INHERITANCE OF ANTIBODY RESPONSE

V. CORRELATED ANTIBODY RESPONSES TO VARIOUS RELATED AND UNRELATED ANTIGENS

By K. M. ADAMS* and W. R. SOBEY*

[*Manuscript received June* 16, 1961]

Summary

A number of correlation coefficients of responses of antibody injections of like and unlike antigens are presented. There is a suggestion that there is present a predisposition to immunity. The findings of negative correlations are discussed in view of suggestions of error of measurement of responses.

I. INTRODUCTION

For some time past it has been known that animals of the same species show a marked variation in their responses to a given antigen.

Experiments have been carried out in the past (Carlinfanti and Cavalli 1945, 1947; Carlinfanti 1947, 1950; Sang and Sobey 1954) on the problem of predisposition for immunity. Carlinfanti (1947) states that a correlation does exist among the titres of antibodies produced by one subject in response to different antigens. He suggests that this correlation decreases, however, until it reaches a value not significant from zero, when antibodies of different types are considered.

The importance of such a predisposition, if real, is great and has great bearing on the whole problem of immunity.

Sang and Sobey (1954) examined the genetic features which control the response of antibodies and have stressed the importance of genetic constitution in determining ability to produce antibodies.

The experiments to be described, using related and unrelated antigens in mice and rabbits, gave information to help in the clarification of this problem.

II. MATERIALS AND METHODS

(*a*) *Antigens for Mice*

Rhizobium meliloti, strain "Sydney University 277/1" and the mouse-adapted strains of influenza virus MEL and LEE were used in this investigation.

Mice were given 5×10^8 rhizobial organisms/ml, in two 0·5 ml intravenous injections spaced by 4 days. They were bled 7 days after the last injection.

The two virus preparations were injected simultaneously; 0·25 ml each of strains MEL and LEE were administered by the intraperitoneal route. Mice were bled 14 days after the last injection for the MEL titration and 18 days after injection for the LEE titration.

* Division of Animal Genetics, C.S.I.R.O., University of Sydney.

(*b*) *Antigens for Rabbits*

Influenza virus strains MEL and LEE, vaccinia virus, tobacco mosaic virus (TMV), and potato X virus were used.

Rabbits were injected intravenously with 0·25 ml of each of the influenza virus preparations simultaneously. They were bled as described for mice injected with this preparation.

Two intravenous injections of 1 ml, each containing 0·5 mg TMV and 0·25 mg potato X virus, were given, spaced by 1 week, to rabbits which were bled 10 days after the last injection.

Vaccinia virus was administered in one 0·5 ml intravenous injection and rabbits were bled 10 days later.

TABLE 1

CORRELATION COEFFICIENTS OF RESPONSES TO VARIOUS ANTIGENS IN MICE

MEL, LEE represent influenza strains MEL and LEE respectively, and O, Vi represent the O and Vi antigens of *Rh. meliloti*. N = neutralizing potency titre; A = antihaemagglutinin titre

No.	Antigen Responses Correlated	Correlation Coefficient*	Degrees of Freedom	No.	Antigen Responses Correlated	Correlation Coefficient*	Degrees of Freedom
1	MEL(N)–LEE(N)	0·51	201	8	O–MEL(N)	−0·09	216
2	MEL(A)–LEE(A)	0·32	194	9	O–MEL(A)	−0·10	212
3	MEL(N)–MEL(A)	0·59	212	10	O–LEE(N)	−0·04	212
4	LEE(N)–LEE(A)	0·71	212	11	O–LEE(A)	0·10	208
5	MEL(N)–LEE(A)	0·47	198				
6	MEL(A)–LEE(N)	0·29	198	12	Vi–MEL(N)	−0·02	216
				13	Vi–MEL(A)	−0·04	212
7	O–Vi	0·34	256	14	Vi–LEE(N)	−0·01	212
				15	Vi–LEE(A)	−0·03	208

* S.E = 0·14.

(*c*) *Serological Techniques*

(i) Rhizobium meliloti.—The method of detection of antibodies to this organism, containing a Vi-like and O antigen, are described in detail in Part IV of this series (Sobey and Adams 1961).

(ii) *Influenza Virus.*—Responses in mice to injection of both strains of this virus were measured for antihaemagglutinin and neutralizing titre, whilst in rabbits antihaemagglutinin titre only was measured. Methods of measurement were as previously described (Sobey and Adams 1961).

(iii) *Vaccinia Virus.*—Production of antibodies to this virus was measured by the antihaemagglutinin method.

(iv) *TMV and Potato X Virus.*—Titration of antisera were measured by the equivalence zone method as described by Sang and Sobey (1954).

(*d*) *Experimental Animals*

(i) *Mice.*—128 daughter/dam pairs of adult albino mice weighing about 25 g, obtained from a randomly bred stock maintained in this Laboratory, were used. The mice were prepared as for an earlier experiment (Claringbold, Sobey, and Adams 1957). For convenience, the experiment was divided into four blocks. Each block comprised 32 boxes of dams and 32 corresponding boxes of daughters. The mice were given standard mouse cubes and water *ad lib.*

(ii) *Rabbits.*—50 randomly bred adult rabbits of both sexes weighing about 2·5 kg were used. The rabbits were given standard rabbit pellets and water *ad lib.*

TABLE 2

CORRELATION COEFFICIENTS OF RESPONSES TO VARIOUS ANTIGENS IN RABBITS

TMV = tobacco mosaic virus; X = potato X virus; V = vaccinia virus; MEL, LEE = influenza virus strains MEL and LEE respectively

No.	Antigen Responses Correlated	Correlation Coefficient*	Degrees of Freedom	No.	Antigen Responses Correlated	Correlation Coefficient*	Degrees of Freedom
1	TMV–X	0·35	50	6	MEL–LEE	0·97	50
2	TMV–MEL	0·53	50	7	MEL–V	0·14	50
3	TMV–LEE	0·62	50	8	LEE–V	0·14	50
4	X–MEL	−0·17	50	9	TMV–V	0·21	50
5	X–LEE	−0·09	50	10	X–V	−0·21	50

* S.E = 0·16.

III. RESULTS

The correlation coefficients of the responses to various antigens tested in mice are shown in Table 1. It is seen that there are strong correlations between responses to like antigens whilst weak or negative correlations are found between responses to unlike antigens; however, the like antigens are two strains of the same virus.

Correlation coefficients of the responses to antigens tested in rabbits are shown in Table 2. No regular pattern of correlation seems to appear from these data.

For example, the animal influenza and vaccinia viruses have weak correlated responses, one with the other, yet between TMV, a plant virus, and the influenza viruses there is a strong correlation. Correlation between potato X and vaccinia or potato X and influenza viruses is of a negative value.

It is of importance to know if an animal which is a good responder to a particular antigen is likely to be a good responder when challenged with another type of antigen, even if the antigens be unrelated.

The total variance found in these two experiments can be apportioned into that found within and between animals. If the latter exceeds the former, as

measured by the usual F test, it can be taken that responses to the antigens are unlikely to be randomly distributed and hence that individual animals tend to produce a similar type of response to each antigen. This calculation is derived from the formula given by Sang and Sobey (1954). The difference between mice gives $F_{210\text{-}2940} = 3{\cdot}75$ and between rabbits gives $F_{49\text{-}441} = 3{\cdot}3$. These significant results suggest a predisposition to immunity in both mice and rabbits.

IV. Discussion

The overall results from both mice and rabbits suggest from positive correlations that there may be a pattern in correlation of response between like antigens whilst unlike antigens give weak or negative correlations.

Suggestion of a predisposition to immunity and the likelihood of individuals producing similar responses to antigens would make it of interest to continue and expand this study to include antigens of similar molecular weight, protein pattern, or origin.

If the arguments advanced by Sobey and Adams (1955, 1961) that there is an error of measurement of response due to antigen complexity resulting in formation of a diverse family of antibodies, is correct, then the absence of an observed correlation does not necessarily rule out a predisposition to immunity. A positive correlation, however, is presumably real since information can be taken from but not added to data.

V. Acknowledgments

The authors would like to thank Professor J. M. Vincent, Faculty of Agriculture, University of Sydney, for the supply of rhizobial organisms, and Dr. M. Zaitlin, formerly of the Division of Plant Industry, C.S.I.R.O., for the potato X virus.

VI. References

Carlinfanti, E. (1947).—Proc. 4th Congr. Int. Microbiol., Copenhagen, 1947. pp. 313–14.

Carlinfanti, E. (1950).—*Sci. Med. Ital.* **1**: 513–33.

Carlinfanti, E., and Cavalli, L. L. (1945).—*Boll. Ist. Sieroter. Milano* **24**: 215–32.

Carlinfanti, E., and Cavalli, L. L. (1947).—*Estr. Riv. Ist. Sieroter. Ital.* **22**: 129–58.

Claringbold, P. J., Sobey, W. R., and Adams, K. M. (1957).—*Aust. J. Biol. Sci.* **10**: 367–73.

Sang, J. H., and Sobey, W. R. (1954).—*J. Immunol.* **72**: 52–65.

Sobey, W. R., and Adams, K. M. (1955).—*Aust. J. Biol. Sci.* **8**: 603–14.

Sobey, W. R., and Adams, K. M. (1961).—*Aust. J. Biol. Sci.* **14**: 588–93.