We have seen that differentially rotating solar models are unstable unless their angular momentum is an increasing function of distance from the rotation axis. This latter condition is violated by all solar models whose interiors rotate sufficiently rapidly to account for Dicke's oblateness measurement. The turbulent motion that would ensue in these unstable models would be characterized by very elongated eddies. Their short dimension (approximately 1 km) would allow rapid exchange of heat with the surroundings, whereas their long dimensions would approach, if not exceed, the local scale height. The circulation time for these energy-containing eddies is on the order of a rotation period. Such eddies would produce very rapid diffusion of angular momentum and complete mixing of the sun would take place in about 10 years.

The sun is subject to a torque by the solar wind (*5*, *6*). This torque will produce differential rotation and therefore turbulence below the solar convective zone. The mixing of material brought about by turbulence will lead to the depletion of lithium and beryllium which are destroyed at temperatures slightly in excess of those at the bottom of the convective layer. From the presence of beryllium (and possibly lithium) in the solar photosphere, we may infer that the sun's angular momentum has not decreased by orders of magnitude since it arrived on the main sequence (unless lithium and beryllium have been formed since then).

The rotational instability that we have described is analogous to a thermohaline instability that was first discovered by Stern (*7*). This instability arises when a layer of warm salty water lies above cold fresh water. Even if the density increases downward the system can still be unstable because the thermal diffusivity is much greater than the diffusivity of salt. A small rising blob of fluid can lose most of its temperature deficiency, while retaining its initial salinity, and consequently be acted upon by a buoyant force. In this context, salt plays the role that angular momentum did in the rotational instability we have been discussing.

PETER GOLDREICH
California Institute of Technology, Pasadena
GERALD SCHUBERT
University of California, Los Angeles

References and Notes

1. R. H. Dicke, *Phys. Rev. Letters*, **18**, 313 (1967).
2. ———, *Nature* **202**, 432 (1964).
3. S. Chandrasekhar, *Hydrodynamic and Hydromagnetic Stability* (Oxford Univ. Press, London, 1961).
4. P. Goldreich and G. Schubert, in preparation.
5. J. C. Brandt, *Astrophys. J.* **144**, 1221 (1966).
6. E. J. Weber and L. Davis, Jr., *Astrophys. J.* **148**, 217 (1967).
7. M. E. Stern, *Tellus* **12**, 172 (1960).
8. We are grateful to Drs. F. H. Busse, A. P. Ingersoll, and W. V. R. Malkus for many helpful discussions.

4 April 1967

Limited Heterogeneity of Gamma Globulin in Hypogammaglobulinemia

Abstract. *When serums of 11 patients with hypogammaglobulinemia were examined by acrylamide-gel electrophoresis, combined with diffusion analysis, for the gamma chain of immunoglobulin G, the electrophoretic distribution of immunoglobulin G differed from that of normal individuals. The differences consisted of limited heterogeneity and bimodal distributions of the proteins at times. Isolated immunoglobulin G from four of the patients showed similar phenomena. The findings indicate a deficient gene population in these patients.*

We investigated the possibility that detectable structural abnormalities of the immunoglobulins might be found in diseases of immunological deficiency. Studies of the electrophoretic characteristics of immunoglobulin G (IgG) in serums of 11 hypogammaglobulinemic patients show that the mobility of the IgG of each of these subjects differs from that of IgG either in a human serum pool or in individual serum samples from a group of normal persons.

Electrophoretic behavior was assessed by diffusion analyses of serums after electrophoresis in acrylamide (*1*) and by immunoelectrophoretic and acrylamide analyses of isolated IgG. Serum samples containing approximately 150 μg of IgG (0.05 to 0.15 ml total) were applied to 7.5-percent acrylamide gels. At the end of electrophoresis (*p*H 9.5), the gels were sliced longitudinally in half and placed on the surfaces of agar-coated microscope slides. Troughs were cut parallel to the gel and filled with antiserum specific for gamma chain.

The analyses (Fig. 1) showed that limited heterogeneity was a constant feature in the patients. Bimodal peaks (two arcs) were common. The electrophoretic mobility of most of the IgG's fractionated from samples of whole serum tended to be slow, but peaks of intermediate and fast mobility were also seen. When we increased the smaller volume of control serums (those having normal amounts of γ-globulin) by adding serum albumin (70 mg/ml) or normal saline to make it the same as that of the patients, the diffusion pattern of the normal serums was unchanged. All samples tested were obtained from patients before administration of γ-globulin therapy, except for samples from one patient who had not received any γ-globulin for 1 year before the study. We examined the IgG patterns of two sets of parents of our patients and found them normal. The diffusion patterns of patients with hypogammaglobulinemia of secondary etiology (hypoproteinemia) also do not differ from normal when equivalent amounts of γ-globulin are applied to the gel. Conversely, two patients with hypergammaglobulinemia (chronic infection) also showed normal patterns under these conditions (that is, when serum containing 150 μg of IgG was applied to the gel). Similar distributions were also seen when we used antiserum specific for κ- and λ-chains; hence, the restrictions are apparently unrelated to the composition of the light chain.

Immunoglobulin G was isolated from the serums of four male patients; the amounts varied from 85 to 172 mg per 100 ml of serum. None of these samples showed a bimodal distribution; the serum pattern is represented by the lowermost portion of Fig. 1. Fractionation was accomplished by diethylaminoethyl (DEAE)-Sephadex chromatography at *p*H 6.3 with 0.0175*M* phosphate buffer (*2*). When the isolated IgG's were analyzed by immunoelectrophoresis, the samples from the patients tended to have slower mobility and less heterogeneity than the IgG from normal persons (Fig. 2). Analysis in acrylamide gel confirmed the differences between the IgG's of the patients and γ-globulins of normals. After electrophoresis in 7.5-percent neutral gel of equal quantities of proteins from the IgG pools, there was a restricted heterogeneity and slower mobility of the γ-globulin from the

hypogammaglobulinemic patients (Fig. 3). Furthermore, samples from two of the patients showed banding of the γ-globulin in the acrylamide gel; this fine banding is attributable to unit-charge differences between the γ-globulins and is similar to the anomalous patterns seen with Bence Jones and myeloma proteins (*3*). A number of manipulations indicated that the banding observed in the acrylamide-gel electrophoresis was not due to conversion of γ-globulins to proteins of unusual unit-charge distribution as a result of proteolysis or destruction caused by handling (*4*). While IgG from normal human serum undergoes changes if kept at room temperature for 24 hours at neutral *p*H, *p*H 10, or *p*H 3, in no case is banding produced. Further, we observed the banding pattern whether or not urea was used. Even when the serums were handled with special precautions to minimize proteolytic degradation, the banding was still regularly observed. Figure 3 also shows marked difference in dye-binding in IgG samples from two of the patients (B and D); this decrease in dye-binding was always noted with these samples. All of the proteins illustrated in Fig. 3 were subjected to electrophoresis at the same time, the same amount of protein (180 μg) was applied in each case, and the gels were stained simultaneously with the same batch of dye. Although the banding is associated with the more faintly staining specimens, this does not, in itself, explain the difference. Simply binding more dye would not make the normal IgG appear to have a more continuous distribution of mobilities.

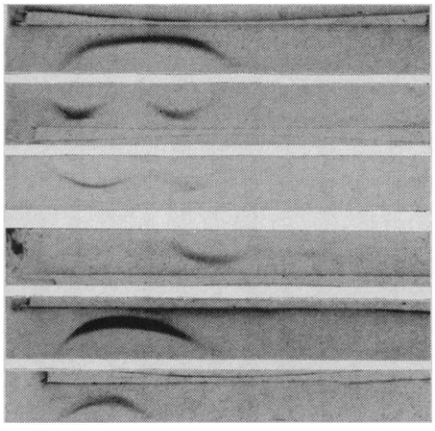

Fig. 1. Diffusion analyses of gamma-chain distribution of representative patients with immunological deficiency. Serum samples adjusted to contain 150 μg of IgG were subjected to electrophoresis in acrylamide gel. The diffusion pattern obtained by reacting a longitudinal slice of the gel with antibody specific for gamma chain of IgG is shown. The pattern from normal individuals is at the top. Patients from whom the IgG was isolated showed reactions typified by the lowermost portion.

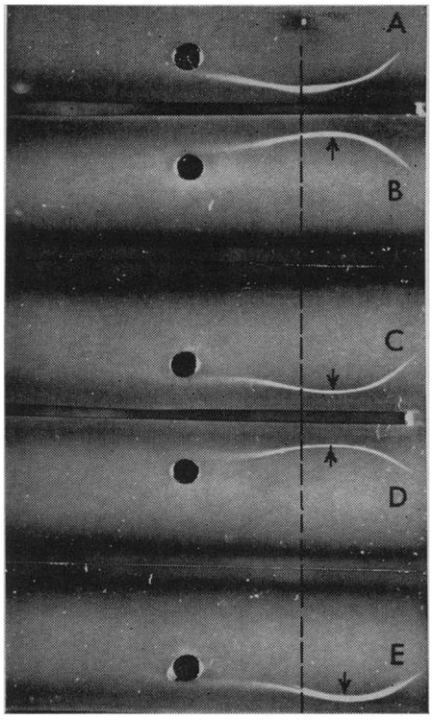

Fig. 2. Immunoelectrophoretic analyses of IgG (2 mg/ml) isolated from four patients. Electrophoresis of the several samples was performed simultaneously. The dotted line passes through the tangent of the normal arc (A). Arrows show the point of tangency for IgG arcs of the patients' serum. Cathode to the right.

These findings show that the IgG's of normal persons differ from those of certain hypogammaglobulinemic patients. The observations may be of significance in etiological considerations of patients with hypogammaglobulinemia and in theories of antibody synthesis. Our results imply an abnormality in protein synthesis in these patients. The electrophoretic characteristics of the IgG fractions obtained from our patients indicate that only a part of the total potential of the IgG production apparatus is functioning normally. This could be the result of a faulty structural gene involving the control of the absent molecules, or selective inability of precursors to differentiate along certain cell lines (a tendency toward oligoclonality).

Schaller *et al.* (*5*) reported an unusual case of immunological deficiency associated with thymic dysplasia, lymphopenia, and hypergammaglobulinemia. They mentioned a sharp peak in the γ-globulin region suggestive of a paraprotein, and they also noted the absence of faster IgG components. An additional parallel to our findings can be found in bacterial mutants. Mutants of *Escherichia coli* and *Neurospora crassa* produce analogs of the enzyme tryptophane synthetase which, although biologically inactive, bear antigenic determinants that cross-react with the normal enzyme. A similar analog has been described for β-galactosidase (*6*). It is impossible to test the hypothesis that the molecules which are present and have been examined are, in this sense, abnormal. The species present may function adequately. However, the diminished total antibody response in these patients is associated with less heterogeneity, and thus the organism's response is impaired.

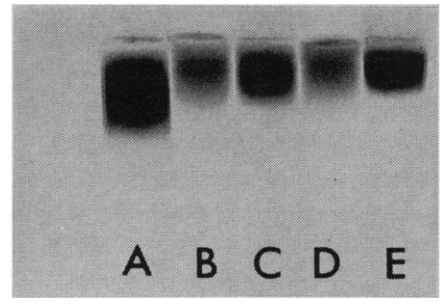

Fig. 3. Acrylamide electrophoresis of isolated IgG (180 μg). Samples were applied in each case. Limited heterogeneity is evident. Samples B and D did show band formation, although these bands are not evident in the photograph.

RICHARD HONG
ROBERT A. GOOD
Variety Club Heart Hospital, Department of Pediatrics, University of Minnesota School of Medicine, Minneapolis 55455

References and Notes

1. L. Ornstein, *Ann. N.Y. Acad. Sci.* **121**, 321 (1964); B. J. Davis, *ibid.* **121**, 404 (1964).
2. H. B. Levy and H. A. Sober, *Proc. Soc. Exp. Biol. Med.* **103**, 250 (1960).
3. R. L. Engle, K. R. Woods, J. H. Pert, *J. Clin. Invest.* **44**, 1045 (1965); J. A. Owen, C. Got, H. J. Silberman, *Clin. Chim. Acta* **3**, 605 (1958); B. Askonas and J. Fahey, *Nature* **190**, 980 (1961); G. M. Edelman and M. D. Poulik, *J. Exp. Med.* **113**, 861 (1961); J. M. Fine and R. Creyssel, *Rev. Franc. Etud. Clin. Biol.* **6**, 766 (1961).
4. U. J. Lewis and E. V. Cheever, *J. Biol. Chem.* **240**, 247 (1965).
5. J. Schaller, S. D. Davis, Y. Ching, D. Lagunoff, C. P. S. Williams, R. J. Wedgwood, *Lancet* **1966-II**, 825 (1966).
6. S. R. Suskind, C. Yanofsky, D. M. Bonner, *Proc. Nat. Acad. Sci. U.S.* **41**, 577 (1955); M. Cohn and A. M. Torriani, *J. Immunol.* **69**, 471 (1952).
7. Aided by grants from PHS (HE-02085, AI-00798, NB-02042, and AI-07726), the National Foundation, the American Heart Association, and the Graduate School Research Fund of the University of Minnesota; and by research career development award K3-HD,511 to R.H.

11 April 1967