whether the growth of solid tumors other than that described herein might be inhibited by immunization with leukemia virus vaccines. This question, as well as the relation between the leukemogenic and sarcomagenic effects exerted by the same virus preparation, is under study.

Summary. Offspring of mice inoculated during pregnancy with a Rauscher virus vaccine prepared from neoplastic spleen cell extracts were resistant to challenge with cells rendered myxofibrosarcomatous by transformation *in vitro* with the Rauscher virus. Offspring of mice similarly inoculated with normal spleen cell extracts showed no such resistance. The results suggest that cells transformed to a myxofibrosarcomatous pattern of growth by infection with the Rauscher leukemia virus *in vitro* share a specific antigen with spleen cell extracts rendered neoplastic by the same virus *in vivo*. The possible significance of the relationship between leukemia induction by the Rauscher virus *in vivo* and myxofibrosarcomatous transformation of cells by the same virus *in vitro* is discussed.

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E. coli Agglutinating Activity of Ulcerative Colitis Sera. (32103)

SIDNEY FINK, ROLAND F. MAIS, ROBERT F. LOCKE, AND ANNIE GLENN HALL
(Introduced by H. M. Schoolman)
Medical Service, Veterans Administration Hospital, and Department of Medicine, Loyola University Stritch School of Medicine, Hines, Ill.

It has been suggested(1) that enteric bacteria play a role in the pathogenesis of chronic ulcerative colitis (UC). It is known that strains of *E. coli* which contain capsular ("K") antigens, particularly of the "B" type, are more pathogenic than non-capsular organisms(2). Serum gamma globulins represent one aspect of the defense against Gram-negative bacteria(3); we therefore measured the antibody titer against "B" antigens in the sera of patients with UC compared with the titer in patients free of gastrointestinal disease and patients with liver disease. The slide agglutination technique was used(4).

Methods. Serum was taken from 16 ambulatory patients with well documented, chronic UC. The patients were in various stages of clinical activity, but none were in full proctoscopic remission. Eight patients were receiving salicylazosulfapyridine, and none were receiving other medication. These 16 sera were compared with sera from 17 individuals free of gastrointestinal disease, 23 patients with advanced Laennec's cirrhosis confirmed by recent liver biopsy, and commercial pooled gamma globulin adjusted to physiologic concentration. The contribution of immunoglobulin-M to the agglutinin titer was determined

TABLE I. Serum *E. coli* agglutinating activity.

	E. coli O 119:B 14			*E. coli* O 119			*E. coli* O 14		
	Control	UC	Cirrhosis	Control	UC	Cirrhosis	Control	UC	Cirrhosis
5+	3	–	6				1	–	–
4+	2	–	9	None over 2 +			–	–	–
3+	6	2	6				1	–	6
2+	2	4	2	5	2	8	3	3	8
1+	4	8	–	6	5	12	8	7	8
0	–	2	–	6	9	3	4	6	1

by comparison of sera before and after immunoglobulin-M inactivation. Two methods were used for this purpose; a modification of the heat-inactivation technique(5) by heating at 57°C for 30 minutes, and reduction with 0.2 M mercaptoethanol(6). *E. coli* antigens were prepared by washing 24-hour slant cultures with saline, diluting the organisms to a final concentration of 20,000 organisms per mm^3 as determined by Coulter counter. Precipitin-ring tests with specific rabbit antisera confirmed the potency of the antigen preparations. The pathogenic strain *E. coli* O 119:B 14, the equivalent non-pathogenic, non-capsular strain *E. coli* O 119, and *E. coli* O 14 were used. The test was performed by mixing one drop (approximately .04 ml) of antigen suspension on a glass slide with one drop of serum. The amount of agglutinating activity was estimated by direct inspection within 10 seconds. Specific hyperimmune rabbit antiserum to *E. coli* O 119:B 14 in saline dilutions of 1:2 to 1:32 was used to prepare standards, and the heavy agglutination seen with 1:2 antiserum was arbitrarily graded 5+, with decreasing values to 1+ for the agglutination with rabbit antiserum diluted 1:32. These standards were used for all slide tests performed.

It has been shown that antisera to *E. coli* O 14 are heterogenetic, but that antibodies to *E. coli* O 119 do not cross-react with *E. coli* O 14 antigen(7). Before testing patients' sera, experiments were performed mixing specific rabbit antisera to *E. coli* O 119 and O 119:B 14 with *E. coli* O 14 antigen, and the absence of cross-reactivity between these strains was confirmed. A slight (1+) reaction was observed when undiluted hyperimmune O 14 serum was mixed with the O 119 antigens.

Results. As shown in Table I, control sera agglutinated all *E. coli* strains tested and gave highest titers against the capsular strain O 119:B 14. In contrast, sera from patients with UC showed significantly lower agglutinating titers against this organism ($p<0.01$ single-sided by Wilcoxon rank sum test). An increase in titer did not occur when the low titer UC sera was retested in dilutions of 1:500. Differences due to drug therapy or the severity of the disease were not apparent. A significant difference was not found between normal and UC titers against *E. coli* O 119 and O 14. The serum from patients with cirrhosis showed significantly elevated titers against *E. coli* O 119:B 14 ($p<0.01$) and O 14 ($p<0.025$) when compared to normal values, and similar titers against *E. coli* O 119.

Thermal inactivation and mercaptoethanol reduction of normal sera caused a fall in agglutinating activity against *E. coli* O 119:B 14 from 3-5+ to 1-2+. This treatment had little or no effect on the already low *E. coli* O 119:B 14 agglutination titers of sera from patients with UC. The altered sera of both groups of patients showed an equal decrease in activity of 1 or 2+ against the other antigens. Commercial pooled gamma globulin adjusted to physiologic concentration gave agglutination titers similar to those of the thermal-inactivated sera from normal subjects with titers of 2+ against *E. coli* O 119:B 14 and 1+ against the other strains.

Discussion. Our data show that sera of patients with UC have normal agglutinin activity against several O antigens of *E. coli,* but decreased activity against one capsular antigen. Tests performed after the inactivation of IgM antibodies suggest that this decrease is wholly or in part due to a relative deficiency of these macroglobulins in the sera of patients with UC. Two complications

of UC should be considered, but do not explain this finding. Liver disease is frequent in patients with UC, but we have found an increased titer of capsular agglutinating activity in sera from patients with Laennec's cirrhosis. Protein loss into the intestinal tract occurs in UC, but our patients had normal agglutination titers against 2 of the 3 *E. coli* strains studied. This would be unusual in protein-losing enteropathy, which is not characterized by selective antibody loss (8). The observation that lymphocytes taken from patients with active UC fail to react in the presence of the K antigen of O 119:B 14 *in vitro*(9) suggests that our findings are due to decreased production of agglutinating antibodies to this antigen.

The low agglutinin titer against the capsular antigens of known pathogens such as *E. coli* O 119:B 14(10) may increase direct damage to the UC colon by these organisms. Alternatively, bacterial invasion could furnish a repeated antigenic stimulus leading to further mucosal damage by an autoimmune mechanism(11). In this context, our finding that UC and normal sera have similar agglutinating activity against *E. coli* O 14, reported to have immunologic similarity to sterile human fetal colon antigen, is of interest(12). It should be notel that we did not study specific components of *E. coli* O 14, such as the common antigen of Kunin(13).

Summary. Sera from patients with chronic ulcerative colitis have low agglutination titers against a pathogenic strain of *E. coli,* due wholly or in part to a decreased content of 19S antibodies.

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Stability of Human Immunoglobulin Levels.* (32104)

M. ALLANSMITH, B. MCCLELLAN, AND M. BUTTERWORTH
(Introduced by S. Raffel)
Department of Medical Microbiology, Stanford School of Medicine, and Department of Statistics, Stanford University, Stanford, Calif.

Immunoglobulin levels vary widely among individuals, but the variation within the individual has not been studied. This information would be useful in understanding immunoglobulin metabolism and in evaluation of patients on whom repeated levels have been obtained. This study reports the amount of variation observed in the immunoglobulin levels of 15 healthy subjects who were bled weekly for 6 months. The results show that levels in the average individual vary within ± 17% (2 standard deviations) of their estimated mean and are, therefore, quite stable.

Materials and methods. Subjects. Seven men and 8 women between the ages of 20 and 35 were bled once a week from a finger stick for 25 consecutive weeks. At the time of bleeding each reported on his general health, time of last meal, any medication

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