after infection, HCC virus behaves as a member of the adenovirus group. The virus can be excreted with the urine for as long as 271 days(11). The virus was "unmasked" in noninoculated dog kidney cell cultures derived from a dog 3 months after recovery from an infection(14). In the same way, adenovirus was detected in cultures made from human adenoid tissue.

As far as we know, HCC virus is not pathogenic for man. The claim of inapparent human infections made by some authors(15) was based on the finding of C.F. antibodies in human sera. This should be reviewed in the light of the relationship between HCC strains and adenoviruses.

It is not yet known if the virus of infectious canine hepatitis is a new member of the adenovirus group or related to one of the human or simian types. Dr. van der Veen informed us that the prototype adenovirus strains of types 1-17 could not be neutralized by our guinea pig antiserum to the Utrecht strain of HCC virus at a serum dilution of 1:4. This serum had a neutralizing titer of 1:320 for the homologous strain. Typing experiments are in progress and will be published. The host range and virulence of HCC virus points to a separate position among the members of the adenovirus group. Future experience will show whether the animal host range is appropriate for the further division of adenoviruses into human, simian and canine subgroups.

Summary. 1) The virus of infectious canine hepatitis was shown to share the 4 main properties of the adenovirus group, including common complement-fixing antigen. 2) The relationship between the disease of the dog and human adenovirus infections is discussed.

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Human Blood Group Substance B and *Escherichia coli* 086. (25036)

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Many investigators have considered selective influences of ABO blood groups on disease conditions. A marked selection against heterozygous fetuses and infants occurs, for example, when the mother is group O and the father is group A or group B(1). Moreover, Race and Sanger(2) have postulated that it is unlikely that the relationship between blood groups and disease would work only through maternal-foetal incompatibilities. A significant association has been found between the ABO groups and duodenal ulcer, carcinoma of stomach, and diabetes mellitus(3). Also, in infectious diseases, individuals of blood group B appear to possess a slightly greater degree of natural resistance to poliomyelitis(4).

McConnell(3) postulated that possibly these associations are merely ethnological, that patients with some diseases are of a racial group with high susceptibility to the disease and that their blood group frequencies are different from the rest of the population. Manuila (5) has also pointed out that natural variation in frequency of blood groups in a limited area, sampling errors, and technical errors may account for assumed association. Studies by Oliver-Gonzalez(6) indicated presence of serologic blood group active polysaccharides in animal parasites and Springer(7) has shown the presence of serologic blood group active substances in animals (gastric mucin of the horse and Castle's intrinsic factor from the hog), plants, several species of the enteric bacteria, and *Pseudomonas aeruginosa.* Springer also indicated that decomplemented high titered human anti-B sera temporarily inhibited growth of *Escherichia coli* 086. These findings suggested a new approach to the possibility of an association between blood groups and infectious disease. Of particular interest was the high group B activity in *Escherichia coli* 086, one of the *E. coli* serotypes associated with epidemic diarrhea of the newborn and the disproportionately high group A activity of the Vi antigen. Significance of the Vi antigen in immunization and protection of mice against challenge with virulent *Salmonella typhosa* is well documented (8), although its role, if any, in human infection is not clear.

Results. It seemed possible that relative susceptibility of different individuals to these and other microbial organisms and their products possessing blood group activity might be influenced by the individuals' blood group. Accordingly, a large number of bacteria, viruses, and toxoids were tested for serologic blood group activity by the hemagglutination-inhibition technic. The bacteria were cultured on meat extract agar plates containing no detectable blood group activity, suspended in saline and adjusted optically to standard density to contain about 2.4×10^9 organisms/ml. Serial dilutions in duplicate of the untreated and heat-killed suspensions of bacteria and of other materials in saline were prepared. Equal volumes of Anti-A and anti-B containing 4 units (4 times minimal quantity of Anti-A or anti-B required for agglutination of a standard suspension of appropriate erythrocytes) were added to each dilution series. Whenever inhibitory activity was found, it was greater with the heat-killed suspension. Purified Vi antigen(9) was consistently reactive for group A activity; solutions containing 6.25 μg/ml of the antigen sufficed for its detection. Slight A activity which was not consistently reproducible was obtained with several Vi-containing organisms (*S. typhosa* strain Ty2, *S. typhosa* strain ViI, *Paracolobactrum ballerup, E. coli* 5396/38) and *Shigella flexneri* 2a. Group B activity was detected only in 5 strains of *E. coli,* all of serotype 086:B7. In each of these strains, approximately 2.4×10^6 organisms sufficed for detectable group B activity. The other organisms tested included 23 serotypes of *E. coli, Salmonella paratyphosa* A, 10 different *Shigella* organisms, an Ogawa and Inaba strain of *Vibrio cholera, Staphylococcus pyogenes, Staphylococcus aureus, Corynebacterium xerose,* and 3 *Leptospira* organisms. Also tested were complement fixation antigens for typhus fever, lymphogranuloma venereum, Western equine encephalomyelitis, Eastern equine encephalomyelitis, mumps, herpes, and lymphocytic chorio-meningitis; poliomyelitis vaccine; diphtheria and tetanus toxoids. None of these organisms or materials reacted.

These findings raised 2 questions relating to antibody formation and resistance to infection with microbes possessing blood group active substances. In the first place, since animals do not respond ordinarily to their own antigenic substances, would the presence of a blood group active substance in a microbe or the microbe's products result in diminished antibody formation in infected individuals of the same blood group? The implied detrimental effect of such immunological response to one's own antigens was dramatized by Ehrlich with the expression "horror autotoxicus." The sera of 204 individuals injected with purified Vi antigen were assayed for Vi hemagglutinin(10) 14 days after injection. Although the geometric mean titer of individuals of Group A and AB was 95 and that of the others was 109, the difference was not significant. These findings may reflect the low level of blood group A activity in Vi

TABLE I. Response of a Rabbit to 4 Intravenous Injections of 1 ml of Washed 30% Human Group B Erythrocytes. Sera were absorbed with group O erythrocytes before testing for hemagglutinins to remove red cell antibodies other than anti-A or anti-B.

Serum	Hemagglutination titers		Bactericidal antibody titers	
	Anti-A	Anti-B	*E. coli* 086	*E. coli* 02
1st day—preimmunization	16	4	2.5	2.5
21st day, 12 days after last inj.—post-immunization	256	256	152.0*	2.5

* Absorption of 21st day serum with group B erythrocytes reduced bactericidal antibody titer against *E. coli* 086 to less than 2.5. Absorption of this serum with heat-killed *E. coli* 086 reduced its bactericidal titer to less than 2.5 and its anti-B titer to 4.

antigen, but are suggestive that ordinarily blood group activity in a microbe would not influence its antigenicity in the human host. Moreover, chimpanzees, which do not respond as well as man to purified Vi antigen (personal communication from Dr. G. Edsall and Major S. Gaines), are predominantly of blood group A(11), but whether this is merely a coincidental rather than a causal relationship is conjectural.

The other question was whether the reactivity of the isoantibodies against organisms possessing blood group activity would contribute to the body's defenses against these organisms. Bactericidal activity of pools of fresh normal human sera(12) against several strains of *E. coli* 086 did not reveal significant differences, however, between sera of individuals of different blood groups. On the other hand, the sera of individuals with elevated anti-B levels were considerably more reactive against *E. coli* 086 than control sera. Mean serum bactericidal antibody titer determined by quantitative photometric assay (13) of 5 mothers of group O who gave birth to group B babies and who were presumably stimulated with group B substance(14) was 6.3. In contrast, sera of 3 mothers obtained after homospecific pregnancies gave a mean titer of 2.7. In addition, in an individual injected subcutaneously with 0.2 ml of blood group specific substance B (obtained from gastric mucosa of horses, product of Knickerbocker Blood Bank, N. Y.) the bactericidal antibody titers against *E. coli* 086 rose from 2.0 to 17.9 or 9-fold; anti-B agglutinin titer rose from 32 to 16,384 or 512 fold. A slight rise in bactericidal antibody titer from 2.2 to 4.3 was noted also against an *E. coli* 02 strain which does not contain detectable blood group substance B.

To elucidate further the relationship between blood group B substance and *E. coli* 086, rabbits were injected with blood group B substance, human group B erythrocytes, heat killed *E. coli* 086, and living *E. coli* 086. The rabbit injected with blood group B substance showed no detectable anti-B hemagglutinin response although the bactericidal antibody titer of its serum against *E. coli* 086 rose slightly from less than one to 2.5. The rabbit injected with human group B erythrocytes responded much better (Table I). The simultaneous rise in anti-A has also been noted by other investigators(15), but rabbit anti-A had no enhanced bactericidal activity against *E. coli* 086. The results obtained with sera of rabbits injected with *E. coli* 086 are outlined in Table II. Antisera to 4 other species of Enterobacteriacea prepared by injections of organisms grown similarly to *E. coli* 086 showed no anti-B response, and therefore, the meat extract agar as a possible source of group B substance in *E. coli* 086 was ruled out. The relatively slight loss in bactericidal activity against *E. coli* 086 as a result of absorption of anti-B from *E. coli* 086 antisera indicated that although the B reactive grouping of *E. coli* 086 is a susceptible target for bactericidal reaction, it is relatively insignificant in the presence of an antiserum directed against the entire antigenic mosaic of the organism.

Summary. Blood group A activity was demonstrated in purified Vi antigen preparations and blood group B activity in whole cells of *Escherichia coli* 086. The immunological implications of these findings were investigated. The antigenicity of Vi antigen was essentially as great in group A or AB individuals as in those of other groups. Anti-B exerted a bactericidal effect upon *E. coli* 086, but further studies are obviously needed

TABLE II. Response of Rabbit #1 to Heat-Killed *E. coli* 086 and of Rabbit #2 to Viable *E. coli* 086. Rabbits were injected intravenously on day 1, 5, 9 and bled on day 1 and on day 21.

Sera—rabbit #1	Anti-B hemagg. titer	*E. coli* 086 agg. titer with heat-killed organisms	Bactericidal antibody titer *E. coli* 086	*E. coli* 02
1st day—pre-immunization	2	64	2.5	2.5
21st day—post-immunization	1024	1024	1960	2.5
Idem, after absorption with group B cells	2	1024	1560	2.5
Sera—rabbit #2				
1st day—pre-immunization	16	16	2.5	2.5
21st day—post-immunization	256	1024	666	2.5
Idem, after absorption with group B cells	2	1024	600	2.5

to determine the protective effect, if any, of anti-B against *E. coli* 086 or, indeed, of either isoantibody against any microbial agent which may possess blood group antigens. Nevertheless, cross-reactivity between blood group substance B and *E. coli* 086 affords a model for the possible influence of blood groups in resistance to infection against those microbial agents which may possess blood group antigens.

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Pyridoxine Deficiency in Congestive Heart Failure. (25037)

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Our previous studies have shown the occurrence of thiamine deficiency in patients with advanced congestive heart failure. The deficiency was demonstrated by the thiamine test dose(1), pyruvic acid levels in the blood (2), and determination of thiamine and cocarboxylase content in myocardial tissues of patients dying of congestive heart failure(3). In view of the fact that Vit. B_6 is a member of the Vit. B complex and is required for a great variety of enzymatic reactions, it appeared desirable to investigate Vit. B_6 metabolism in congestive heart failure.

Methods and material. The presence of Vit. B_6 complex is required for metabolic breakdown of tryptophan. In induced Vit.