Reports of Societies

HUMAN GAMMA-GLOBULIN

A meeting of the Fever Group of the Society of Medical Officers of Health was held on Nov. 30, 1945, with Dr. M. MITMAN in the chair.

Mr. B. R. RECORD, Ph.D. (Lister Institute), who opened the discussion, said that the realization that the various antibodies present in immune serum were associated with the globulin part of the serum, and indeed for the most part with a particular kind of globulin, had stimulated research into methods of separating human plasma into its component parts. The ultra-centrifuge and the electrophoresis apparatus had proved of the greatest value in this work. In the ultra-centrifuge, human plasma showed, broadly speaking, only two sedimenting boundaries, corresponding to a fast-sedimenting component, globulin, and a slower-sedimenting component, the albumin. In the electrophoresis apparatus, on the other hand, at blood *p*H the serum globulin appeared as at least three distinct components, designated α-, β-, and γ-globulin, in descending order of mobility. These different globulins had essentially the same molecular size and shape, and therefore sedimented as a single boundary in the ultra-centrifuge, but they had different ionizable groups, and therefore different rates of migration in an electric field. For this reason electrophoresis had become a most valuable analytical method in studies on the fractionation of plasma protein. Electrophoresis had not so far been developed for the separation of plasma components on a large scale During the war Cohn and his co-workers had made an extensive study of the alcohol fractionation of human plasma, and this method was used in America for the large-scale preparation of various components of human plasma. Most of the antibody activity had been found to be associated with the γ-globulin fraction, which had been used clinically in the prophylaxis and treatment of measles.

Clinical Trials

Dr. W. GUNN (L.C.C.) said that the development of the clinical use of the various components of human plasma protein followed naturally Cohn's fundamental researches on their separation by high-speed centrifugalization and electrophoresis, and subsequent analysis of their biochemical and immunological characters. The main component, albumin, comprising 50 to 60% of the protein, was shown to have a very high osmotic activity. It was used on a considerable scale in a 25% solution to combat shock among American Service casualties. The globulin fraction originally designated Fraction II, now generally referred to as γ-globulin, represented about 11% of the total protein, and contained all the immune substances in the circulating blood. Though the amino-acid constitution of this fraction differed appreciably from that of α- and β-globulins, attempts to identify and isolate pure antibody, and to correlate its immunological properties with its chemical constitution, had hitherto failed.

Gamma-globulin was prepared in a specially buffered solution having a protein content of $16.5 \pm 1.5\%$ in 5-c.cm. ampoules, each representing approximately 125 c.cm. of the parent plasma (from a pool obtained from several thousand donors). It was relatively stable compared with unaltered human serum and could be heated at 57° C. for four hours without loss of potency; this destroyed the agent of homologous serum jaundice. Samples of Cohn's original Fraction II, and several batches of γ-globulin prepared by different American manufacturers, were made available by the courtesy of the American Red Cross for clinical trial in this country.

Preliminary tests revealed that, volume for volume, γ-globulin was approximately twice as potent against measles as an average pooled convalescent serum. In the trials the recommended American dosage of 0.1 c.cm. per lb. (454 g.) body weight was followed; this was found sufficient for protection at ages under 1 year and over 5 years, but in the most susceptible age group, 1 to 5 years, protection failed in 10 to 15%. In nearly all there was moderate to pronounced attenuation, except in respect of one particular batch. The majority of the inoculations were given to home and hospital, or nursery, measles contacts in and around London, and in Glasgow, where the trials, carried out under the supervision of Dr. T. Anderson at Knightswood Fever Hospital, gave substantially the same results. Some degree of success had been claimed for it by American workers in the prevention of infectious jaundice. The speaker referred to a small unctrolled series of whooping-cough and chicken-pox cases successfully protected, and suggested that its use might be extended to the control of all the ordinary infectious diseases. In the treatment of measles its action had been found less certain, but more clear-cut results might be expected from the intravenous administration of the latest preparation, which Cohn had recently claimed to be free from risk.

Comparison with Convalescent Serum

Dr. NORMAN D. BEGG (L.C.C.) described a comparative test between γ-globulin and a dried, reconstituted, batch of convalescent measles serum. As modification of attack and not prevention was the aim, dosage had been pitched low. He summarized the experience of five outbreaks of measles in whooping-cough wards. Of 22 susceptible contacts injected with 2.5 c.cm. of the convalescent measles serum, 12 developed measles and only 4 of these were very sharply attenuated; 24 contacts of comparable ages from the same outbreaks injected with 1.2 c.cm. of γ-globulin produced 8 cases of measles, of which 6 were very much modified. The result of this limited experience indicated that γ-globulin had a measles antibody content at least twice that of convalescent measles serum, but further experience was necessary to fix dosage more precisely, and to decide on the importance of adjusting dosage to body weight at various ages.

For the prevention of measles in exposed contacts he had tried the American recommendation of 0.1 c.cm. per lb. body weight, with results which indicated that, with adequate preliminary field-testing of individual batches, γ-globulin would give high protection rates in this dosage. The results of treating established measles had been disappointing. One case in particular given 15 c.cm. of γ-globulin intramuscularly when the first Koplik's spots were visible, and 54 hours before the skin eruption appeared, had later developed an entirely unmodified attack of measles.

Treatment of Poliomyelitis

Dr. W. H. KELLEHER (L.C.C.) said that the value of any serum in the treatment of poliomyelitis was doubtful. He had abandoned the use of convalescent poliomyelitis serum for this purpose, but decided to treat a series of cases with γ-globulin. The results in 10 cases of poliomyelitis, given an average dose of 34 c.cm., were entirely negative. Inconclusive results had been obtained in treating two cases of acute toxic polyneuritis, and no improvement resulted from the use of γ-globulin in one case of acute myelitis. He had noted a failure to develop paralysis in poliomyelitis contacts with definite cerebrospinal-fluid changes who had been injected with γ-globulin, but this was a naturally occurring phenomenon and probably without significance. In reply to a question he said that he had not given γ-globulin intrathecally, and that there were physiological reasons against antibody reaching the anterior horn cells by that route.

Dr. H. J. PARISH (Beckenham) thought that the apparent complete failure of γ-globulin in the treatment of measles indicated that its antibody content might not be so high as was thought; and he suggested that it would be worth while preparing γ-globulin from convalescent measles serum in an attempt to produce a therapeutic measles serum.

Changes in the industrial service provided by the Royal Society for the Prevention of Accidents are to have effect in April. This is due to the ending of the arrangements made with the Ministry of Labour and National Service in 1940, by which a free wartime basic service of accident-prevention material was supplied to several thousand firms engaged on war work. Under the new arrangement the industrial side of the society will revert to a membership basis, though it will continue to work in the closest touch with the Government. Service will be provided on a co-operative, non-profit-making basis. A new membership scheme will replace the earlier one in operation up to 1940. As support from industry is increased, services will be extended and improved according to a definite plan which has been worked out during the past eighteen months. Notice of the change has been given to industrial undertakings in a circular issued from Terminal House, 52, Grosvenor Gardens, London, S.W.1.