B Cell antigen D8/17 as a marker of susceptibility to rheumatic fever in Australians

and

The sharp end of the needle:

Rheumatic fever prophylaxis and concepts of care for Yolngu patients

A thesis in two parts

Submitted for the degree of Masters of Science (Health Sciences) at

Flinders University, March 2005

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Acknowledgements

For part 1, this work was carried out with the assistance of a research scholarship from the Cooperative Research Council of Aboriginal and Tropical Health. The National Heart Foundation of Australia provided funding for the research.

I would like to thank my supervisors Bart Currie and Jonathan Carapetis for their conceptualisation of this study and subsequent guidance and assistance. I am grateful to Kumar Visvanathan and Narelle Skinner for their contribution in the laboratory and enthusiasm for teaching me all I know about laboratory processes. Susan Jacups was helpful in dozens of practical ways at critical moments. Michael Harrington relived his student days by becoming a laboratory assistant in rather humid conditions. Michael Christie's language tuition and assistance in translation was appreciated greatly.

The warmest thanks goes to the people of Galiwin'ku for their willingness to contribute to this project, to Basma Ganalarritj for recruiting people from her home town, Dorothy Bepuka and Dorothy Yungirrnya for translating the information sheets and expanding my Yolngu matha vocabulary in order that I could speak fluently about rheumatic fever in Djambarrpuyngu, to Ngalkanbuy Health for facilitating this work, and to *Yalu Marŋgithinyaraw* (Yalu nurturing centre) for cultural advice and general support.

For part 2, this work was supported by a scholarship provided by the Cooperative Research Council of Aboriginal and Tropical Health. Funding for a co-worker and

project costs was supplied by a grant from the Department of Health and Ageing Regional Health Services Program.

Thank you to my supervisors David Thomas and Bart Currie for generating the question, the means of finding the answers, and all the subsequent encouragement I needed to complete the task.

Joy Bulkanhawuy was indispensable to the completion of this project. Her dedication, professionalism, good advice were all highly valued - *mirrithirr manymak djäma dhuway!*

Members of the *Yalu Marŋgithinyaraw* gave useful advice and support. Thanks to the staff of Ngalkanbuy Health and Marthakal, who were enthusiastic and helpful participants in this study. Michael Christie's assistance with *Yolngu matha* tuition and translation was much appreciated. The patients and families of Galiwin'ku who gave freely of their time and thoughts are deeply appreciated.

And to David and Jahan, who were continually entangled in the whole happy process…

Statement of work undertaken

In part 1, the project was conceptualised by Prof. Bart Currie and Prof. Jonathan Carapetis. I principally performed the data and sample collection, the statistical analysis and interpretation of the D8/17 results. I undertook the D8/17 staining of the community samples, with assistance from Mr Michael Harrington. Kumar Visvanathan and Narelle Skinner stained the samples in the laboratory. The D8/17 flow cytometry was performed by Dr Kumar Visvanathan.

In part 2, I conceptualised and planned this study, with the assistance of my supervisor, David Thomas. My co-researcher, Joy Bulkanhawuy and I developed the interview structure and carried out the interviews in a bilingual fashion. Joy translated the interviews, and then participated in the analysis of the data. I performed the bulk of the analysis and write-up of the data. Joy assisted with the feedback to the community, and the review of the final conclusions.

Declaration

I certify that this thesis does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Abstract

Aboriginal Australians have some of the world's highest rates of rheumatic fever. Two approaches to reducing the burden of rheumatic fever are discussed in this thesis. The B cell antigen D8/17 has a strong association with rheumatic heart disease and may be a universal marker of inherited susceptibility to rheumatic fever. Identifying a population at increased risk of rheumatic fever provides an opportunity to focus primary prevention measures. **In part one of the thesis** I evaluate the accuracy of D8/17 as a marker of past rheumatic fever amongst Australians from the Northern Territory. D8/17 levels were measured and compared in patients with acute rheumatic fever, rheumatic heart disease or past rheumatic fever, first-degree relatives and healthy, unrelated controls. The mean percentage of B cells positive for D8/17 was 83.7%, 38.9%, 20.2% and 11.6% respectively. The difference between the groups was significant ($p<0.0001$). A receiver operator curve analysis indicated that 22.1% of B cells positive for D8/17 was the most accurate cut-off to distinguish patients with acute or past rheumatic fever from healthy subjects. These results indicated that the B cell antigen D8/17 is an accurate marker of past rheumatic fever in Aboriginal Australians and could be a helpful addition to the Jones Criteria for strengthening or excluding a diagnosis of acute rheumatic fever. The intermediate levels of D8/17 expression in the relatives of index cases supports the hypothesis that D8/17 is a marker of an inherited susceptibility to rheumatic fever, although prospective trials are required to provide conclusive proof of this hypothesis.

Non-compliance with secondary prophylaxis was suspected to be the cause of increasing rates of rheumatic fever in the Top End. **In part two of the thesis** I discuss the 'problem of compliance' with respect to Aboriginal patients, and investigate the

factors that affected the delivery and uptake of prophylaxis for rheumatic fever in an Aboriginal community. Patients, relatives and health practitioners were interviewed on the topic of the care of patients with rheumatic heart disease. The data were analysed using the principles of grounded theory.

The main finding was the desire for more personalised care and support for patients with rheumatic heart disease from the community clinic, rather than simple medical care. These ideas crystallised through two Yolngu terms to describe care: *djäka* (to physically care for) and *guŋga'yun* (to encourage). Thus even from the outset there was divergence in the focus of the 'consumer'- holistic care - and that of the health-care professional/ researcher – improving the rate of secondary prophylaxis coverage.

With regards to service provision, a significant reason for failure to receive secondary prophylaxis was the differing approaches of urban and community health services, patient mobility, and a differing understanding of the responsibilities of patients and health service providers in the different settings. Other factors pertaining to service provision, such as staff motivation, administrative issues and program coordination affected the uptake of secondary prophylaxis to a lesser extent. With regards to treatment uptake, individual patient factors inhibiting uptake of treatment were apparent in some cases, but treatment refusal was rare. Pain was not found to be a deterrent. No simple relationship was found between treatment compliance and biomedical knowledge of the disease. There was no simple relationship between patient passivity and sense of responsibility that guaranteed compliance.

This study demonstrated that the failure to achieve good uptake of prophylaxis for rheumatic fever related as much to factors of service provision as patient factors and

that providing holistic care within a familiar and supportive framework is important to Yolngu patients. However, there are real difficulties for health services as they are currently structured to meet the expectations of patients and families.

Abbreviations

ALPA	Arnhem Land Progress Association
ARDS	Aboriginal Resource and Development Society
JB	Joy Bulkanhawuy
NT	Northern Territory
PBMC	Purified blood mononuclear cells
RF	Rheumatic fever
RHD	Rheumatic heart disease
ROC	Receiver operator characteristics
SD	Standard deviation
WHO	World Health Organisation
ZH	Zinta Harrington

TABLE OF CONTENTS

INDEX OF TABLES AND FIGURES

TABLES

FIGURES