

Aid is usually given generously when occasion arises. During the Italian floods last autumn over £20,000 was sent to the Red Cross by members of the British public. It was spent as received, together with £3,000 from the Society's own funds, on sweaters, blankets, and vitamin and water-purification tablets. When the coal-tip fell down the hillside at Aberfan a local Red Cross team at once went into action. Trained nurses and V.A.D.s worked day and night in the mortuary, washing and helping to identify the bodies. Because the Red Cross is world-wide and has long experience of training in all types of emergency aid, it is well placed to provide the short-term relief so badly needed immediately after a disaster until the responsible authorities can undertake more permanent measures.

Antinuclear Factors

The term antinuclear factor may be applied to any constituent of the serum that has an affinity for combining with the material of cell nuclei. The existence of such factors was first suggested by the observation of M. M. Hargraves, H. Richmond, and R. Morton¹ that marrow smears from patients with systemic lupus erythematosus (S.L.E.) contain cells with peculiar cytoplasmic inclusions apparently derived from the nuclei of disrupted cells. That these so-called L.E. cells result from the presence of a specific factor in the serum of patients with S.L.E. was subsequently shown by the work of J. R. Haserick and his associates.²

The serum factor behaves like an opsonin for cell nuclei, facilitating their phagocytosis by normal phagocytic cells, but is incapable of intracellular penetration. Its effects are therefore most readily detected in vitro, where some degree of mechanical trauma facilitates the reaction. The discovery that the L.E. cell factor resided in the γ -globulin fraction³ of the serum soon led to the application of an immunofluorescent method for its detection. A positive reaction is shown by a brilliant apple green fluorescence of the cell nuclei, and the term antinuclear factor is customarily restricted to those factors detected by the immunofluorescent technique.

The presence of these antinuclear factors in the γ -globulin fraction of serum suggests their antibody nature, and the application of other immunological techniques, notably complement fixation³ and tanned-cell agglutination, soon disclosed in patients with systemic lupus erythematosus a number of different antibodies directed against different nuclear constituents, among them desoxyribonucleoprotein, desoxyribonucleic acid, nucleohistone, and other nuclear proteins. It also soon became apparent that the antinuclear factors are by no means confined to patients with S.L.E., but that they occur sometimes in the related connective-tissue disorders such as rheumatoid arthritis, dermatomyositis, and systemic sclerosis.⁴ But their incidence in these disorders is considerably lower than in S.L.E., for in that disease they are found in well over 90% of all active cases. Their precise incidence in other diseases is difficult to determine, since much depends on selection of cases and even more on the sensitivity of the methods used to detect them, but most of the published figures for rheumatoid arthritis lie between 3 and 27% of cases.⁵

Recent analyses⁶ have shown that the antinuclear factors causing immunofluorescent staining occur in all three major

classes of immunoglobulins—namely, IgG, IgA, and IgM—but their distribution can be of some diagnostic value. For example, the antinuclear factor of systemic lupus erythematosus is found predominantly in the IgG fraction, whereas the similar factor in rheumatoid arthritis is mainly in IgM. It should be emphasized that these are predominant distributions, and in any individual patient in which antinuclear factor is present traces can always be found in the non-dominant fractions. It has, however, recently been claimed⁷ that antinuclear factor found exclusively in the IgM fraction is seen especially frequently in patients with Sjögren's syndrome.

Different patterns of immunofluorescent staining have also suggested that there are varieties of antinuclear factor with affinities for different nuclear components. J. S. Beck⁸ described three such patterns, homogeneous, speckled, and nucleolar, and some evidence indicates that the homogeneous pattern is characteristic of the IgG antinuclear factor, while the speckled pattern is chiefly due to the IgM factor. Another variation known as "flaming" or "shaggy," in which streams of fluorescent material radiate from the nuclei, has been particularly associated with highly active cases of systemic lupus erythematosus.⁹

Several attempts have been made to correlate the presence of the antinuclear factors with the various clinical manifestations of the connective-tissue diseases, especially in patients with rheumatoid arthritis. In the series reported by D. J. Ward, G. D. Johnson, and E. J. Holborow⁵ subcutaneous nodules, vascular lesions, eye lesions, and Felty's syndrome were commoner in the patients with antinuclear factor, but in a similar series described by J. J. Condemni and his associates¹⁰ the only positive association was with subcutaneous nodules, though in general the disease was more severe in those patients with antinuclear factors. In an interesting study in Manchester by D. A. Pitkeathly and G. Taylor⁷ the difficulty of distinguishing the borderline cases of rheumatoid arthritis and systemic lupus erythematosus was avoided by considering all the cases of connective-tissue disorder as one group subdivided exclusively on the presence or absence of antinuclear factors. Since the group with antinuclear factors must have included some cases of systemic lupus erythematosus it is perhaps not surprising that it also showed a higher incidence of such features as skin rashes, vasculitis, and renal disease.

It is evident from these somewhat conflicting reports that the relationships between the antinuclear factors and clinical symptoms still remain to be established. The factors are, however, mainly if not exclusively associated with the connective-tissue group of diseases, and despite the absence of any certain evidence it may be safely concluded that they have some role in the pathogenesis of the disease.

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