Inquiry failed to reveal any increase in the incidence of infective hepatitis during the period under review in the North-West Region, the population of which is 3,250,000. In another part of England the attack rate per 1,000 per annum was 0.06 in 1945, 0.07 in 1946, and 0.04 in 1947 in a population of 2,600,000 (McFarlan—personal communication).

In the production of small-pool plasma a record of the donors who contributed to each pool was available, and a follow-up of these donors was carried out so far as was possible, but in only one out of the 63 donors traced was there a history of jaundice. In this case jaundice occurred three months after blood donation. No information such as history of contact with infective hepatitis or of inoculation was given. The donors whose bloods were involved in homologous serum jaundice in the whole-blood series were also followed up, but with negative results.

Summary

In the follow-up of 4,430 patients who had received transfusion therapy 134 (3%) cases of jaundice were discovered, of which seven (0.2%) terminated fatally.

Large-pool plasma and combined large-pool plasma and blood transfusions were responsible for 100 (74.6%) of the cases, six of which were fatal.

The incidence rates of homologous serum jaundice for small-pool plasma (1.3%) and for whole blood (0.8%) are not significantly different (difference/S.E. of difference = 1, approx.), but these rates differ very considerably from that of large-pool plasma (11.9%).

The findings suggest that at least 0.35% of donors are probably carriers of the icterogenic virus.

REFERENCES

- Brightman, I. J., and Korns, R. F. (1947). *J. Amer. med. Ass.*, **135**, 268.
Lancet, 1943, **1**, 83. (Memo by Medical Officers of the Ministry of Health.)
 MacNalty, A. S. (1938). Annual Report of the Chief Medical Officer, Ministry of Health for 1937, London, p. 38.
 Sawyer, W. A., Meyer, K. F., Eaton, M. D., Bauer, I. H., Putnam, P., and Schwentker, F. F. (1944). *Amer. J. Hyg.*, **39**, 337; **40**, 35.
 Spurling, N., Shone, J., and Vaughan, J. (1946). *British Medical Journal*, **2**, 409.

One of the German casualties of the war was the *Archiv für Schiffs- und Tropenhygiene*, and for over four years the Germans have been without a national journal devoted to tropical medicine. This gap has now been filled by the publication of the *Zeitschrift für Tropenmedizin und Parasitologie*, which is edited by workers at the Bernhard Nocht-Institut für Schiffs- und Tropenkrankheiten, Hamburg, and published by Georg Thieme, of Stuttgart. In their prefatory note the editors point out that, while opportunities for German workers in the Tropics are now almost non-existent, many problems concerning tropical medicine can be investigated in the laboratory at home, and that as a result of the war many cases of tropical disease in Germany make ample material available for clinical investigation. Subscription to the new journal is approximately £4 per annum. Dutch investigators also suffered a setback when publication of the *Geneeskundig Tijdschrift voor Nederlandsch Indië* was stopped by the Japanese in March, 1942, after having appeared without interruption since 1852. This journal was replaced in 1946 by the *Medisch Maandblad*. Both these journals have the disadvantage, so far as English readers are concerned, of being almost entirely in Dutch. To overcome this difficulty the Dutch have now commenced publication of an English-language quarterly journal of tropical medicine and hygiene, *Documenta Neerlandica et Indonesica de Morbis Tropicis*, with an editorial board representative both of the Netherlands and its overseas territories. Subscription to this journal is £1 2s. 6d. per annum, and it is published at Rivierenlaan 268, Amsterdam Z.

ISO-IMMUNIZATION BY BLOOD-GROUP FACTORS A AND B IN MAN

BY

PIERRE O. HUBINONT, M.D.

(From the Laboratoires d'Hygiène et de Bactériologie de la Faculté de Médecine, Université Libre de Bruxelles)

Much has been written about the possibility of the blood-group factors A and B acting in the same way as the Rh factor in the pathogenesis of haemolytic disease of the newborn. Jonsson (1936) gave the first immunological evidence, of a statistical nature, that heterospecific blood-group pregnancy (where the O or B mother bears a foetus of group A or AB) was accompanied by a rise of the anti-A haemolysin. Smith (1945) demonstrated that the anti-A or anti-B agglutinin titre rose only in the cases in which the heterospecific foetus was a secretor. The heterospecific pregnancy is then capable of inducing an immune response, but there are very few heterospecific foetuses that demonstrate haemolytic disease. In consequence, there must be some protective mechanism, several of which were reviewed by Tovey (1945).

There are, however, certain facts which focus the attention on the antibody itself. In 1946 we found in the blood of pregnant women who had previously been delivered of stillborn babies anti-A agglutinins reacting far more strongly at 37° than at 4° C. (Millet and Hubinont, 1946a; Hubinont and Millet, 1946). Bruynoghe (1947) found an anti-B agglutinin of the same type in a case of haemolytic disease of the newborn. Since then we have met with several similar cases in which the clinical course was somewhat different from the classical haemolytic disease of the newborn. In all cases the foetus died *in utero* a few days before delivery or during labour.

Many authors—the first of them being Levine, Katzin, and Burnham (1940)—have emphasized that anti-Rh agglutinins react more strongly at 37° than at 4° C. Inversely, it is very well known that natural anti-A or anti-B agglutinins possess a thermal optimum at 4° C.

We verified that several normal agglutinins of rabbit serum (Millet and Hubinont, 1946b; Hubinont, 1948a) and guinea-pig serum (Hubinont, 1947) showed, through immunization, the same change of thermal optimum that we found in our patients. Further investigations on the rabbit showed that hyperimmunization with sheep erythrocytes was often followed by the production of a blocking antibody, giving a prozone phenomenon in quantitative agglutination tests (Hubinont, 1948b).

We recently had the opportunity of studying the immune-response of a group B individual who was transfused by mistake with A₁ blood and eventually recovered: 75 ml. of whole blood had been injected before alarming symptoms appeared.

The serum was tested at regular intervals with A₁ and A₂ cells collected from the same donors. The tests were performed by the usual technique in tubes, using 0.9% saline as diluent, each test being performed simultaneously at 4° and 37° C. The results are shown in the Table.

On the day of transfusion both A₁ and A₂ cells were agglutinated with the same titre and thermal optimum. On the fourth day there was a small increase in titre, noticeably higher for A₁ than for A₂ cells. On the eighth day the thermal optimum for A₁ agglutination turned to 37° C. Finally, on the 30th day the agglutination was stronger at

37° C. for both A₁ and A₂ cells. Further, there was a prozone phenomenon in the test for A₁ agglutination at 4° C. It was shown by a blocking test (Race, 1944; Wiener, 1944) that this prozone was due to the presence of an anti-A blocking antibody.

Time of Test	Cells	Temp.	Serum Dilutions											T
			1/1	1/2 ¹	1/2 ²	1/2 ³	1/2 ⁴	1/2 ⁵	1/2 ⁶	1/2 ⁷	1/2 ⁸	1/2 ⁹		
Day of transfusion	A ₁	37° C.	½	++	+	w	—	—	—	—	—	—	—	
	A ₂	4° C.	3½	3½	3½	2½	2	—	++	++	—	—	—	
		37° C.	++	+	w	2	1	++	++	—	—	—	—	
4th day	A ₁	37° C.	2	2	1	+	w	—	—	—	—	—	—	
	A ₂	4° C.	4	4	4	3	3	—	—	—	—	—	—	
		37° C.	++	++	(+)	?	?	++	+	—	—	—	—	
8th day	A ₁	37° C.	4	4	4	4	4	3	2	1	½	++	—	
	A ₂	4° C.	4	4	4	4	4	3	2	2	++	(+)	—	
		37° C.	4	4	4	3½	3	2½	1	++	++	++	—	
30th day	A ₁	37° C.	2½	4	3	3½	3½	3½	3	2½	2	2	—	
	A ₂	4° C.	++	(+)	+	++	3½	3½	3	3	2	1	++	—
		37° C.	2	2	+	+	3	3	3	2	2	1	1½	—

Scores for agglutination are given in arabic signs (for visual agglutination) and the signs usually employed for microscopical agglutination in Rh work (M.R.C. Memorandum, 1943).

Unfortunately the patient could not be followed up, and we are not aware of his actual agglutination pattern for A₁ and A₂ cells. Nevertheless, his immune response to an incompatible transfusion confirms our observation of ABO iso-immunization in pregnant women and of experimental hetero-immunization in rabbits.

Upon immunization with an antigen corresponding to a natural agglutinin present in the animal's serum (anti-A or anti-B in man, anti-sheep in rabbits), the first noticeable change would be a slight rise in titre, followed quickly by an inversion of the thermal optimum in quantitative agglutination tests. A further step would be the apparition of a prozone corresponding to the production of "blocking antibodies."

The *in-vitro* differences in the behaviour of "natural" cold anti-A and anti-B agglutinins and the "immune" warm anti-A and anti-B antibodies are probably dependent on their chemical structure, which would account for their harmfulness to the foetus. It is a significant fact that we found these warm agglutinins in the only instances quoted above with their particular clinical course, and that they were not found in uneventful heterospecific blood-group pregnancies.

Summary

A case of immune response to an incompatible blood-group transfusion is described. There is a definite difference *in vitro* between natural and immune anti-A agglutinins.

The same difference is found in maternal iso-immunization, the particular form of haemolytic disease following A and B sensitization being the death of the foetus *in utero*, either during the last days of pregnancy or at the time of delivery.

REFERENCES

- Bruynoghe, R. (1947). Quoted by R. Heffinck, *Pr. méd.*, **55**, 823.
 Hubinont, P. O. (1947). Unpublished data.
 — (1948a). *C.R. Soc. Biol., Paris*, **142**, 1457.
 — (1948b). *Ibid.*, **142**, 1458.
 — and Millet, M. (1946). *Gynéc. et Obstét.*, **45**, 718.
 Jonsson, B. (1936). *Acta path. microbiol. scand.*, **13**, 424.
 Levine, P., Katzin, E. M., and Burnham, L. (1940). *Proc. Soc. exp. Biol., N.Y.*, **45**, 346.
 Millet, M., and Hubinont, P. O. (1946a). *Acta clin. belg.*, **1**, 452.
 — (1946b). *C.R. Soc. Biol., Paris*, **140**, 1227.
 Race, R. R. (1944). *Nature, Lond.*, **153**, 771.
 Smith, G. H. (1945). *J. Path. Bact.*, **57**, 113.
 Tovey, G. H. (1945). *Ibid.*, **57**, 295.
 Wiener, A. S. (1944). *Proc. Soc. exp. Biol., N.Y.*, **56**, 173.

DIAGNOSIS AND TREATMENT OF CUTANEOUS ANTHRAX

BY

JOHN A. HOLGATE, M.B., Ch.B.

Demonstrator, Department of Physiology, University of Leeds; Formerly House-physician to the Department of Dermatology, General Infirmary at Leeds

AND

REGINALD A. HOLMAN, M.B., Ch.B.

Demonstrator, Department of Bacteriology, University of Leeds

Anthrax—a rare disease in this country—has many interesting and unusual facets. Probably first recorded by Virgil, it became prominent initially in Britain about the middle of the last century coincidentally with the importation of alpaca and mohair to Bradford. It was first notifiable so far as factories and workshops were concerned in 1896, and activity was rapidly directed towards its prevention in view of the high proportion of fatalities among affected workers—then some 20 to 30%. Local precautions in the form of protective clothing, the posting of information regarding the disease, washing facilities, and exhaust ventilation for certain processes were advocated by the Anthrax Investigation Board set up in Bradford by the Chamber of Commerce. Despite these the incidence remained high, though the dread and fatal form of pulmonary infection showed a rapid decline between 1881, when Mr. John Spear made his investigations, and 1905, when Dr. T. M. Legge gave the classical Milroy Lectures on industrial anthrax.

A further Anthrax Investigation Committee set up in 1913 advocated, in 1918, a process for wool and hair disinfection. Following up the committee's suggestions, Parliament passed the Anthrax Prevention Act in 1919, and by 1921 an experimental disinfecting station had been set up in Love Lane, Liverpool, to carry out the "Duckering process"—named after the secretary of the above committee—for wool and hair disinfection, and in succeeding years this process has proved its efficacy. Mention should be made of the excellent bacteriological investigations carried out for both the board and the committee by the late Dr. F. W. Eurich, professor of forensic medicine at the University of Leeds.

From 1890 to 1920 an increase in the incidence of anthrax was also noticed in the cattle of Great Britain, though the numbers were never comparable to those encountered in Russia, Siberia, China, and parts of India. Knowledge about the means of spread of the disease and the life history of the organism enabled measures to be taken which may be briefly summarized under the headings of—notification, isolation, and destruction of the sick animal or carcass, disinfection of the surroundings, and inoculation of other animals. These not only rapidly controlled the disease among cattle but also diminished the incidence among butchers, veterinarians, shepherds, and others associating with animals, the true index of which was never known, since only cases occurring in certain trades were then notifiable. This anomaly of notification was widely commented upon in coroners' courts, medical journals, and Parliament at the time.

In the four or five years following 1915 the incidence of anthrax increased both here and in America, the source being shaving-brushes made from infected hair. This source was soon recognized as being especially dangerous, since it was not confined to any particular trade or industry, claiming among its victims a professor of law and a