughout the body. Specific antigens consist of glycoproteins which contain varying percentages of galactose, fucose, hexosamine, N-acetyl-glucosamine and N-acetyl-galactosamine (15).

Antigens similar to blood group substances have been identified among the *Enterobacteriaceae* (16) and have led to the hypothesis that such strains cannot be recognized as foreign, thus evading immune response (17–19). These antigens are not limited to common bacteria, having been demonstrated in such

¹Department of Clinical Microbiology, Tel-Aviv Medical Center, 6 Weizman Street, Tel Aviv 64239, Israel.

²Department of Laboratory Medicine, Yale-New Haven Hospital, Yale University School of Medicine, New Haven, Connecticut, USA.

Table 1: Association of human blood type with infectious diseases.

Disease or organism	Blood group or substance	Clinical observation	References
Bacterial			
Plague	O	increased disease incidence	(53)
Cholera	O	increased disease severity	(49, 61)
Tuberculosis	O	increased disease incidence	(9, 12)
		decreased disease incidence	(10, 71)
Leprosy	B	increased disease incidence	(70, 71)
	ABO	no relationship to incidence	(69)
	A	increased incidence of lepromatous form	(109, 110)
	B	increased incidence of lepromatous form	(111)
	O	increased incidence of tuberculoid form	(109, 110, 112)
Yaws	ABO, Rh	no relationship to incidence	(13, 113)
Syphilis	M	increased disease among homozygotes	(52)
<i>Streptococcus pneumoniae</i>	ABO, Rh	no relationship to incidence	(114)
	B	decreased disease incidence	(28)
<i>Neisseria meningitidis</i>	ABO	increased incidence in nonsecretors	(78)
<i>Haemophilus influenzae</i>	ABO	increased incidence in nonsecretors	(78)
Gonorrhea		increased incidence in nonsecretors	(80)
Staphylococcal infection	B	increased disease incidence	(79, 115)
	ABO	no relationship to incidence	(116, 117)
<i>Staphylococcus aureus</i>	ABO	no relationship to incidence	(118)
Dental caries	ABO Rh	no relationship to incidence	(119)
Rheumatic fever	M	decreased disease incidence	(74)
	N	increased disease incidence	(74)
	ABO, MN	no relationship to incidence	(73)
	ABH	increased disease in nonsecretors	(75, 76)
	A	increased disease in incidence	(77)
Hematogenous osteomyelitis	A, AB	increased disease incidence	(120)
	O	increased disease incidence	(121)
	<i>Escherichia coli</i>	increased incidence of urinary tract infection	(47)
	P	no increase in renal scarring	(46)
		increased incidence of bacteremia	(45)
<i>Enterobacteriaceae</i>	A, Kell	stimulation of production of anti-Kell and anti-A antibody	(31)
	B	increased incidence of septicemia	(27)
	ABO	increased virulence of strains with antigens related to blood group substances	(17, 18)
	B	increased incidence of upper urinary tract infection	(24)
Viral			
Epstein Barr virus	N	anti-N antibody, hemolytic anemia	(81)
	i	anti-i cold agglutinin, hemolysis	(82)
Influenza	O	increased viral antibody present	(85)
		increased disease incidence	(122)
	A	increased disease severity	
	ABO	no relationship to incidence	(86–89)
	Rh, MN	no relationship to incidence	(123)
Smallpox	A, AB	increased disease incidence	(54)
Adenovirus	A	conflicting findings	(87, 123)
Kuru	ABO, MN, Rh	no relationship to incidence	(124)
Mumps	O	increased disease incidence	(93)
Hepatitis B	O, Rh negative	increased prevalence of carriage	(5)
	A	increased prevalence of carriage	(6)
	AB	increased prevalence of carriage	(7)
		no relationship to carriage	(8)
Fungal			
<i>Candida albicans</i>	ABO	increased incidence of superficial infection among nonsecretors	(78)
<i>Trychophyton</i> spp.	ABO, Rh	no relationship to incidence	(78)
Parasitic			
Vivax malaria		no relationship to incidence	(125)
	P positive	increased disease incidence	(126)
	A	increased disease incidence	(61, 62)
	Duffy negative	decreased disease incidence	(58, 66)
	ABO	no relationship to incidence	(60)