

ALLOGRAFT REJECTION
and the
RETICULOENDOTHELIAL SYSTEM

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TABLE OF CONTENTS

| | |
|-------------------|--|
| SIGNED STATEMENT | viii |
| ABSTRACT | ix |
| <u>CHAPTER I</u> | <u>Introduction and Review of Literature</u>1 |
| <u>CHAPTER II</u> | <u>Materials and Methods</u>49 |
| | Experimental animals.....49 |
| | Mice.....49 |
| | Rabbits.....49 |
| | Bacterial strains.....49 |
| | Radioactive isotope labelling of bacteria.....50 |
| | Opsonisation of bacteria.....51 |
| | Opsonic activity of mouse serum.....52 |
| | Bacterial clearance studies.....52 |
| | Organ distribution of isotopically labelled bacteria.....54 |
| | Skin grafting in mice.....54 |
| | Donor skin.....55 |
| | Graft removal.....57 |
| | Splenectomy in mice.....58 |
| | Washing of glassware.....58 |

| | |
|---|----|
| Preparation of cell suspensions..... | 59 |
| Lymphoid cells..... | 59 |
| Peritoneal cells..... | 59 |
| Viability counts..... | 60 |
| Cell counts..... | 61 |
| (i) Peripheral white cell counts..... | 61 |
| (ii) Differential counts..... | 61 |
| (iii) Bacterial counts..... | 61 |
| Collection of sera..... | 62 |
| (i) Mouse serum..... | 62 |
| (ii) Pig serum..... | 62 |
| Antibody production..... | 63 |
| (i) Antigen employed..... | 63 |
| (ii) Immunisation of mice with sheep erythrocytes..... | 63 |
| (iii) Estimation of haemagglutination titre..... | 64 |
| (iv) Immunisation of mice with bovine serum albumin (BSA)..... | 64 |
| (v) Estimation of anti BSA antibody levels (Precipitation)..... | 64 |
| (vi) Diazotisation of BSA onto sheep erythrocytes (Haemagglutination)... | 66 |
| Histological studies | 67 |

| | |
|--|----|
| Carbon | 67 |
| Preparation of rabbit anti mouse lymphocyte serum..... | 68 |
| Absorption of anti mouse lymphocyte serum..... | 69 |
| Assay of anti mouse lymphocyte serum..... | 69 |
| Leukocyte agglutination..... | 70 |
| Skin graft assay..... | 71 |

CHAPTER III

| | |
|--|-----------|
| <u>The effect of skin allograft rejection on the activity of the reticuloendothelial system.....</u> | <u>72</u> |
| Introduction..... | 72 |
| Phagocytic activity in allografted animals..... | 74 |
| The temporal relationship between allograft rejection and changes in phagocytic activity.... | 76 |
| Dose dependency of changes in phagocytic activity..... | 78 |
| Phagocytic activity in animals bearing F ₁ grafts.. | 78 |
| Organ changes during skin allograft rejection.... | 79 |
| Organ distribution of radioactivity..... | 81 |
| Phagocytic activity in splenectomised mice..... | 82 |
| Transfer of antigenic information and its relationship to changes in phagocytic activity.... | 84 |
| Stimulation of the reticuloendothelial system by adoptive transfer..... | 86 |
| Summary..... | 89 |

| | | |
|-------------------|---|-----|
| <u>CHAPTER IV</u> | <u>Studies on the effect of heterologous anti-lymphocyte serum on the reticulo-endothelial system in mice</u> | 92 |
| | Allograft survival I - the effect of the timing and the dosage of antiserum..... | 94 |
| | Allograft survival II - the effect of the route of administration of the antiserum..... | 96 |
| | Allograft survival III - the effect of allograft size..... | 97 |
| | Allograft survival IV - the specificity of antiserum..... | 97 |
| | Allograft survival IV - tissue specificity..... | 98 |
| | Phagocytic activity in anti-lymphocyte serum treated mice..... | 99 |
| | The effect of anti-lymphocyte serum on the reticuloendothelial system - morphological studies..... | 100 |
| | Liver weights..... | 101 |
| | Spleen weights..... | 101 |
| | Lymph node weights..... | 102 |
| | The effect of antiserum on the reticulo-endothelial system - morphological studies II.... | 103 |
| | Peripheral white cell count in anti-lymphocyte serum treated animals..... | 108 |
| | Allograft rejection in antiserum treated animals.. | 108 |
| | Allograft rejection in antiserum treated animals - histologic studies..... | 110 |
| | Summary..... | 112 |

| | | |
|-------------------|---|-----|
| <u>CHAPTER V</u> | <u>Antibody production and immunity in allografted and antiserum treated mice</u> | 115 |
| | Antibody production in allografted mice..... | 116 |
| | Susceptibility to infection of mice treated with anti-lymphocyte serum..... | 117 |
| | The antibody response to sheep erythrocytes in antiserum treated mice..... | 118 |
| | Antibody response to bovine serum albumin in antiserum treated mice..... | 120 |
| | Summary..... | 122 |
| <u>CHAPTER VI</u> | <u>Discussion</u> | 125 |
| | <u>Acknowledgements</u> | 140 |
| | <u>Bibliography</u> | 141 |

ABSTRACT

While further evidence has been provided that skin allografts stimulate the reticuloendothelial system as indicated by an increased rate of clearance of ^{32}P labelled Salmonella typhimurium (C5) from the circulation, it has been shown that the magnitude of this increase is directly related to the size of the graft employed.

Splenomegaly was observed in these allografted mice and this as with the increased rate of clearance of labelled bacterial particles occurred just prior to macroscopic rejection of the graft. Splenectomy did not, however, alter the subsequent survival of the graft or the changes in the activity of the reticuloendothelial system. The distribution of the radioactive label indicated that the phagocytic cells of the liver were primarily responsible for the increased rate of clearance observed. This increased rate of clearance which reflected one aspect of the activity of the reticuloendothelial system was not paralleled by an increased ability of such an animal to produce antibodies when challenged with another antigen.

The demonstration of changes in phagocytic activity following removal of the graft at varying intervals and the relationship of this response to macroscopic and histologic graft rejection suggests that the release of antigens from the graft stimulates the reticuloendothelial

system rather than graft rejection per se. This, however, does not appear to be a direct effect of the antigens on the cells of the reticulo-endothelial system but results from a factor released by the lymphoid cells after interaction with the antigen.

These studies have also shown that the measurement of phagocytic activity may be of value in indicating the presence of a host versus graft reaction.

The utilisation of heterospecific anti-lymphocyte serum and its associated immunosuppressive properties has made it possible to investigate the phagocytic activity of animals clearly incapable of rejecting an allograft. The initial step was to establish a satisfactory time, dose and route of administration for the antiserum. These studies revealed that the time of commencement of the antiserum in relation to the day of grafting as well as the dose were of importance to the subsequent survival of the graft, whereas the route of administration was unimportant.

Apart from achieving prolongation of allograft survival the antiserum used in the various experiments was also found to produce marked hyperplastic changes in the lymph nodes and spleens with the appearance of large numbers of pyronin-positive cells. The observation that these changes correlated well with allograft survival suggested a relationship between this histologic picture and

the disturbed immune function.

The clearance studies indicated that the antiserum treated animals had an adequately functioning reticuloendothelial system. However, commencing a given antiserum regime prior to antigenic challenge was more effective than the same regime commenced after this challenge, suggesting that the antiserum had a significant effect on the initiation of the immune response.

Two important practical points have emerged; firstly antiserum treated animals were not more susceptible to infection; secondly, while it was not possible to produce tolerance to a purified protein the simultaneous administration of anti-lymphocyte serum and antigen resulted in a significantly reduced secondary response to the same antigen.