insufficient immunosuppression, and some in-vitro tests of lymphocyte function have been devised. A simple, rapid technique for predicting failure of immunosuppression would be of great value. A. Munro and colleagues4 have recently described a "rosette inhibition" test which does appear to do this.

The name is descriptive in the technique depends on interaction between a central cell, usually a monocyte or lymphocyte, and surrounding red cells. Clusters are formed in suspension, and when these are spread out on a slide the appearance of a rosette is produced. The earliest observations on rosetting were made during studies on the destruction of red cells by antibodies in man, when rosette-like agglutinates involving anti-D (rhesus) sensitized red cells and granulocytes from a D-sensitized person were seen. Subsequently it was shown that spleen and lymph-node cells from animals immunized with sheep red blood cells could bind red cells to form rosettes, the number of cells able to do this increasing during the immune response.

When compared to the Jerne plaque test, another technique designed to quantitate antibody-forming cells, the rosette test appeared to be more sensitive.8 Further studies showed that small and medium lymphocytes, lymphoblasts, plasma cells, and macrophages could all act as the central cell.

An important development was the observation that some non-immunized animals carry small numbers of cells capable of forming rosettes with foreign red cells. J.-F. Bach has presented evidence from experiments in mice that these cells are derived from the thymus and that they are special cells for recognizing antigen. He has shown that antilymphocyte serum and some immunosuppressive drugs can inhibit the phenomenon, enabling it to be used as a test of their potency. In a recent review of the technique its use at several centres to assay three samples of antilymphocyte serum is mentioned, with reasonable correlation between the results.

Munro and colleagues have used a system in which human white blood cells react with sheep red cells. It was thought that cells subjected in vivo to the action of immunosuppressive agents might be more susceptible in vitro to the inhibitory action of an antilymphocyte serum of known potency, and it was hoped that the amount of antilymphocyte serum needed to lower the number of rosetting cells would correlate with some aspect of their immune competence. Their results are impressive in that this simple, rapid technique did seem to be able to predict rejection crises in renal allografting.

The immunological basis of this technique is less clear. The method used for separating off the white blood cells is likely to leave a mixed population of lymphocytes, monocytes, and some polymorphs. In addition, different investigators record widely differing figures for the number of rosetting cells per thousand white cells and for the number of individuals whose cells were capable of reacting in this way. R. R. A. Coombs and colleagues15 have expressed doubt whether the phenomenon has an immunological basis at all, in that it cannot be blocked by anti-immunglobulin sera.

While work remains to be done on the theoretical aspects of this test, the empirical observations of Munro and colleagues remain of great interest. Further data will be eagerly awaited, particularly on the question of whether the test can be of general use when more precise control of immunosuppressive therapy is needed.

Control of Oral Anticoagulant Treatment

The dosage of oral anticoagulant drugs of the coumarin type depends on strict laboratory control by the prothrombin time test.1 In this test blood plasma is clotted in the presence of a powerful tissue thromboplastin. With the national reference preparation, the British Comparative Thromboplastin (BCT), the normal prothrombin time is 11-13 seconds. Patients with effective anticoagulation have prothrombin times between 21 and 36 seconds, giving prothrombin ratios (patient's prothrombin time divided by control prothrombin time) of 1.8 to 3.0.2 There are many ways of making thromboplastin extracts, and many different tissues and different species are used in such preparations. Thus different prothrombin times are obtained with the same patient's blood with the various thromboplastin extracts. Without some system of standardization several problems arise. Among them are variation in the intensity of anticoagulation from dangerous overdosage to homoopathic levels; results at one hospital are meaningless at another; levels of anticoagulation in clinical trials are difficult to correlate with the results elsewhere; commercial manufacturers and hospitals who produce their own thromboplastin reagent have no yardstick to apply to successive batches, and considerable variation between batches occurs. All these difficulties have made anticoagulant treatment difficult to apply and empirical.

In Great Britain many hospitals use the same thromboplastin extract—namely, the Manchester Comparative Reagent (MCR) for all their routine tests for anticoagulant control. The MCR is produced at Withington Hospital, Manchester, and at the moment nearly half the larger hospital centres use it. Most of the remaining hospitals in Britain receive a sample of the national reference reagent (BCT), which is also produced at Withington Hospital and for clinical purposes is identical with the MCR. It has been subjected to the strict quality control scheme of the British Committee for Standards in Haematology. Hospitals use a small sample of this reagent to calibrate their commercial or own home-made reagent at regular intervals.3

The second important feature of the British system is that in addition to the national thromboplastin reagent we have a nationally adopted method for reporting prothrombin results—namely, the British Corrected Ratio. This is the ratio which it is calculated would have been obtained had the BCT been used instead of the local thromboplastin.

3 Cameron, J. S., Journal of the Royal College of Physicians, 1971, 5, 282 and 301.
8 Zaalberg, O. B., Meul, V. A. van der, and Twink, M. J. van, Journal of Immunology, 1968, 100, 45.
All hospitals are asked to give the ratio with every prothrombin time result whatever the local system of reporting prothrombin times may be. Previous systems of reporting (prothrombin time, ratio, activity, and index) resulted in clinical confusion. The last twelve months have seen further developments in the British system. National laboratory trials have confirmed the statistical validity of the recommended system and have demonstrated the necessity of follow-up quality control to ensure that the standardization is being correctly applied.

On the international scene the situation is less advanced than in Britain, because there is no agreed standardization of reagents or expression of results. However, the progress made here may provide the basis for international standardization by providing a model for other countries to follow in preparing national thromboplastins. Several countries in the Commonwealth and Europe are now in fact turning to the British system as their model.

1 British Medical Journal, 1969, 4, 125.


Uncharted Territory

On 1 October operation of the Industrial Relations Act started in earnest when the Registrar of Trade Unions and Employers’ Associations opened the register of employers’ and workers’ organizations. The Representative Body at Leicester this year had decided the B.M.A.’s strategy towards the Act by approving in principle that the Association should apply, with certain important provisos, for admission to the Act’s Special Register.

At its meeting last week the Council (see Supplement, p. 23, having been assured that the provisos sought by the Representative Body had been met, discussed the tactical approach to the Act and decided four things: firstly, to make an immediate application for enrolment on the Special Register; secondly to give advance notification to the Health Departments and other employers of doctors that the B.M.A. intended to apply for sole bargaining agencies; and, thirdly, to apply promptly as soon as it was registered. Finally, the Council agreed to set up a working party to study the implications of the Association seeking an “agency shop” agreement.

Since the start of the N.H.S. the B.M.A. and its autonomous committees have been recognized by the Government as the main negotiating bodies for the profession. Other employers of doctors, such as local authorities and most nationalized industries, have similarly recognized the B.M.A. As by far the largest voluntary organization representing all doctors it is appropriate that the Association should seek to be the sole bargaining agent for the profession. This would give it exclusive negotiating rights for each group of doctors in different kinds of employment (that is, N.H.S., local authority, etc.), and each group would then be defined as a bargaining unit. (Definitions of some of the terms in the Act are reproduced in the Supplement, at p. 29.)

The B.M.A.’s claim to be the sole bargaining agent for doctors is intended to guarantee the continuation of existing negotiating machinery, which has stood the test of time. However, the B.M.A. is not in a position to decide that it will be the sole bargaining agent either in the N.H.S. or elsewhere. For the Health Service the Health Departments as employers within the meaning of the Act must agree, and, furthermore, any challenges that may come from other organizations claiming to represent doctors would have to be met before the B.M.A. could achieve its objective. Another problem is that while the position of hospital doctors as employees under the Act is clear, general practitioners though specifically included in the Act by the Government are classified as workers and not employees, a distinction which has raised some uncertainty as to whether they can be recognized in any formal bargaining group.

The relationship of the Health Departments to individual doctors in the N.H.S. at one time threatened to complicate the usefulness of the Act to the profession. Though the Departments are responsible for negotiating centrally with doctors, they do not legally employ them—they are in contract with hospital boards or executive councils—and the Bill was based primarily on the relationship between employer and worker. However, for the purposes of the Act the Departments have now accepted the role of employer so this anomaly should not hinder the continuation of the existing negotiating machinery.

The setting up of a working party to study the “agency shop” position is sensible. If the B.M.A. is recognized as sole bargaining agent and as a further step achieves an agency shop agreement, then every doctor in the field of work covered by the agreement will have to pay an “agency fee” to the Association as a contribution to the costs of negotiation. Members would of course already be paying this fee. In the case of conscientious objection to such a payment a doctor would have to pay an equivalent amount to charity. The B.M.A., however, has always stood against the closed shop principle, and in doing so it has undoubtedly represented the views of nearly all doctors. Though the Government has, with certain limited exemptions, now outlawed the closed shop, an agency shop comes uncomfortably near to being the same thing. While the B.M.A. would welcome 100% voluntary membership by doctors, subscriptions reluctantly given as a legal obligation would cause resentment among many in the profession. On the other hand, running a representative organization is increasingly expensive, and, with every N.H.S. doctor benefitting from the B.M.A.’s efforts whether or not he contributes to the B.M.A., those who do contribute might be glad of some help in sharing the burden. These and other advantages and disadvantages of the agency shop will need careful study.

The practical effects of the Act will to an extent depend on the emergence of “case law.” Furthermore, in the immediate future the Registrar will no doubt have his hands more than full with the activities of T.U.C.-affiliated unions, so it could be some time before the doctors’ negotiating position in the N.H.S. is finally set in the new “industrial environment.” In this uncharted territory, with long-established patterns of negotiations under review, there will be ample opportunity for any and every organization to claim to represent this or that group. This will be a testing time for the B.M.A. and its autonomous committees, and decisions should not be reached hastily. Of all the major issues which will shortly bring major changes in medicine—entering Europe, the reorganization of the N.H.S., reform of the G.M.C., and the new industrial legislation—it is possible that the last will have the greatest practical impact on doctors and on the future of the B.M.A.

1 British Medical Journal Supplement, 1971, 3, 97.