diode because of the known (often linear) relation between current and intensity [T. E. Cohn, *Am. J. Optom. Arch. Am. Acad. Optom.* **49**, 1028 (1972)]. Our light control circuitry provided adjustable steady levels and superimposed square pulse modulations of adjustable amplitude and selectable polarity. Rise and fall times were less than 0.1 msec. Steady levels were always in the low photopic range (calibrated United Detector Technology radiometer).

13. In more compact notation the 28 stimuli were characterized by different ratios: $E_L/E_R = \pm 0$, ± 0.22, ± 0.48, ± 0.80, ± 1.25, ± 2.09, ± 4.28, and $\pm\infty$.
14. The control knob was returned to zero (no stimulus to either eye) between settings.
15. The order of presentation of stimuli was quasi-random.
16. See, for example, W. P. Tanner, Jr., and J. A. Swets, *Psychol. Rev.* **61**, 401 (1954).
17. We have conducted control experiments using two-alternative forced-choice techniques to verify the essential features of the data shown in Fig. 1. As many as four stimulus alternatives were randomized in a given run. Such testing precludes the effects of both criterion variation and motivational change, since the subject cannot know the type of stimulus to be presented in advance and because the criterion may be presumed to be fixed on a given trial. Control runs with four types of stimulus combination were made. In the first, we used equal modulation luminance changes (the monocular stimuli had been previously found to be of equal detectability) in order to verify that increment-decrement detectability is slightly less than increment-increment or decrement-decrement detectability. Data consistent with this hypothesis were found for all subjects tested. The second control compared the detectability of monocular increments with that of binocular increments [T. E. Cohn and R. D. Freeman (*5*)]. Binocular detectability lay between that predicted by probability summation and that predicted by energy summation. The third control used stimuli all chosen to lie in the second and fourth quadrants, for example, four combinations of increment to one eye and decrement to the other eye differing only in the modulation ratio. The results of this test were consistent with the curvilinear nature of the threshold contour in the second and fourth quadrants (Fig. 1). The fourth control experiment used an increment to one eye presented with one of four low-amplitude increments or decrements to the other eye. This control was designed to test the asymmetrical nature of the threshold contour about horizontal and vertical axes. The results of this test were consistent with the hypothesis that a monocular increment is slightly more detectable when presented with a small monocular increment than with a small monocular decrement.
18. We have tested a total of six subjects, none of whom manifested binocular abnormalities in clinical tests. All exhibited elliptical threshold contours. Two of the subjects made a total of 35 determinations of the threshold contour. No systematic departures from the elliptical shape fit to data points have been observed.
19. This type of data display was first shown by C. Rashbass [*J. Physiol. (London)* **210**, 165 (1970)]. He found elliptical threshold contours for incremental and decremental monocular stimuli separated in time.
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21. Suggestions of a subtractive mechanism between two eyes can also be found in the writings of B. Julesz [*Sci. Am.* **212**, 38 (Feb. 1965)], S. M. Anstis [*Vision Res.* **10**, 1411 (1970)], and E. Welpe [*ibid.* **15**, 1283 (1975)]. The visual evoked response data of L. Cigánek [*ibid.* **11**, 1289 (1971)] might also be interpreted as favoring the existence of a binocular subtraction mechanism.
22. The relation

$$E_L^2 + E_R^2 + 2KE_LE_R = 1$$

is derived in the appendix of T. E. Cohn and D. J. Lasley [*Vision Res.* **15**, 387 (1975)]. Assumptions critical to the derivation are (i) monocular thresholds equal unity, (ii) independent gaussian noise of unity variance in both summing and subtracting mechanisms, and (iii) likelihood ratio processing of outputs of the two mechanisms. The symbol K expresses the relative strengths of the mechanisms.

23. We think that the suprathreshold binocular visual phenomenon called stereoscopic luster [J. P. C. Southall, Ed., *Helmholtz's Treatise on Physiological Optics* (Optical Society of America, 1925), vol. 3, p. 525 (reprint by Dover, New York, 1962), p. 515] would also be expected of a visual system that contained interocular summing and subtracting mechanisms. When a dark target in one eye is fused with a light target in the other eye, the fused object appears transparent or lustrous, as if it were polished metal, even though the components may have been various shades of gray matte paper. We hypothesize that a subtraction mechanism would signal strongly in these circumstances and thus provide a percept noticeably different from the usual one comprising brightness and texture, which would be provided by a summing mechanism.

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Complement-Dependent Immunoglobulin G Receptor Function in Lymphoid Cells

Abstract. *Lymphoid cells are unable to lyse antibody-coated target cells in the presence of normal immunoglobulin G (IgG), presumably because their surface receptors for IgG are blocked. However, when target cells are sensitized with antibodies and complement, IgG receptors are unblocked and cytotoxicity occurs even in the presence of normal IgG. Thus, IgG receptors may function in vivo despite the relatively high concentrations of IgG in serum and interstitial fluid.*

Cell-mediated cytotoxicity induced by immunoglobulin G (IgG) antibodies to target cell (antibody-dependent cell-mediated cytotoxicity, ADCC) has been advocated as a possible mechanism involved in allograft rejection (*1*), viral infections (*2*), tumor immunity (*3*), and autoimmune diseases (*4*). However, no direct evidence of its participation in vivo has been obtained. Furthermore, ADCC is inhibited by normal IgG (*5*) at concentrations below those in normal serum or interstitial fluid (*6*). I now report an in vitro model in which ADCC is induced even in the presence of inhibitory concentrations of IgG, providing an experimental basis for a possible in vivo function of the IgG receptors.

Effector cells were obtained from spleens surgically removed from patients undergoing staging laparotomies (*7*). A cell suspension was prepared and mononuclear cells were concentrated by Ficoll-Hypaque centrifugation (*8*). Sheep red blood cells (SRBC), used as target cells, were labeled with 100 μc of ^{51}Cr ($Na_2{}^{51}CrO_4$, New England Nuclear) (*9*) and treated with different antibody preparations. The following groups of sensitized target cells were prepared: EA-G, SRBC coated with IgG antibodies (*10*); EA-M, SRBC sensitized with IgM antibodies; EAC-M and EAC-G, SRBC sensitized with IgM or IgG antibodies and complement (C); EA-M-G, SRBC sensitized with IgM first and subsequently with IgG; EAC-M-G, SRBC sensitized with IgM and C and subsequently with IgG.

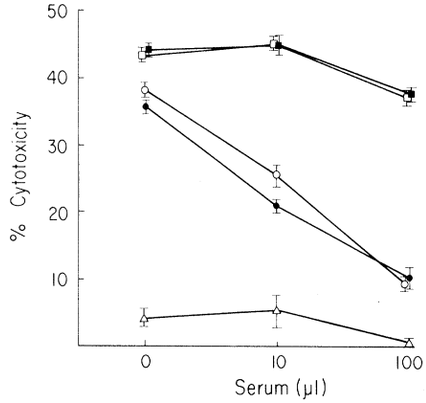

Fig. 1. Inhibition of cytotoxicity by human serum. Human serum, obtained from normal donors, was pooled, inactivated by heat, and absorbed with SRBC. Cytotoxicity was induced by human spleen lymphoid cells against SRBC sensitized in different ways. △, EAC-M; ●, EA-G; ○, EA-M-G; ■, EAC-G; □, EAC-M-G. The total volume of the cell mixture was 1 ml. The bars correspond to the range of duplicate determinations.

Effector cells (30×10^6) and target cells (2×10^6) were placed in plastic petri dishes (35 by 10 mm; Falcon Plastics) in 1 ml of Ham's F-10 medium (Grand Island) supplemented with 20 percent fetal calf serum and 50 μg of gentamicin (Schering) per milliliter. Inhibitors were added prior to the addition of the target cells. The cell mixtures were incubated (on a rocking platform) in an atmosphere of 5 percent CO_2 at 37°C for 18 hours and the percentage of cytotoxicity was determined (*11*). Values were expressed as specific cytotoxicity after subtraction of nonspecific lysis obtained in the absence of spleen cells. Nonspecific lysis was determined for each type of target cell (EA-G, EAC-G, EAC-M, and others).

Lymphoid cells carry on their surface receptors for the third component of complement (C3), which enable them to bind SRBC coated with C (*12*). However, such a binding does not induce lysis of the target cell, an observation

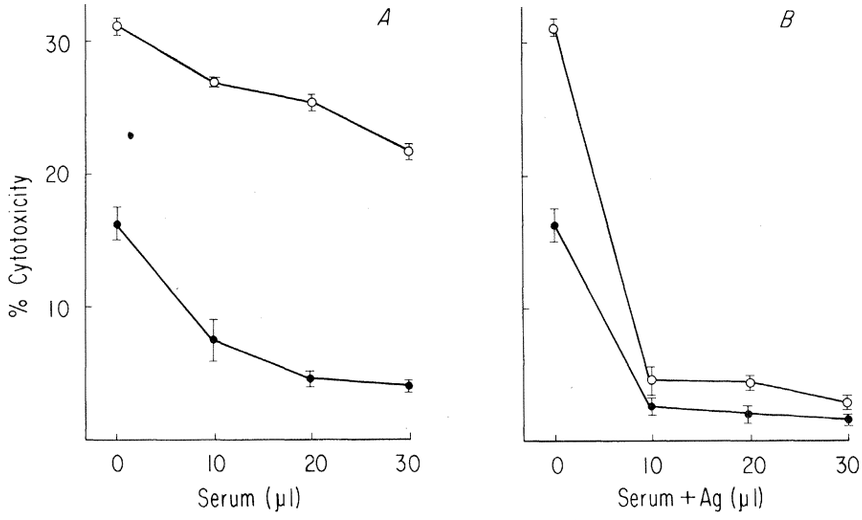

Fig. 2. Inhibition of cytotoxicity by rabbit serum and antigen-antibody complexes. Cytotoxicity was induced by human spleen lymphoid cells in a total volume of 1 ml. The target cells used were as follows: ●, EA-G; ○, EAC-G. Lysis of EAC-M was 2.2 percent. (A) Effect of increasing concentrations of rabbit antiserum to *Candida albicans* antigens. (B) Effect of the rabbit antiserum plus equal volume of *Candida albicans* antigen. No inhibition of cytotoxicity was observed with 10, 20, or 30 μl of the antigen preparation in the absence of the rabbit antiserum. The bars correspond to the range of duplicate determinations.

that has lead to the suggestion that the C3 receptor does not have a major role in ADCC (*13*). The following results indicate that the C3 receptor does have a major role since it allows the induction of ADCC in the presence of inhibitory concentrations of serum IgG. Lysis of EA-G is inhibited by human serum at dilutions of 10^{-2} and 10^{-1}. However, lysis of EAC-G is inhibited to a much lesser extent, and a significant degree of cytotoxicity is still observed at the higher concentrations of serum (Fig. 1). The same effect is observed when C is bound to the erythrocyte by IgM antibody, and IgG antibody is added later (EAC-M-G); the lysis of EA-G is not affected by the simultaneous presence of IgM (EA-M-G). Similar results were obtained in four independent experiments (*14*).

An excess of free molecules of serum IgG may block the IgG receptors but not the C3 receptors. However, since the binding through C3 receptors does not trigger lysis of the target cells, an explanation must be offered for the cytotoxicity of EAC-G (but not of EA-G) obtained in the presence of serum IgG. Taking into account that the IgG antibody must be present on the target cell for the induction of cytotoxicity and that the binding of free monomeric IgG molecules to the IgG receptors is weak (*15*), then it can be postulated that the intimate contact between effector and target cell, brought about through the C3 receptor, promotes the displacement of the free IgG from the lymphocyte receptor by the IgG antibody bound to the target cell, making possible the occurrence of ADCC. If this hypothesis is correct, blocking of the IgG receptors with soluble antigen-antibody complexes, whose binding with the IgG receptor is stronger than that of free IgG (and more difficult to displace), should lead to a pronounced inhibition of the lysis of EAC-G.

The following experiments support this possibility. Serum from a rabbit immunized against *Candida albicans* antigens (*16*) produced significant inhibition of cytotoxicity of EA-G, but little effect on the lysis of EAC-G (Fig. 2A). However, when the antigen was also added to the cell mixture, cytotoxicity for both EA-G and EAC-G was inhibited (Fig. 2B). Antigen alone did not inhibit cytotoxicity. In other experiments, antigen-antibody complexes did not inhibit binding of EAC-G (*17*).

The foregoing results suggest that the antigen-antibody complexes do not block the C3 receptors, and hence binding of EAC-G ensues unaffected. Antigen-antibody complexes do block IgG receptors, in a reaction not easily reversible; and lysis of target cells does not occur in their presence. Thus, the lysis of EAC-G obtained in the presence of monomeric serum IgG represents an induction of the classical ADCC, generated through the IgG receptors.

Most cells that carry IgG receptors (B lymphocytes, granulocytes, monocytes, macrophages), which are efficient effector cells for ADCC (*11, 18*), also carry C receptors (*12*). This may be a structural arrangement designed for a cooperative function of C and IgG receptors (*19*).

In conclusion, the classical mechanism of ADCC may operate in the presence of normal IgG, provided that both IgG antibody and C are present on the target cell. The function of the C3 receptor is to promote the binding of effector and target cells, generating favorable conditions for the interaction of the IgG antibody and the lymphocyte receptor, and overcoming the inhibitory effect of normal IgG.

The occurrence of IgG antibodies and the presence of C on target cells or tissues are features frequently found in some autoimmune diseases (*4*) and in allograft reactions (*20*). Consequently, the above results suggest that the participation of ADDC in those situations is not only possible but is also likely to occur.

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17. Spleen cells attached to plastic petri dishes treated with poly-L-lysine [J. C. Kennedy and M. A. Axelrod, *Immunology* **20**, 253 (1971)], were incubated with ^{51}Cr-labeled target cells (E, EA-G, EA-M, EAC-M, EAC-G) for 1 hour at 37°C in a rocking platform. Each petri dish was then washed three times with saline and immersed three more times in a beaker with saline. The target cells that remained attached to the spleen cells were lysed with distilled water, and radioactivity was measured in a well-type gamma counter [J. C. Scornik and B. Drewinko, *J. Immunol.* **115**, 1223 (1975)].
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Antiserum to Somatostatin Prevents Stress-Induced Inhibition of Growth Hormone Secretion in the Rat

Abstract. *Plasma growth hormone levels fall and remain low for several hours after stress in the rat. When antiserums to somatostatin are administered to rats prior to stress, growth hormone secretory pulses are partially restored. The results provide evidence that circulating somatostatin plays a prominent role in stress-induced inhibition of growth hormone secretion in the rat.*

Growth hormone (GH) secretion in the rat is characterized by pulsatile or episodic release (*1*). In freely behaving, nonstressed male rats surges of GH secretion occur at intervals of 3.2 to 3.4 hours, reaching plasma concentrations of 300 to 400 ng/ml (*2*). Between bursts, levels of GH are undetectable (< 1 ng/ml). The surges in GH are entrained to the light-dark cycle with major secretory episodes occurring at 1030 to 1230 hours and at 1330 to 1500 hours when lights turn on at 0600 hours (*2, 3*). Pulsatile GH surges are blocked by administration of somatostatin (GH-release inhibiting hormone), a tetradecapeptide isolated from the hypothalamus (*4*), and by bilateral lesions placed in the hypothalamic ventromedial nuclei (*1*).

Stress in the rat results in acute inhibition of GH secretion (*5*). The mechanism of this suppression is unknown, although it is hypothesized to be mediated by the hypothalamus (*5*). We now report that stress suppresses pulsatile GH release for at least 5 hours and that antiserum to somatostatin administered prior to stress partially restores the GH secretory pattern.

Male Sprague-Dawley rats (300 to 350 g) were prepared with permanent indwelling intra-atrial catheters and adapted to small isolation boxes to permit repeated blood sampling without disturbance to the animal (*1*). This experimental procedure is important since even minor stress, such as handling, inhibits GH secretion (*1, 6*). Cage adaptation was carried out by housing the animals in the isolation chambers for a period of 48 to 72 hours prior to sampling. All animals had reached their presurgical body weight before study. Each rat was given free access to water and Purina rat chow; the light-dark (LD) cycle was 12 : 12, with lights on from 0600 to 1800 hours. Blood samples (0.4 ml) were taken every 15 minutes from 0930 to 1500 hours to encompass two GH secretory episodes. The plasma was separated and frozen; red blood cells were resuspended in physiologic saline and returned to the animal after the removal of the next sample. This technique prevented a fall in hematocrit and allowed multiple samples to be taken without hemodynamic disturbance. Plasma GH was measured in duplicate samples by radioimmunoassay using materials supplied by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

To develop a model to study the effects of stress on GH secretion, two different stressful conditions were used. In the first, the effect of an intraperitoneal injection was evaluated. Six normal rats were sampled for 5 hours (1000 to 1500 hours) on two separate occasions. Three of the animals were first sampled without handling and three were injected with 0.5 ml of physiological saline intraperitoneally at 0830 hours. The sequence was reversed 2 to 4 days later. The area encompassed by a single GH secretory episode was calculated by planimetry. In order to standardize the determination, a period of 3.5 hours was taken from the onset of each secretory episode. Both saline-injected (Fig. 1A) and control groups had a normal pulsatile pattern of GH release. However, animals that were injected had a significantly lower, mean integrated GH level ($P < .05$) compared to the noninjected group (62.9 ± 7.2 compared to 105.6 ± 12.5 ng/ml per 3.5 hours) (*7*) (Table 1). These results demonstrate that a minor stress can alter the subsequent secretion of GH without completely abolishing the pulsatile pattern.

In a second experiment, the effect of a more severe stress on GH secretion was assessed. After the baseline blood samples were obtained, each animal was removed from its isolation cage at 1000 hours, placed in a large water bath at 37°C and forced to swim for 30 minutes. Each rat was then returned to the isolation cage and sampled for 3.5 to 5.0 hours. Six control rats showed complete suppression of pulsatile GH secretion for up to 5.0 hours after stress, confirming previous reports (*5, 6*) that acute stress causes inhibition of GH in the rat and demonstrating that this suppression is due to abolition of pulsatile GH release.

If the GH suppression to stress is mediated by somatostatin, we hypothesized that its effects might be blocked or diminished by administration of a large dose of antiserum to somatostatin. Two different antiserums to somatostatin were used. One antiserum (AS 1) was generated in normal rabbits by injecting somatostatin bound to thyroglobulin, and the second (AS 2) by injecting somatostatin bound to bovine serum albumin. At a dilution of 1 : 2000 both antiserums bound more than 50 percent of ^{125}I-labeled tyrosine-1 somatostatin and at a dilution of 1 : 300 they bound more than 95 percent. The antiserums were specific for somatostatin and showed no cross-reactivity to thyrotrophin releasing hormone, lute-