number of occasions attention has been drawn to the time relationship between the disappearance of foetal haemoglobin in infants and the onset of their susceptibility to malignant malaria (Lehmann, 1953; Allison, 1954; Davidson, 1955; Gilles, 1957). One of the possible explanations is a protective role of foetal haemoglobin. Haemoglobin-S/high-haemoglobin-F individuals and haemoglobin-C/high-haemoglobin-F individuals might then be especially favoured.

Summary

Two Ghanaian families are reported whose members illustrate interaction between the high F gene and the genes responsible for haemoglobins A, S, and C. Persistence of a high level of foetal haemoglobin was not associated with anaemia or morphological abnormality, except for numerous target cells in the haemoglobin C-F combination. The possible significance of the high F gene is discussed.

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"Representatives of the Library Association met the Libraries Committee of the Association of Municipal Corporations to discuss the provision of better library services in hospitals. Agreement was reached upon a number of principles which should govern the administration of these services and a memorandum embodying the views of the two Associations was subsequently circulated to the other associations of local authorities and to the voluntary bodies concerned. It was decided that if agreement could be reached between all the organizations interested, a deputation should be sent to the Minister of Health asking him to initiate action along the lines agreed." (*Annual Report, 1961*, Library Association.)

RICKETTSIAL AND VIRAL ANTIBODIES IN MULTIPLE SCLEROSIS

BY

CONSTANCE A. C. ROSS, M.D.

Senior Registrar in Virology, University Regional
Virus Laboratory, Ruchill Hospital, Glasgow

The presence of micro-agglutinating antibodies in sera from cases of multiple sclerosis has been reported by Le Gac (1960) and by Le Gac, Giroud, and Dumas (1960), the most common being antibodies to *Rickettsia burneti* (Q fever). Although no control cases were examined Le Gac concluded that rickettsiae might be causal agents in many cases of multiple sclerosis, and on the basis of his findings he advocated treatment with broad-spectrum antibiotics.

During the past year we have been carrying out a virological investigation of specimens from cases of multiple sclerosis. Part of this investigation has comprised serological examination by complement fixation (C.F.) for antibodies to several viral agents which have been associated with disturbance of neurological function. In view of the findings of Le Gac and his colleagues we have also examined the sera for C.F. antibodies to various rickettsial agents. It was realized that if a viral or rickettsial agent were responsible for initiating the disease it might have done so many years previously and that the antibody might no longer be detectable by C.F. technique. On the other hand, if the agent were latent in the central nervous system it might provide a constant antigenic stimulus manifesting itself in high C.F. antibody.

No control cases were included in this preliminary investigation as its purpose was to assess the distribution of several viral and rickettsial antibodies in sera from cases of multiple sclerosis so that subsequently, in an adequately controlled series of cases, there need be no examination for antibodies which were absent in the preliminary investigation.

Materials and Methods

Single specimens of sera were obtained from 36 patients aged 28 to 64 with chronic multiple sclerosis. From four other patients aged 19 to 47 paired sera were obtained during an acute relapse (in two of these cases the disease was of less than one year's duration), the first serum being taken early in the relapse and the second serum 10 to 14 days later. In all 40 cases the diagnosis of multiple sclerosis had been made by a neurologist.

All 40 sera were examined by C.F. technique as previously described (Ross, 1961a). Rickettsial C.F. antigens comprised *R. burneti* (Q fever), *R. mooseri* (the causative agent of murine typhus but sharing a common C.F. antigen with epidemic typhus), and *R. akari* (the causative agent of rickettsialpox but sharing a common C.F. antigen with other members of the spotted-fever group). Viral C.F. antigens comprised psittacosis-lymphogranuloma group (P-LGV), louping-ill, lymphocytic choriomeningitis, herpes, and mumps. Both mumps soluble (S) and viral (V) antigens were used, as mumps S antibodies disappear within a few weeks of infection whereas V antibodies remain high for many years. Antigens and uninfected control antigens were prepared as follows: mumps S, mumps V, and P-LGV

from fertile hens' eggs—chorioallantoic membrane, allantoic fluid, and yolk-sac respectively; louping-ill and herpes as previously described (Ross, 1961a and 1961b respectively). *R. burneti* and lymphocytic choriomeningitis were kindly supplied by the Central Public Health Laboratory, Colindale; typhus and rickettsialpox by Cyanamid of New York. For the test each antigen was used at optimal dilution as determined by chessboard titration against homologous standard positive serum.

Results

The range of serological C.F. titres against the various antigens is shown in the accompanying Table. Negative results (titres <8) were obtained in all sera for Q fever, typhus, and louping-ill. Neutralization tests for louping-ill, which were carried out by Dr. J. S. Porterfield, on the first 28 sera received were also all negative (see

Complement-fixation Titres in 40 Cases of Multiple Sclerosis

Titre	No. of Cases in Tests							
	Q Fever (<i>R. burneti</i>)	Typhus (<i>R. mooseri</i>)	Rickettsialpox (<i>R. akari</i>)	Psittacosis- lympho- granuloma	Louping-ill	Lymphocytic Chorio- meningitis	Herpes	Mumps S
≤ 8	40	40	38	36	40	38	7	36
8-32	0	0	2	3	0	2	20	4
Over 32	0	0	0	1	0	0	13	0
								Mumps V
								11
								28
								1

Appendix). Rickettsialpox tests were negative in all but two cases, both sera giving titres of 8; as one of the sera gave a titre of 64 with psittacosis the rickettsialpox titre was probably a cross-reaction. Lymphocytic choriomeningitis tests were negative except in two cases, both with serum titres of 8.

Fixation with P-LGV group antigen was detected in four cases. From one of these, a chronic case of multiple sclerosis, paired sera had been obtained during an acute relapse and showed a rising titre from 4 to 16. No history of recent contact of patient with psittacine birds could be obtained. A further specimen of serum obtained from this patient 14 months later showed no detectable antibody to P-LGV.

Herpes and mumps antibodies were detected in most of the patients: herpes in 33 (82.5%), mumps V in 29 (72.5%).

Discussion

Our mainly negative results for rickettsial antibodies are not in keeping with the findings of Le Gac *et al.* (1960), who reported that rickettsial or neorickettsial antibodies were present in sera from 23 of 27 cases of multiple sclerosis, the commonest being antibodies to *R. burneti* (10 cases) and to *R. prowazeki* (6 cases). It is possible that their technique—namely, micro-agglutination—was more sensitive than C.F. This seems unlikely, as Wentworth (1955) has reported that C.F. antibodies for *R. burneti* persist longer than tube-agglutinating antibodies (no comparison of the relative sensitivity of tube-agglutinating and micro-agglutinating antibodies has been found). Thus, because of this failure to corroborate the findings of Le Gac and his colleagues, and because of the absence of control cases in their series, there would seem to be no indication for treatment of multiple sclerosis with broad-spectrum antibiotics.

The absence of controls in the present investigation again means that no significance can be placed on our positive findings. The high proportion of positive

results for herpes and mumps V antibodies might well be the same in a control group, as herpes and mumps are common infections of childhood. The finding of antibodies for P-LGV in four cases was more surprising: Grist (1954, 1960) found that, in Glasgow, positive C.F. reactions to P-LGV were rare. To establish the significance of these findings a further study of antibodies to herpes, mumps, and psittacosis-lymphogranuloma is now being carried out in an adequately controlled series.

Summary

Sera from 40 cases of multiple sclerosis were examined by complement fixation against several rickettsial and viral antigens—namely, Q fever, typhus, rickettsialpox, psittacosis-lymphogranuloma, louping-ill, lymphocytic choriomeningitis, herpes, and mumps. The majority of the sera were also examined for louping-ill antibodies by a tissue-culture neutralization test.

Mainly negative C.F. results were obtained with rickettsial antigens; thus we failed to support the positive rickettsial microagglutination results of Le Gac *et al.* (1960).

As there were no control cases in this preliminary investigation the significance of our positive findings for herpes, mumps, and P-LGV requires further study in an adequately controlled series of cases.

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APPENDIX BY DR. J. S. PORTERFIELD, NATIONAL INSTITUTE FOR MEDICAL RESEARCH, MILL HILL, LONDON

Tests for neutralizing antibodies to louping-ill virus were carried out by a modification of the plaque-neutralization technique described for yellow-fever virus (Porterfield, 1959). Equal parts of a 1:20 dilution of each serum to be tested and louping-ill virus diluted to contain 200 plaque-forming units per ml. were incubated for two hours at 36° C. together with known negative and positive control sera. Each mixture was then applied to duplicate chick fibroblast cultures in Petri dishes, which were incubated for a further two hours at 36° C. The cultures, together with other Petri dishes infected with control dilutions of virus, were overlaid with agar containing 5% of newborn calf serum (Porterfield, 1962) and the number of plaques which developed was recorded on the fifth and sixth days. None of the sera from cases of multiple sclerosis reduced the plaque count as much as 20%; a control louping-ill immune serum gave complete neutralization at 1:20 and 97% neutralization at 1:100 dilutions of serum.

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