INFECTION AND IMMUNITY, Mar. 1985, p. 659–664
0019-9567/85/030659-06$02.00/0

Vol. 47, No. 3

Depressing Hepatic Macrophage Complement Receptor Function Causes Increased Susceptibility to Endotoxemia and Infection

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Received 12 September 1984/Accepted 3 December 1984

Previous work has demonstrated that in vivo hepatic macrophage complement receptor clearance function is depressed after thermal injury. To determine whether impairment of complement receptor function is important in host defense, the present study evaluated the effect of the depression of complement receptor function in uninjured animals on susceptibility to endotoxin shock and bacterial infection. Hepatic complement receptor clearance function was evaluated by measuring the hepatic uptake of a test dose (2.9×10^8/100 g) of rat erythrocytes coated with anti-erythrocyte immunoglobulin M (EIgM) or EIgG in rats. Depression of hepatic complement receptor function was induced by the injection of EIgG. The hepatic uptake of the test dose of EIgM or EIgG was depressed after the injection of 8.7×10^8 EIgG per 100 g and 17.4×10^8 EIgG per 100 g but not after the injection of 2.9×10^8 EIgG per 100 g. This effect was shown not to be due to a decrease in hepatic blood flow or a depletion of serum C3 and was, therefore, due to a depression in hepatic macrophage complement receptor clearance function. Susceptibility to endotoxin shock was increased with the dose of 8.7×10^8 EIgG per 100 g, and susceptibility to infection with *Pseudomonas aeruginosa* was increased with the dose of 17.4×10^8 EIgG per 100 g. Therefore, depression of hepatic macrophage complement receptor clearance function with EIgG is associated with depressed host defense.

Hepatic macrophages have complement receptors on their surface. The function of these receptors is considered to be the clearance of complement-coated bacteria and yeasts as well as large immune complexes from the blood (19). A recent study from this laboratory has demonstrated that there is a depression of hepatic macrophage complement receptor clearance function after experimental thermal injury (5). Since thermal injury is associated with an increase in susceptibility to infection (1, 17), it was speculated that a depression in complement receptor function may contribute to the impairment of host defense.

The present study used erythrocytes coated with anti-erythrocyte immunoglobulin M (EIgM) and EIgG to determine hepatic macrophage complement receptor clearance function. Complement receptor function was depressed in uninjured animals by the injection of EIgG. The effect of the depression of complement receptor clearance function in this manner on the mortality rate after the injection of endotoxin or *Pseudomonas aeruginosa* was determined.

MATERIALS AND METHODS

Preparation of EIgM and EIgG. Inbred, male, Sprague-Dawley rats (weight, 200 to 250 g) were used for all experiments. Blood was collected in acid citrate-glucose solution, and the erythrocytes were washed three times in phosphate-buffered saline (PBS) (0.9% NaCl and 5 mM phosphate buffer [pH 7.4]). Erythrocytes were treated with IgM or IgG fractions of rabbit anti-rat erythrocyte antisera. Antisera were obtained from U.S. Biochemical Corp. or from immunized New Zealand white rabbits. These rabbits had received six injections of 2.5×10^{10} erythrocytes (half of each injection was given intraperitoneally and half was given intravenously [i.v.]) over 2 weeks.

Antisera were collected 5 days after the last injection, and the 40% ammonium sulfate precipitate was separated into IgM and IgG fractions by gel filtration (Sephacryl 400) chromatography. Fractionation was verified by immunodiffusion against appropriate antibodies, and the small amount of IgG present in the IgM fraction was removed with protein A. For treatment with IgM or IgG, packed erythrocytes were diluted to a concentration of 2×10^9/ml in PBS containing 1% gelatin. The antibody was diluted in a volume of PBS-gelatin equal to the volume of the erythrocyte suspension and added over 3 min to the erythrocytes with constant stirring. The mixture was incubated at 37°C for 30 min, and the EIgM or EIgG were washed twice in PBS. The concentration of antibody used for treatment was adjusted to obtain a 65 to 80% hepatic localization of the dose of 2.9×10^8 EIgM or EIgC per 100 g at 10 min after injection. All antibody-treated erythrocytes were used on the day of preparation.

Clearance of EIgM and EIgG from the blood. EIgM and EIgG used for clearance studies were labeled with ^{51}Cr before treatment with antibodies. Animals were anesthetized with ether or sodium pentobarbital (30 mg/kg i.v.) before giving injections and taking blood samples. Erythrocytes, EIgM, or EIgG were injected i.v. at a dose of 2.9×10^8/100 g. Blood radioactivity was monitored over 2 h, and localization in the liver and spleen was determined at 10, 30, and 120 min after injection. Organ localization data were not corrected for the blood present in the organs, and blood volume was assumed to be 6% body weight. To verify the complement dependence of the clearance of EIgM and EIgG, cobra venom factor (CVF) was injected intraperitoneally (20 U/100 g) 18 h before the clearance determination.

Determination of hepatic complement receptor clearance function. The clearance function of hepatic macrophage complement receptors was determined on the basis of the hepatic uptake of the test dose of EIgM and EIgG. The test dose of EIgM and EIgG was 2.9×10^8/100 g. Hepatic uptake of the test dose of EIgM and EIgG was determined at 10 and 30 min after injection, respectively.

Effect of EIgG on hepatic complement receptor clearance function. EIgG were injected as a means of depressing

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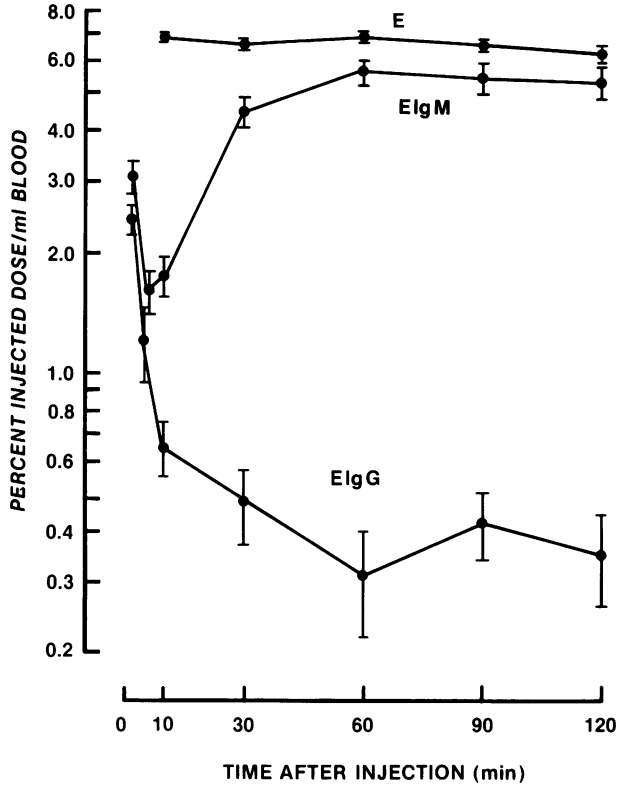

FIG. 1. Blood levels of rat erythrocytes (E), EIgM, and EIgG from 2 to 120 min after injection into rats. Erythrocytes were labeled with ^{51}Cr and injected at a dose of 2.9×10^8/100 g. Data are expressed as the percentage of the ID per milliliter of blood. Values are the mean ± standard error with six animals per group.

hepatic complement receptor clearance function. Initial studies were carried out to characterize the blood levels and organ localization of different doses of EIgG. EIgG labeled with ^{51}Cr were injected at doses of 5, 15, 30, or 45 mg of hemoglobin per 100 g, which on the basis of a mean corpuscular hemoglobin of 1.72×10^{-8} mg per cell gave 2.9×10^8, 8.7×10^8, 17.4×10^8, and 26.2×10^8 erythrocytes per 100 g. Hemoglobin measurements were carried out by the cyanomethemoglobin method. Unlabeled EIgG were injected 30 min before the determination of complement receptor clearance function. As a control, erythrocytes not coated with IgG were injected (17.4×10^8 erythrocytes per 100 g) before the determination of complement receptor clearance function.

Determination of hepatic blood flow. Since the liver is the principal organ for the clearance of EIgM and EIgG, a sufficient decrease in hepatic blood flow could decrease the clearance of these test particles (18). Hepatic blood flow was measured by the fractional clearance technique (7). Gelatinized lipid emulsion was used as the test particle and was injected at a dose of 5.0 mg/100 g. At this dose, the rate-limiting factor in the clearance of this test particle is hepatic blood flow and not hepatic phagocytic function (20). Blood samples were taken every 30 s for 3 min from a cannulated carotid artery in anesthetized animals. The clearance rate constant, which is the proportion of the blood volume cleared of the test particle per minute, was multiplied by the blood volume to give the hepatic blood flow. Blood volume was estimated by extrapolating the clearance line to zero time and assuming uniform distribution of the test particle throughout the vascular compartment.

Hepatic blood flow was decreased in normal animals by acute hemorrhage. Mean arterial blood pressure was reduced to 35 mmHg (ca. 4665.5 Pa) over 2 to 3 min by withdrawing 1 ml of blood every 30 s. Hepatic blood flow or the clearance of the test dose of EIgM or EIgG was determined beginning 5 min after the start of blood withdrawal. Blood pressure was monitored during the clearance of EIgM and EIgG, and additional blood was removed or saline was injected to maintain the blood pressure at 35 to 40 mmHg (ca. 4666.5 to 5332.0 Pa). Hepatic blood flow was also measured after injection of the larger doses of EIgG.

Determination of serum C3 levels. Since the rapid clearance of both EIgM and EIgG was shown to be dependent upon adequate levels of C3, a sufficient depression of C3 could cause a depression in the clearance rate of these test particles. Serum C3 levels were determined by the radial immunodiffusion method, using rabbit anti-rat C3 IgG (U.S. Biochemical Corp.) (16). Purified CVF was used to determine the extent to which C3 levels had to be depressed before the clearance of EIgM and EIgG was depressed. CVF was injected intraperitoneally at doses of 20 U/100 g or 1 U/100 g 18 h before the clearance measurements. C3 levels were also determined after the injection of each dose of EIgG.

Endotoxin shock. Endotoxin (*Salmonella enteritidis*, lipopolysaccharide B; Difco Laboratories) was injected i.v. at a dose of 0.4 mg/100 g 30 min after the injection of EIgG. None of the animals died before 6 h, and the mortality rate was recorded at 24 h after the injection of endotoxin.

Bacterial infection. The injection of *P. aeruginosa* (PA1348A) was used to induce bacterial infection. The bacteria were grown on nutrient agar plates for 18 h, washed twice in PBS, and enumerated by optical density against pour plate standards. The bacteria were injected i.v. at a dose of 10^9 per animal, and the mortality rate was recorded 48 h later. This strain of *P. aeruginosa* is resistant to killing by serum when grown on nutrient agar (6).

Statistics. Data were expressed as the mean ± standard error. Two group comparisons were analyzed by Student's *t* test, and multiple group comparisons were analyzed by the one-factor analysis of variance. Survival data were analyzed by the Fisher exact test. The level of confidence was placed at 95% for all experiments.

RESULTS

Hepatic complement receptor clearance function was assessed from the hepatic uptake of a test dose (2.9×10^8/100 g) of labeled EIgM or EIgG. Both EIgM and EIgG were removed rapidly from the blood over the first 5 to 10 min after injection (Fig. 1). Blood levels of EIgM subsequently increased, whereas the blood levels of EIgG remained low. Hepatic localization of EIgM and EIgG reflected the blood levels over this time period with hepatic localization of EIgM rising and then falling, whereas hepatic localization of EIgG remained high (Fig. 2). Splenic localization of EIgM was ca. 2% of the injected dose (ID) at 10 min after injection and then increased to 5% ID at 30 and 120 min after injection. EIgG splenic localization was 8 to 10% ID for each observation time. Lung localization of EIgM and EIgG was always less than 3% ID. On this basis, the organ localization of EIgM was determined at 10 min after injection and that of EIgG at 30 min after injection for all subsequent studies. Lable recovery was 90 to 110% for all experiments, and no

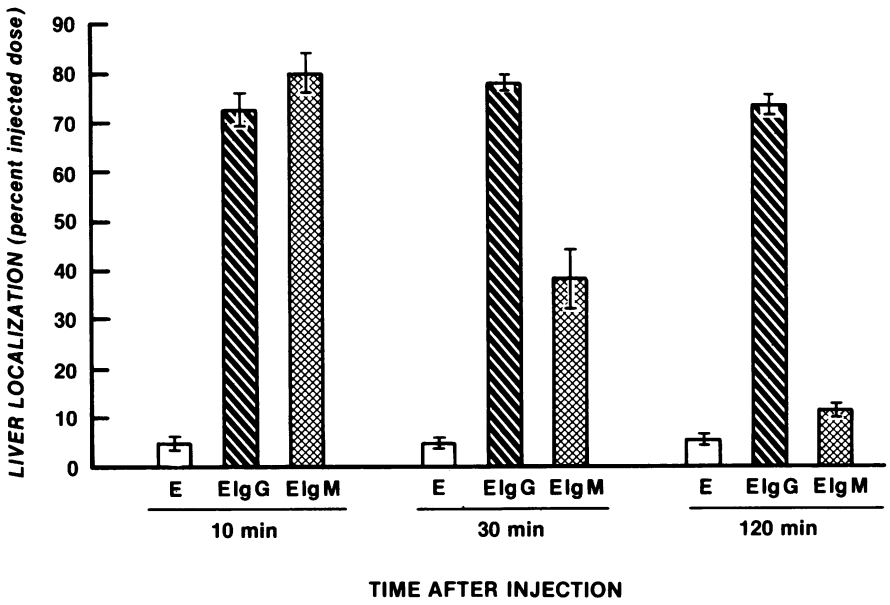

FIG. 2. Hepatic localization of erythrocytes (E), EIgM, and EIgG at 10, 30, and 120 min after injection. Erythrocytes were injected at a dose of 2.9×10^8/100 g. Data are expressed as the percentage of the ID present in the liver. Values are the mean ± standard error with six animals per group.

more than 3% of the injected radioactivity was present in the plasma, indicating that there was very little lysis of the erythrocytes.

Injection of purified CVF (20 U/100 g) reduced the hepatic localization of the test dose of EIgM to 8% of control and that of EIgG to 37% of control. Since this dose of CVF decreased C3 levels to 9% of control, the rapid hepatic uptake of these test particles was dependent on an intact complement system.

Before the studies on the effect of injecting EIgG on hepatic complement receptor clearance function, the clearance characteristics of different doses of EIgG were determined. Blood levels of EIgG tended to decrease more slowly as the dose was increased (Fig. 3). The number of EIgG in the liver and spleen at 30 min after injection increased as the dose was increased (Table 1). The hepatic localization of erythrocytes increased as the dose was increased, and this represented a constant 3 to 4% of the ID.

Hepatic complement receptor clearance function was determined beginning 30 min after the injection of unlabeled EIgG at a dose of (per 100 g) 2.9×10^8, 8.7×10^8, or 17.4×10^8. The smallest dose of EIgG had no effect, whereas the two larger doses depressed the hepatic uptake of the test dose of EIgM and EIgG (Fig. 4). Splenic localization was unchanged, and pulmonary localization did not increase above 1% ID. The blood levels of the test dose of EIgM and EIgG were increased in proportion to the decrease in hepatic uptake. Injection of erythrocytes not coated with IgG at a dose of 17.4×10^8/100 g had no effect on the hepatic uptake of the test dose of EIgM or EIgG.

Reduction of arterial blood pressure to 35 mmHg by acute hemorrhage decreased hepatic blood flow to 38.3% of the control value. Animals hemorrhaged to a similar degree did not show a depression in the hepatic uptake of the test dose of EIgM or EIgG. For EIgM, the hepatic localization in nonhemorrhaged animals was 64.7 ± 3.7% ID, and in hemorrhaged animals it was 66.8 ± 4.0% ID. For EIgG, the respective values were 73.4 ± 1.0 and 76.3 ± 3.0% ID. Therefore, a depression of hepatic blood flow greater than that caused by acute hemorrhage is required to cause a depression in the clearance of the test doses of EIgM and EIgG. At 30 min after injection of 17.4×10^8 EIgG per 100 g, hepatic blood flow was decreased to 70% of control. These data indicate that the depression in the hepatic uptake of test doses of EIgM and EIgG after the injection of EIgG was not due to a decrease in hepatic blood flow.

As indicated above, the dose of 20 U of CVF per 100 g caused a substantial depression in the hepatic uptake of the test dose of both EIgM and EIgG. This dose of CVF did not depress hepatic blood flow. Injection of 1 U of CVF per 100 decreased serum C3 levels to 57.6% of control but did not depress the hepatic uptake of the test dose of EIgM or EIgG. Therefore, a greater depression of C3 than that caused by the 1 U of CVF per 100 g is required to cause a depression in the hepatic uptake of the test particles. Serum C3 levels at 30 min after the injection of 2.9×10^8/100 g, 8.7×10^8/100 g, and 17.4×10^8/100 g were 99.2 ± 3.92%, 96.4 ± 3.22%, and 89.0 ± 3.30% ($P < 0.05$) of control, respectively. Therefore, the depression of hepatic uptake of the test doses of EIgM and EIgG caused by EIgG was not due to a depression of serum C3 levels.

Susceptibility to endotoxin shock was increased after the injection of EIgG (Table 2). The dose of 8.7×10^8 EIgG per 100 g and all of the larger doses caused a decrease in the survival rate after the injection of endotoxin. Therefore, the doses of EIgG that depressed hepatic complement receptor clearance function caused an increase in susceptibility to endotoxin shock. Survival rate was not affected by the injection of erythrocytes not coated with IgG, indicating that any contamination of the erythrocyte preparation with pyrogens or bacteria was not responsible for the observed results.

Susceptibility to infection with *P. aeruginosa* was also increased after the injection of EIgG (Table 3). However, a larger dose of EIgG (17.4×10^8/100 g) was required to cause a decrease in survival rate with bacterial infection than was required to depress complement receptor clearance function and increased susceptibility to endotoxin shock. Suscepti-

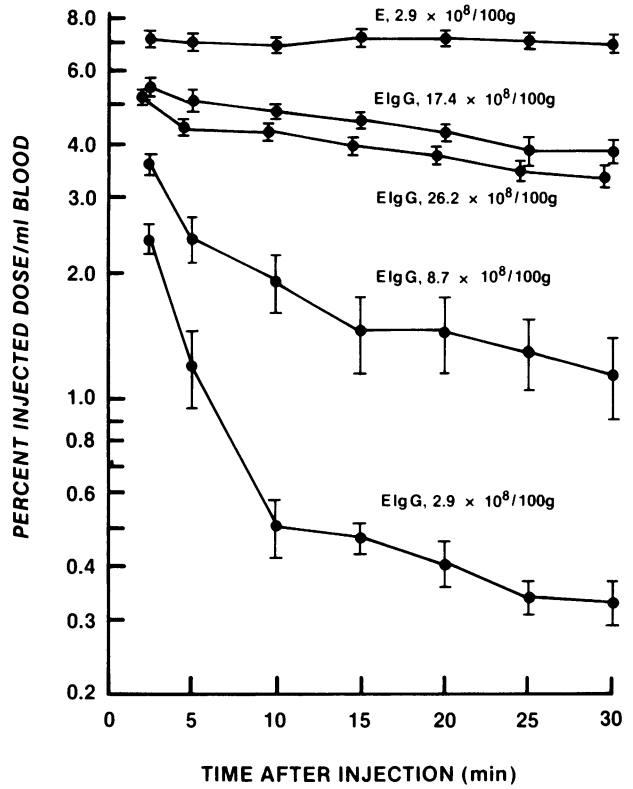

FIG. 3. Blood levels of different doses of EIgG from 2 to 30 min after injection. The dose of 2.9 × 10^8 erythrocytes (E) per 100 g is included for comparison. Data are expressed as the percentage of the ID per milliliter of blood. Values are the mean ± standard error with six animals per group.

bility to infection was not affected by the injection of erythrocytes not coated with IgG.

DISCUSSION

The overall pattern of the clearance and organ localization of EIgM and EIgG was similar to that previously observed in guinea pigs and in humans (9). The EIgM and EIgG were rapidly removed from the blood by the liver over the first 5 to 10 min after injection. Depletion of C3 with CVF caused a large decrease in the hepatic uptake of both EIgM and EIgG, indicating that the hepatic clearance was complement dependent. The clearance was probably due to interaction of the test particles with complement, followed by binding to complement receptors on the hepatic macrophages. After the rapid clearance phase, EIgM were released from the liver and reappeared in the blood. This temporary binding of EIgM to the hepatic macrophages did not affect subsequent complement receptor function. The hepatic uptake of the test dose of EIgM was depressed at 10 min but not at 1 h after the injection of 17.4 × 10^8 EIgM per 100 g (unpublished data). The release of EIgM back into the blood was probably due to the action of C3b inactivator (2). The rate of return of the EIgM to the blood in the present study was somewhat faster than that previously observed in guinea pigs or in humans (9). In contrast, the EIgG that were taken up by the liver remained in the liver, presumably due to the interaction of the IgG with the Fc receptors and subsequent phagocytosis of the erythrocytes (9). On this basis, the rapid hepatic clearance of EIgM and EIgG was taken as an indication of the clearance function of hepatic macrophage complement receptors. The methods employed did not allow the determination of which complement component or subcomponent mediated the clearance, although it is most likely that C3b binding to the CR_1 receptor was primarily responsible (9, 19). The lack of lysis of the EIgM or EIgG

TABLE 1. Liver and spleen localization of different doses of erythrocytes and EIgG at 30 min after injection[a]

Dose (per 100 g)	No. (× 10^8) present in:	
	Liver	Spleen
2.9 × 10^8/100 g		
E	0.29 ± 0.02	0.15 ± 0.02
EIgG	5.26 ± 0.21	0.70 ± 0.03
8.7 × 10^8/100 g		
E	1.03 ± 0.03	0.47 ± 0.01
EIgG	9.40 ± 0.36	3.44 ± 0.32
17.4 × 10^8/100 g		
E	1.64 ± 0.12	0.97 ± 0.13
EIgG	13.22 ± 0.87	6.58 ± 0.55
26.2 × 10^8/100 g		
E	2.51 ± 0.09	1.67 ± 0.11
EIgG	21.67 ± 1.14	9.76 ± 0.67

[a] Erythrocytes (E) or EIgG were injected at the indicated doses. Values are the mean ± standard error with six animals per group.

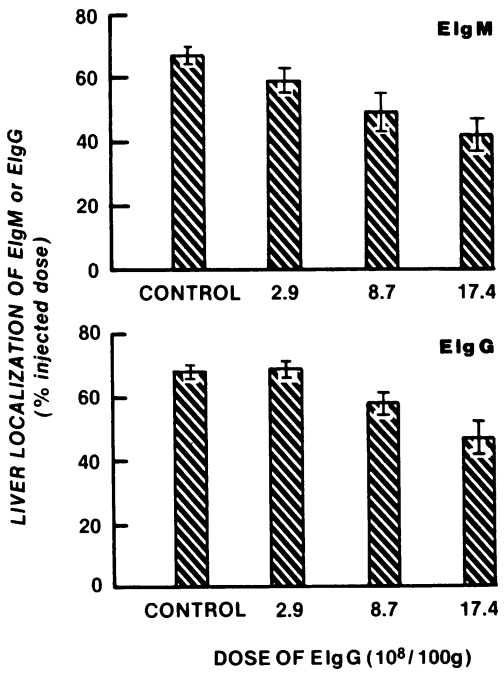

FIG. 4. Effect of different doses of EIgG on hepatic complement receptor clearance function as determined from the hepatic uptake EIgM and EIgG. Unlabeled EIgG were injected at doses of (per 100 g) 2.9 × 10^8, 8.7 × 10^8, and 17.4 × 10^8 30 min before the injection of the test doses of labeled EIgM and EIgG. The test doses of EIgM and EIgG were 2.9 × 10^8/100 g. Hepatic localization of EIgM and EIgG were determined 10 and 30 min after injection, respectively. Values are the mean ± standard error with six animals per group. There was a significant ($P < 0.05$) depression in hepatic localization of both EIgM and EIgG with the doses of 8.7 × 10^8 EIgG per 100 g and 17.4 × 10^8 EIgG per 100 g.

was probably due to the low lytic activity of complement for homologous erythrocytes (13).

As the dose of EIgG was increased, there was a decrease in the rate of removal from the blood but an increase in the number of EIgG taken up by the liver. This is characteristic of other particulates that are removed from the blood by the liver, such as colloidal carbon, gelatinized lipid emulsion, and Formalinized sheep erythrocytes (3, 4, 21). The hepatic uptake of the test dose of EIgM and EIgG was depressed after the injection of 8.7×10^8 EIgG/100 g and 17.4×10^8 EIgG/100 g. Lowering hepatic blood flow by acute hemorrhage and depression of complement with CVF to levels lower than those caused by the injection of EIgG did not depress the hepatic uptake of the test dose of EIgM or EIgG. Therefore, it is concluded that the depression in hepatic uptake of the test doses of EIgM and EIgG was at the level of binding to the hepatic macrophages and represents a depression in hepatic macrophage complement receptor clearance function. A similar approach was used previously to demonstrate that complement receptor function was depressed after experimental thermal injury (5).

Depression of complement receptor function with EIgG was associated with an increase in susceptibility to endotoxin shock and bacterial infection. A larger dose of EIgG was required to cause a decrease in survival rate after the injection of bacteria than after the injection of endotoxin. With regard to the number of EIgG taken up by the liver (Table 1), 9.4×10^8 were required to depress complement receptor function and increase susceptibility to endotoxin, whereas 13.2×10^8 were required to increase susceptibility to infection. Thus, there was a close relationship between the effect of EIgG on hepatic macrophage complement receptor function and on host defense. However, slightly different mechanisms may be responsible for the increased susceptibility to endotoxin than the mechanisms mediating susceptibility to infection.

In a previous study, we demonstrated that thermal injury in rats was associated with the hepatic uptake of 1.71% of the unlysed erythrocyte mass (10). This represents a hepatic uptake of 15×10^8 erythrocytes, which is more than the number of EIgG required to depress receptor function and increase susceptibility to endotoxin shock and bacterial infection (Table 1). Therefore, it may be concluded that the hemolysis associated with thermal injury is sufficient to depress hepatic macrophage receptor function and host defense.

The mechanism of the increased susceptibility to endotoxin shock and bacterial injection remains to be determined. The depression of complement receptor clearance function suggests the possibility of depressed clearance of the bacteria. Erythrocyte stroma, which has been shown to depress complement receptor clearance function, depresses the hepatic uptake of pneumococcus (5, 11). Additionally, erythrocyte stroma depresses the hepatic killing of pneumococcus (11). Hand and King-Thompson (12) have shown that the in vitro phagocytosis of erythrocytes depresses superoxide generation and chemiluminescence by macrophages. Therefore, it is possible that both bacterial clearance and killing function of the hepatic macrophages were depressed by the EIgG. Our previous studies have shown that sequestration of erythrocytes by the spleen can depress host defense (10, 22). It was shown that splenic uptake of ca. 20×10^8 heat-damaged or phenylhydrazine-treated erythrocytes was required to increase susceptibility to endotoxin shock or septic peritonitis. In the present study, splenic uptake of EIgG was less than half this number (Table 1). Therefore, splenic uptake of EIgG could have contributed to the depression of host defense caused by EIgG but could not, by itself, account for this finding. The increased susceptibility to endotoxin shock caused by EIgG was not due to a depletion of complement, because it has been shown that depletion of more than 90% of complement activity with CVF does not affect the susceptibility of rats to endotoxin shock (15).

Whatever the mechanism of the depressed host defense caused by EIgG, this study suggests that monitoring complement receptor clearance function may provide information on host defense status. This is a realistic proposal because antibody-coated erythrocytes have been used in patients to evaluate macrophage receptor function (8, 14). IgM-coated erythrocytes may be the best test particle for this purpose, because fewer of these erythrocytes are phagocytized than erythrocytes coated with IgG (9).

TABLE 2. Effect of EIgG on the survival rate after endotoxin shock[a]

Dose (per 100 g)	% Survival	n
Control	92.5	40
43.6×10^8 E	90.0	20
2.9×10^8 EIgG	70.0	20
8.7×10^8 EIgG	53.5[b]	40
17.4×10^8 EIgG	60.0[b]	20
26.2×10^8 EIgG	30.0[b]	40
43.6×10^8 EIgG	10.0[b]	10

[a] Endotoxin (*S. enteritidis*) was injected i.v. at a dose of 0.4 mg/100 g into controls and 30 min after the injection of erythrocytes (E) or EIgG. Survival was recorded at 24 h.
[b] $P < 0.05$.

TABLE 3. Effect of EIgG on the survival rate after bacterial infection[a]

Dose (per 100 g)	% Survival	n
Control	90	20
17.4×10^8 E	100	20
2.9×10^8 EIgG	100	22
8.7×10^8 EIgG	82	20
17.4×10^8 EIgG	20[b]	20
26.2×10^8 EIgG	20[b]	10

[a] *P. aeruginosa* was injected i.v. at a dose of 10^9 into controls and 30 min after the injection of erythrocytes (E) or EIgG. Survival was recorded at 48 h.
[b] $P < 0.05$.

ACKNOWLEDGMENTS

This work was supported by Public Health Service grant GM-26102 from the National Institute of General Medical Sciences.

We thank A. L. Baltch (Veterans Administration Medical Center, Albany, N.Y.) for generously supplying the *P. aeruginosa* (PA 1348A) culture. The excellent technical assistance of Lisa Gary and Carol Fryc and the secretarial assistance of Maureen Davis are also acknowledged.

LITERATURE CITED

1. **Alexander, J. W.** 1968. Effect of thermal injury upon the early resistance to infection. J. Surg. Res. **8**:128–137.
2. **Atkinson, J. P., and M. M. Frank.** 1974. Studies on the *in vivo* effects of antibody. Interaction of IgM antibody and complement in the immune clearance and destruction of erythrocytes in man. J. Clin. Invest. **54**:339–348.
3. **Biozzi, G., B. Benacerraf, and B. N. Halpern.** 1953. Quantitative study of the granulopectic activity of the reticuloendothelial

system. II. A study of the kinetics of the granulopectic activity of the RES in relation to the dose of carbon injected. Relationship between the weight of the organs and their activity. Br. J. Exp. Pathol. **34**:441–457.
4. **Cornell, R. P., and T. M. Saba.** 1971. Vascular clearance and metabolism of lipid by the reticuloendothelial system in dogs. Am. J. Physiol. **221**:1511–1516.
5. **Cuddy, B. G., D. J. Loegering, and F. A. Blumenstock.** 1984. Depression of *in vivo* clearance function of hepatic macrophage complement receptors following thermal injury. Proc. Soc. Exp. Biol. Med. **176**:443–451.
6. **DeMatteo, C. S., M. C. Hammer, A. L. Baltch, R. P. Smith, N. T. Sutphen, and P. B. Michelsen.** 1981. Susceptibility of *Pseudomonas aeruginosa* to serum bactericidal activity. J. Lab. Clin. Med. **98**:511–518.
7. **Dobson, E. L., and H. B. Jones.** 1952. The behavior of intravenously injected particulate material. Acta Med. Scand. **144**(Suppl. 273):1–71.
8. **Frank, M. M., T. J. Lawley, M. I. Hamburger, and E. J. Brown.** 1983. Immunoglobulin G Fc receptor-mediated clearance in autoimmune diseases. Ann. Intern. Med. **98**:206–218.
9. **Frank, M. M., A. D. Schreiber, J. P. Atkinson, and C. J. Jaffe.** 1977. Pathophysiology of immune hemolytic anemia. Ann. Intern. Med. **87**:210–222.
10. **Grover, G. J., and D. J. Loegering.** 1982. Effect of splenic sequestration of erythrocytes on splenic clearance function and susceptibility to septic peritonitis. Infect. Immun. **36**:96–102.
11. **Grover, G. J., and D. J. Loegering.** 1984. Effect of red blood cell stroma on the reticuloendothelial system clearance and killing of Streptococcus pneumoniae. Circ. Shock **14**:39–47.
12. **Hand, W. L., and N. L. King-Thompson.** 1983. Effect of erythrocyte ingestion on macrophage antibacterial function. Infect. Immun. **40**:917–923.
13. **Hansch, G. M., C. H. Hammer, P. Vanguri, and M. L. Shin.** 1981. Homologous species restriction in lysis of erythrocytes by terminal complement proteins. Proc. Natl. Acad. Sci. U.S.A. **78**:5118–5121.
14. **Jones, E. A., M. M. Frank, C. J. Jaffe, and J. M. Vierling.** 1979. Primary biliary cirrhosis and the complement system. Ann. Intern. Med. **90**:72–84.
15. **Loegering, D. J.** 1983. RES uptake of red blood cell stroma: time course of effects on phagocytic function and susceptibility to endotoxin shock. Circ. Shock **11**:319–327.
16. **Mancini, G., A. O. Carbonara, and J. F. Heremans.** 1965. Immunochemical quantification of antigens by single radial immunodiffusion. Immunochemistry **2**:235–256.
17. **McRipley, R. J., and D. W. Garrison.** 1964. Increased susceptibility of burned rats to *Pseudomonas aeruginosa*. Proc. Soc. Exp. Biol. Med. **115**:336–338.
18. **Normann, S. J.** 1972. Reticuloendothelial system function. V. Studies on the correlation between phagocytic rate and liver blood flow. J. Reticuloendothel. Soc. **12**:473–484.
19. **Ross, D. G.** 1982. Structure and function of membrane complement receptors. Fed. Proc. **41**:3089–3093.
20. **Saba, T. M., and N. R. Di Luzio.** 1969. Surgical stress and reticuloendothelial function. Surgery **65**:802–807.
21. **Schneidkraut, M. J., and D. J. Loegering.** 1981. Fixed sheep red blood cells as an *in vivo* reticuloendothelial system test particle in rats. J. Reticuloendothel. Soc. **30**:73–77.
22. **Schneidkraut, M. J., and D. J. Loegering.** 1984. Effect of intravascular hemolysis on the RES depression following thermal injury. Exp. Mol. Pathol. **40**:271–279.