The Binding of Human Immunoglobulin G1 Monomer and Small, Covalently Cross-Linked Polymers of Immunoglobulin G1 to Human Peripheral Blood Monocytes and Polymorphonuclear Leukocytes

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ABSTRACT Covalently cross-linked dimers and oligomers composed of 2–4 subunits of monoclonal human IgG1 were prepared by incubation of purified monomeric IgG1 with glutaraldehyde followed by gel-filtration chromatography. Monomers, dimers, and oligomers then were labeled with ^{125}I and used to compare the binding properties of IgG Fc receptors on human peripheral blood monocytes and polymorphonuclear leukocytes (PMN). Binding of IgG1 to monocytes at 37°C and of IgG1 polymers to PMN at 4°C could be readily measured and were found to be reversible and saturable. Scatchard plots of binding were linear in each instance. Monocytes bound a mean of 20,200±6,800 molecules/cell of IgG1 monomer at saturation and comparable amounts of dimer or oligomer. The mean association constant (*K*a) for binding of IgG1 monomer to monocytes was $8.6 \times 10^8 M^{-1}$ and the *K*a for binding of dimer and oligomer were three- to fivefold greater.

In contrast, PMN bound a mean of 460,000±130,000 molecules of IgG1 dimer at saturation and comparable amounts of oligomer. The *K*a of binding in both cases was 100–1,000-fold lower than the *K*a for binding of the same preparations to monocytes.

Binding of labeled IgG1 to both cell types was more potently inhibited by unlabeled IgG1 and IgG3 than by IgG4 or IgG2. Binding of labeled polymers of IgG1 to monocytes was 10–100-fold more easily inhibited by monomeric IgG1 than was binding to PMN. Thus, there are significant quantitative and qualitative differences between the binding properties of Fc receptors present on monocytes and PMN.

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INTRODUCTION

Human polymorphonuclear leukocytes (PMN)[1] and monocytes possess Fc receptors on their membranes that bind the Fc portion of IgG and may, as a consequence, initiate the adherence and destruction of IgG-coated target cells (1–3). This IgG-dependent, leukocyte-mediated destruction may be important in host defense against infectious organisms (4), in the destruction of autologous cells in immune hemolytic anemia (5), or immune thrombocytopenia (6), and perhaps in other immunologic disorders.

Despite qualitative similarities in Fc receptor function, prior studies have indicated that monocytes are much more effective in binding and destroying target cells coated with small amounts of IgG than PMN (1, 7, 8), but that destruction mediated by PMN is much less readily inhibited by unbound IgG than that mediated by monocytes (8, 9). In the following studies, comparing the binding of monoclonal human IgG1 to PMN and monocytes, marked differences in the number of Fc receptors per cell and in the avidity with which these receptors bind IgG are noted and it is suggested that these differences in the binding properties of the Fc receptors may be responsible for the

[1] *Abbreviations used in this paper*: B_{max}, maximal binding capacity; BSA, bovine serum albumin; K_a, association constant; PBS, phosphate-buffered saline; PMN, polymorphonuclear leukocyte(s); SDS-PAGE, SDS-polyacrylamide gel electrophoresis.

differing capacities of these cells for interaction with target cells coated with IgG antibody.

METHODS

Phosphate-buffered saline (PBS), RPMI 1640 medium, and fetal calf serum were purchased from Gibco Laboratories (Grand Island Biological Co., Grand Island, N. Y.). Dextran (200,000 mol wt), glutaraldehyde (25%), bovine serum albumin (BSA), papain (two times crystallized in 0.05 sodium acetate) and fluorescein isothiocyanate isomer I (10% on celite) were purchased from Sigma Chemical Co. (St. Louis, Mo.). $Na^{125}I$ (17 Ci/mg) was purchased from New England Nuclear (Boston, Mass.). Sodium heparin was obtained from Upjohn Co. (Kalamazoo, Mich.). Ficoll-Hypaque was obtained from Pharmacia Fine Chemicals, Div. of Pharmacia Inc. (Piscataway, N. J.). The reagents used to stain cells containing esterase were obtained from Technicon Instruments Corp. (Tarrytown, N. Y.).

Preparation of IgG1. Monoclonal IgG1 kappa was purified from the serum of a patient with multiple myeloma that contained >10 mg 100 ml of monoclonal IgG1-kappa, by precipitation with 50% ammonium sulfate, and DEAE cellulose ion-exchange chromatography (10). The purified IgG1 was dialyzed against PBS with 0.1% sodium azide (PBS-Na_3N) and stored at 4°C. Before use in studies requiring IgG1 monomer, this preparation either was passed through a column of Sepharose 4B or spun at 100,000 *g* for 30 min to eliminate aggregates of IgG1, which might have formed during storage.

To prepare covalently linked polymers, purified IgG1 (0.3 mM) in PBS-Na_3N was incubated for 18 h at 4°C with two times molar equivalent of glutaraldehyde, a bifunctional cross-linking agent (11). Covalently linked dimers and oligomers of IgG1 were purified from the resultant mixture of IgG1 polymers by passage through a set of columns (100 × 1.5 cm) containing Sephadex G-200 (Pharmacia Fine Chemicals.), and Ultrogel AcA22 (LKB, Rockville, Md.) using the method of Segal and Hurwitz (12, 13). In addition, polymers that eluted through these columns faster than oligomer, (designated "IgG1 aggregates") were also pooled and concentrated.

Purified human monoclonal IgG proteins of subclasses IgG1, IgG2, IgG3, and IgG4 were kindly provided by Dr. W. Yount of North Carolina Memorial Hospital, Chapel Hill, N. C. These samples were spun at 100,000 *g* for 30 min to remove IgG aggregates just before use in inhibition assays.

IgG concentrations were calculated assuming an extinction coefficient ($E^{1\%}_{1cm}$) of IgG1 of 14.3 (14). To facilitate the comparison of data obtained using preparations of covalently linked polymers, IgG1 molarities were calculated after the method of Segal and Hurwitz (12), assuming a molecular mass of IgG1 of 160,000 daltons, regardless of the degree of polymerization of the IgG1 preparation being studied.

Fc and Fab fragments were prepared from monomeric IgG1 using papain and cysteine by published methods (15). The concentration of Fc and Fab fragments was determined using standard methods (16), assuming a molecular mass of 55,000 daltons for Fc and Fab fragments.

The composition of polymer preparations was assessed by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) using unreduced 3.5% acrylamide gels and Coomassie Blue to stain proteins (17). The relative concentration of each polymer was estimated using a Beckman model CDC-200 densitomer (Beckman Instruments Inc., Science Essentials Co., Mountainside, N. J.).

In some studies, the electrophoretic mobility of radiolabeled IgG1 was assessed after incubation with leukocytes by SDS-PAGE. In these instances, after electrophoresis, gels were cut into 5-mm slices, and each slice was assessed for radioactivity.

Labeling of IgG1 with ^{125}I. Radioiodination of IgG1 (6–60 × 0.1 nM/procedure) was performed using chloramine T at 5 M excess according to Unkeless and Eisen (18) method. At least 95% of radioactivity in the labeled protein preparations could be precipitated by 10% TCA. The specific activity of the labeled protein varied from 4–40 × 10^7 cpm/nM of IgG1. Labeled protein was stored at 4°C and was used within 2 wk of its date of preparation.

Fluoresceination of IgG1 polymers. A preparation of IgG1 aggregates was fluoresceinated using published methods (19) and stored at −20°C.

Preparation of leukocytes. Mixed mononuclear cell suspensions were prepared from heparinized peripheral blood obtained from normal human donors by Ficoll-Hypaque density gradient centrifugation (10, 20). Monocytes from this mixture were permitted to adhere to plastic tissue culture dishes treated with fetal calf serum, and then were released with medium containing 0.2% EDTA (21). 85–95% of the cell suspensions prepared by this procedure had the appearance of monocytes on Giemsa stain and had nonspecific esterase activity in their cytoplasm as determined using alpha naphthol butyrate as the substrate (22). The remaining esterase-negative cells were small lymphocytes.

Paraformaldehyde fixed monocytes were prepared by incubating freshly prepared monocytes with a 1% solution of paraformaldehyde in PBS for 30 min at 37°C. Cells were then washed three times with PBS.

PMN were separated from the erythrocyte pellet obtained after Ficoll-Hypaque density centrifugation, by dextran sedimentation, followed by treatment with Tris-buffered ammonium chloride (pH 7.2) to lyse the remaining contaminating erythrocytes (23). The final suspension contained in excess of 95% neutrophils and 0–5% eosinophils as determined using Giemsa stain. Over 90% of cells in each of the leukocyte preparations excluded trypan blue.

Quantitation of binding of IgG to leukocytes. All assays of binding were performed in PBS containing 0.2% BSA and 0.1% Na_3N (PBS-BSA-Na_3N). Binding was assessed by incubating duplicate samples containing 2–5 × 10^5 monocytes or 5–10 × 10^5 PMN with varying amounts of radioiodinated IgG1 in the presence or absence of a large excess of unlabeled IgG1 (2 μM IgG1 monomer in assays of binding to monocytes and 20 μM IgG1 aggregate in assays of binding to PMN). Binding of IgG1 was quantitated after sedimenting cells through a layer of phthalate oils using the method of Segal (12). Nonspecific binding in the presence of excess unlabeled IgG1 usually constituted <20% of total counts bound. Specific binding in molecules of IgG1 bound per leukocyte was calculated as described by Segal and Hurwitz (12). Duplicate samples usually differed by <10%.

To assess the rate of dissociation of bound IgG1, cells either were washed two times to remove unbound, labeled, IgG1 and resuspended in fresh medium (with or without excess unlabeled IgG1 monomer), or 300-fold excess of unlabeled IgG1 was added directly without washing away unbound, labeled IgG1. In either case, the residual binding of labeled IgG1 was assessed serially over 2–3 h.

Statistical methods. The line best describing the results of semi-log plots of kinetic data, or Scatchard plots of equilibrium binding data were derived using the least squares method program of a TI-55 calculator (Texas Instruments, Inc. Digital System Div., Houston, Tex.).

RESULTS

Composition of the polymer preparations. SDS-PAGE of samples of IgG1 incubated with glutaraldehyde demonstrated the presence of varying amounts of unpolymerized IgG1 monomer, and a mixture of IgG1 polymers composed predominantly of from two to five subunits. Purified dimer separated from this mixture by two passages through the Sephadex G-200-LKB AcA22 column combination contained 80–85% dimer with 5–10% contamination with trimer and a similar degree of contamination with monomer. The oligomer preparations isolated from the crude mixture were more heterogeneous, containing ~20–30% dimer, 40–60% trimer, 20–30% tetramer, and trace amounts of larger polymers of IgG1 (Fig. 1).

Kinetics of binding of IgG1 to monocytes and PMN. Monocytes readily bound ^{125}I-labeled IgG1 monomer, dimer, or oligomer at 37°C. Binding in the presence of a 6.3 nM solution of labeled IgG1 in each instance reached equilibrium within 2 h. In contrast, binding of IgG1 proceeded to equilibrium very slowly at 4°C requiring in excess of 18 h of incubation. This difference in the rate of binding was not due to cellular metabolic activity at 37°C since the same pattern was noted when binding at 4°C and 37°C were compared using paraformaldehyde fixed monocytes (which no longer excluded trypan blue, or transformed from a pattern of diffuse to patchy fluorescence after incubation with fluorescein-labeled IgG1 aggregates at 37°C for 1 h).

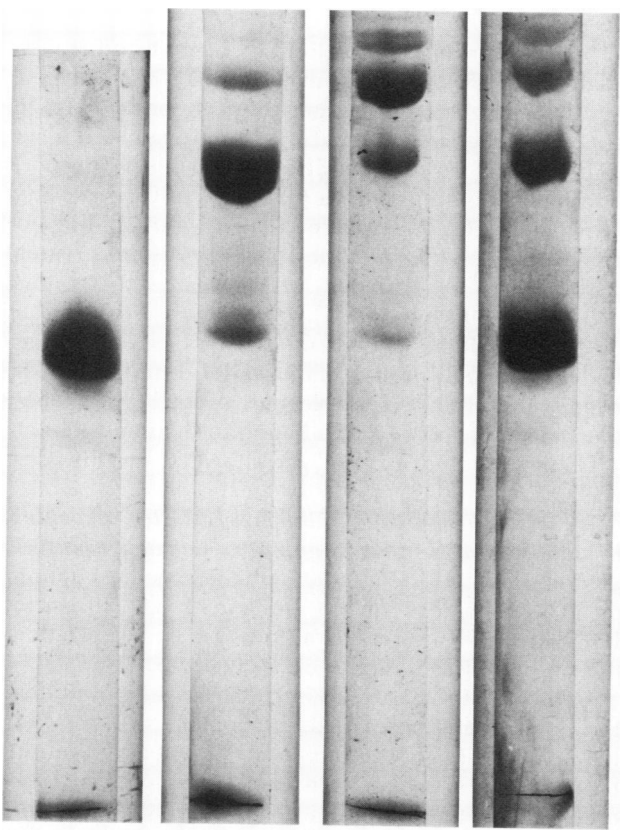

FIGURE 1 SDS-polyacrylamide gels demonstrating the composition of cross-linked IgG1 preparations prepared using glutaraldehyde; from left to right (1) untreated IgG1, (2) purified dimer prepared from mixed polymer preparations by gel-filtration chromatography, (3) purified oligomer prepared from mixed polymer preparation by gel-filtration chromatography, (4) unpurified mixed polymer preparation after treatment of IgG1 with glutaraldehyde.

PMN bound small amounts of IgG1 monomer but at comparable concentrations bound 10–100-fold more dimer or oligomer per cell. Because the amount of IgG1 monomer specifically bound to PMN was very small, no further studies of the interaction of PMN with IgG1 monomer were attempted.

In the presence of 6.3 nM solution of labeled IgG1, binding of dimers or oligomers reached plateau within 2 h at 37°C or 4°C but at equilibrium three- to sixfold more IgG1 bound at 4°C than at 37°C.

The kinetics of dissociation of IgG1 from monocytes and PMN. Over 80% of IgG1 monomer bound to monocytes at 37°C dissociated within 3 h after unbound labeled IgG1 was washed away and replaced by fresh PBS-BSA-Na_3N. Dimer and oligomer dissociated much more slowly under these conditions (Fig. 2A), but the rate of dissociation of these polymers also was nearly comparable to that of IgG1 monomer if dissociation was measured in the presence of BSA-BSA-Na_3N containing 6.3 μM of unlabeled IgG1 monomer (Fig. 2B). Dissociation of labeled dimer or oligomer from PMN after washing or the addition of excess unlabeled IgG1 was much more rapid (Fig. 3).

Over 80% of the labeled IgG1 monomer or polymer that dissociated from monocytes or PMN after unbound IgG1 was washed away precipitated in 10% TCA and in each instance, SDS-PAGE confirmed that the dissociated labeled IgG1 retained the same mobility as the starting preparation (without evidence of smaller proteolytic fragments).

Quantitation of equilibrium binding of IgG1. Binding of labeled IgG1 monomer, dimer, or oligomer to monocytes at 37°C was saturable and Scatchard plots in each case were linear (Fig. 4, Table I). The K_a for binding of monomer was $8.6 \pm 2.3 \times 10^8$ M^{-1} and dimer or oligomer bound ~ three- to fivefold more avidly than monomer. The maximal binding capacity (B_{max}) for IgG1 monomer was $20.2 \pm 6.8 \times 10^3$ sites/monocyte and B_{max} for binding dimer and oligomer were comparable (Table I).

In contrast to the results of prior studies (24), careful washing to remove plasma IgG before Ficoll-Hypaque

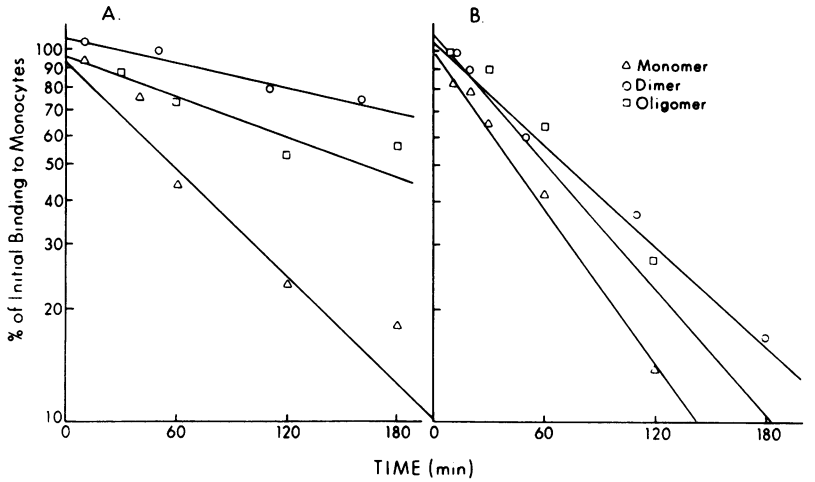

FIGURE 2 Comparison of the rate of dissociation of IgG1 monomer, dimer, and oligomer from monocytes at 37°C. Cells to which IgG1 had bound during incubation with 6.3 nM solutions of IgG1 at 37°C for 2 h were washed twice, and resuspended either in (A) PBS-BSA-Na_3N or in (B) PBS-BSA-Na_3N containing 6 μM of unlabeled IgG1 monomer.

centrifugation did not markedly alter the estimates of B_{max} obtained in these studies.

Because IgG1 polymers bound to PMN poorly at 37°C, equilibrium binding to PMN in most studies was quantitated after a 2-h incubation at 4°C with labeled IgG1. Under these conditions binding of both IgG1 dimer and oligomer were saturable and Scatchard plots of binding of both preparations were linear (Fig. 5). The K_a for binding of either polymer to PMN at 4°C was over a 100-fold smaller than K_a for binding to monocytes at 37°C, but the B_{max} was 20-fold greater (Table II).

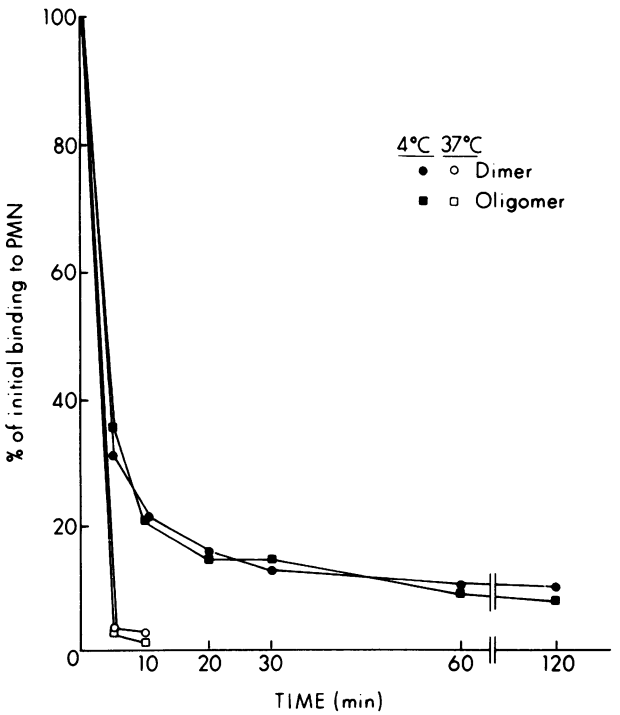

FIGURE 3 Comparison of the rate of dissociation of IgG1 dimer and oligomer from PMN at 37°C and 4°C. After a 2-h incubation with 6.3 mM solution of labeled IgG1 at 4°C, 300-fold excess of unlabeled IgG1 was added, and the rate of dissociation measured serially with time.

Binding to PMN at 37°C was even less avid. In the presence of 3,000 nM of labeled IgG1 oligomer, the highest concentration of labeled IgG1 tested, PMN bound only 100×10^3 molecules of IgG1/cell, one-fourth as much as could be bound to the same cells at 4°C, and binding was not yet saturated by this concentration of IgG1.

Inhibition of binding of labeled IgG1 to leukocytes by unlabeled IgG or its fragments. Fc fragments (6.7 μM) of IgG1 inhibited >90% of the specific binding of IgG1 monomer to monocytes and of IgG1 dimer to PMN, but Fab fragments at the same concentration did not inhibit binding to either cell type.

Unlabeled IgG1 and IgG3 proteins readily inhibited the binding of labeled IgG1 monomer to monocytes, but IgG4 and IgG2 were much less potent in inhibiting binding. The same pattern of subclass potency was observed for the inhibition of binding of labeled dimers of IgG1 to PMN but 10–100-fold greater concentrations of unlabeled IgG were required to inhibit binding to PMN (Table III).

Similarly, much more unlabeled IgG1 monomer was required to inhibit the binding of labeled polymers to PMN than to inhibit the binding of the same polymers to monocytes (Table IV).

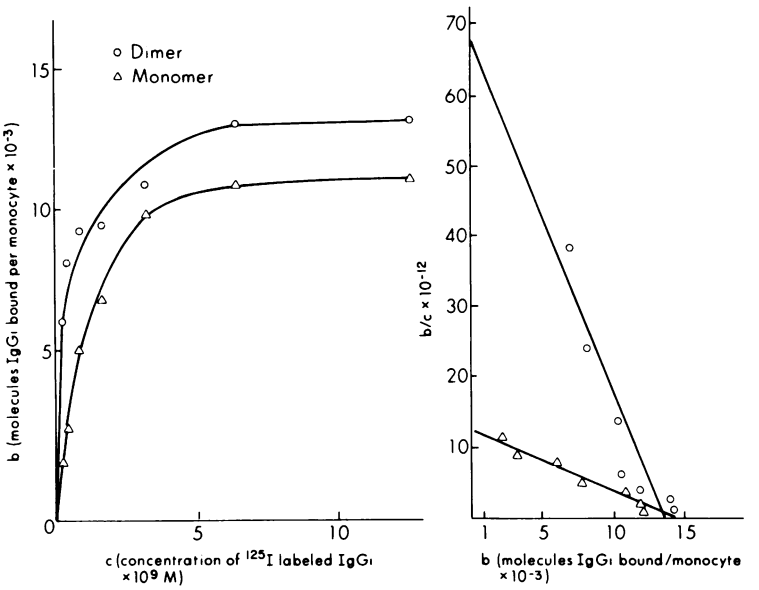

FIGURE 4 Left panel—equilibrium binding of labeled IgG1 monomer and dimer to monocytes at 37°C. Right panel—Scatchard plots of the same data, demonstrating that B_{max} for binding of either preparation is similar (14×10^3 sites/cell) but that the K_a for binding for dimer (4.8×10^9 M^{-1}) is considerably greater than K_a for binding of monomer (8.7×10^8 M^{-1}).

DISCUSSION

Prior investigators have characterized the Fc receptors present on human monocytes (25), activated U-937 cells (which resemble human macrophage) (26), and HL-60 cells (derived from human promyelocytes) (27) by measuring the binding of labeled monomeric human IgG to these cells. Human PMN also can bind monomeric human IgG (28), but perhaps because of the low avidity of this binding (29), the interaction of human IgG with Fc receptors on PMN has not been thoroughly studied previously. These studies demonstrate that by using small, covalently cross-linked polymers of human IgG to enhance the avidity of binding to PMN, it is possible to characterize the Fc receptors on PMN and compare them with the Fc receptors of human monocytes.

Monocytes in these, as in prior studies (24, 30) appear to possess a relatively small number of Fc receptors that bind IgG1 quite avidly at 37°C. As expected based on prior experiments using murine cells (12), small polymers of IgG1 once bound to the surface of

TABLE I
Binding of Labeled IgG1 to Monocytes

Monocytes incubated with radiolabeled IgG1	Number of experiments	r*	$K_a \times 10^8$* M^{-1}	B_{max}* $\times 10^3$ molecules/cell	$C\frac{1}{2}_{max} \times 0.1$ nM‡
Monomer	8	0.97±0.03§	8.6±2.3§ (6.2–13.3)	20.2±6.8§ (10.2–30.5)	16.0±6.0 (7.5–28.0)
Dimer	6	0.97±0.02	30.0±8.4 (17.6–41.0)	18.5±6.7 (9.0–26.0)	3.2±0.8 (2.2–4.1)
Oligomer	6	0.95±0.03	29.5±10.5 (19.0–43.2)	22.2±6.9 (10.3–29.8)	4.2±1.6 (1.6–5.9)

* Data derived from least squares analysis of Scatchard plots of binding.
‡ Concentration of IgG1 at which half the available Fc receptors are occupied as estimated from plots of binding vs. concentration of labeled IgG1.
§ Data represent mean±SD.

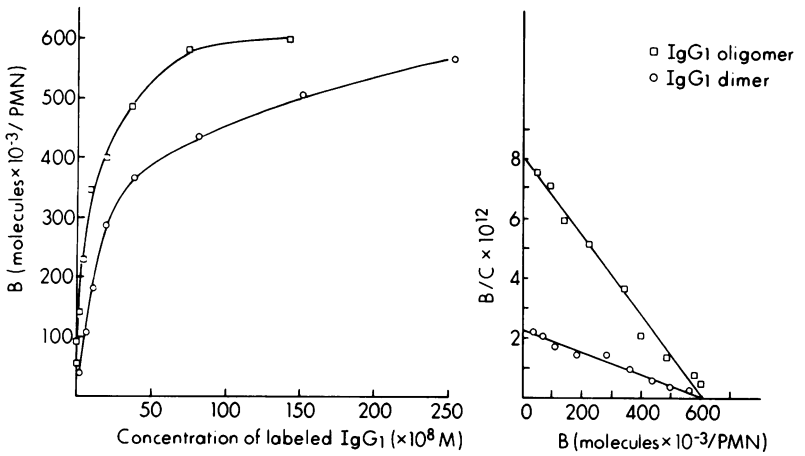

FIGURE 5 Left panel—equilibrium binding of labeled IgG1 dimer and oligomer to PMN at 4°C. Right panel—Scatchard plots of the same data demonstrating that B_{max} for binding of either preparation is similar (6.1×10^5 binding sites/cell) but the K_a for binding of oligomer (1.3×10^7 M^{-1}) is considerably greater than K_a for binding of dimer (3.6×10^6 M^{-1}).

monocytes dissociate more slowly than monomeric IgG1, and as a consequence, the K_a for the binding of IgG1 dimer or oligomer to monocytes is greater than K_a for binding of monomer. Despite this difference in the avidity of binding, in these, as in prior studies (12), estimates of the total number of binding sites obtained from Scatchard plots of binding of monomer, dimer, or oligomer are similar.

In contrast to the avid binding of IgG1 to monocytes, IgG1 binds to PMN very loosely at 37°C, and even at 4°C, where binding is more stable, IgG1 polymers bind to PMN 100–1,000-fold less avidly than they bind to monocytes at 37°C. No prior quantitative studies comparing the binding of human IgG to monocytes and PMN have been published; however, Alexander, Titus, and Segal (30), measuring the binding of labeled trimers of rabbit IgG to human leukocytes, found both effectors to bind rabbit IgG with equal avidity (i.e., a K_a of $\sim 4 \times 10^7$ M^{-1}) (28). The discrepancy between these results and those obtained in the current study illustrates the limitations of the use of heterologous sources of IgG for assessing Fc receptors on human cells. Whereas PMN bind trimers of rabbit IgG and oligomers of human IgG1 with comparable avidity, monocytes bind rabbit trimers much less avidly than they bind comparable polymers of human IgG1.

The surprisingly large amount of IgG1 polymer bound to PMN in these studies has been noted also by Alexander, Titus, and Segal (30). If the amount of IgG polymer bound is an accurate indicator of the total number of Fc binding sites, then PMN possess 10–20-fold more Fc receptors per cell than monocytes, and about as many receptors per cell as reported to be present on the surface of murine cells (18, 31, 32).

Consistent with the results of prior studies (28), both PMN and monocytes bind IgG1 and IgG3 with roughly

TABLE II
Binding of IgG1 to PMN

PMN incubated with radiolabeled IgG1	Number of experiments	r*	$K_a \times 10^6$ M^{-1}*	B_{max}* $\times 10^3$ molecules/cell	$C^1/_{2_{max}} \times 0.1$ nM‡
Dimer	3	0.98±0.02§	5.5±1.6§ (3.6–6.6)	460±130§ (382–613)	20.7±3.5§ (18.3–24.7)
Oligomer	3	0.98±0.01	18±5.0 (13–23)	486±108 (426–610)	6.7±1.4 (4.8–7.7)

* Data derived from least squares analysis of Scatchard plots of binding.
‡ Concentration of IgG1 at which half the available Fc receptors are occupied as estimated from plots of binding vs. concentration of labeled IgG1.
§ Data represent mean±SD.

TABLE III
*Inhibition of Binding of Labeled IgG1 to Leukocytes by Unlabeled Monoclonal IgG**

Protein	IgG subclass and light chain class	Monocytes‡	PMN§
Reference	IgG1κ	7.4×10^{-9}	7.6×10^{-7}
Pit	IgG1λ	1.6×10^{-8}	2.6×10^{-7}
Car	IgGlκ	1.3×10^{-8}	6.7×10^{-7}
Bel	IgG2κ	$>2.1 \times 10^{-7}$ ‖	$>4.7 \times 10^{-6}$ ‖
Hor	IgG2κ	$>2.1 \times 10^{-7}$ ‖	2.5×10^{-6}
Whi	IgG3κ	6.0×10^{-9}	7.3×10^{-8}
McD	IgD3λ	8.6×10^{-9}	1.8×10^{-7}
Pen	IgG4κ	5.3×10^{-8}	2.0×10^{-6}
Ger	IgG4κ	1.4×10^{-7}	3.3×10^{-6}

* Concentration of unlabeled IgG1 required to inhibit binding by 50%.
‡ Monocytes incubated in the presence of labeled reference IgG1 monomers (6.3 nM) for 3 h at 37°C.
§ PMN incubated in the presence of labeled reference IgG1 dimers (6.3 nM) for 2 h at 4°C.
‖ Less than 50% inhibition was produced by the maximal concentration of unlabeled IgG tested.

comparable avidity, and bind IgG4 and IgG2 much less avidly.

These studies suggest that the low avidity with which Fc receptors on PMN bind human IgG compared with monocytes may account for the lesser capacity of PMN to interact with target cells lightly coated with IgG (7–9). On the other hand, since PMN are less capable of interacting, even though they have a markedly greater number of receptors on their surface than monocytes, at least in the range of receptor density encountered in these studies, the number of receptors per cell appears not to be a critical determinant of effector-target interaction.

TABLE IV
*Inhibition of Binding of Labeled IgG1 Monomer and Polymers by Unlabeled IgG1 Monomer**

Leukocytes incubated with labeled IgG1 (6.3 nM)	Monocytes	PMN
Monomer	3.7×10^{-9}	ND
Dimer	1.74×10^{-8}	8.3×10^{-7}
Oligomer	2.9×10^{-8}	1.76×10^{-6}

* Molar concentration of unlabeled IgG1 monomer required to produce 50% inhibition of binding of labeled IgG1.
ND, not determined.

As would be expected in view of the low avidity with which monomeric IgG1 binds to PMN, much more unlabeled IgG1 monomer was required to inhibit the binding of labeled IgG1 polymers to PMN than to inhibit binding to monocytes. Presumably this same explanation may account for the published observation (8, 9) that the interaction of PMN with IgG-coated target cells is much less readily inhibited by unbound IgG than the interaction of monocytes with the same IgG-coated targets.

Although the capacity of both monocytes and PMN to bind labeled IgG1 in the presence of unlabeled IgG monomer is enhanced by polymerization of the labeled IgG1, neither effector could bind the polymers used in these experiments in the presence of high concentrations of IgG1 monomer comparable to those in human plasma. Since comparable immune complexes (33) and IgG-coated targets (34) are bound and cleared in vivo despite the presence of IgG in plasma, it is likely that additional factors not well defined in these studies or alternatively effectors bearing Fc receptors different from those present on PMN or monocytes, play an important role in the clearance of IgG complexes (and of IgG-coated target cells) in vivo. A clearer delineation of the causes of this discrepancy is a major goal for future studies.

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