Summary

XV Lancefield Symposium on Streptococci and Streptococcal Diseases

An impressive ceremony on Sunday 6th October marked the opening of the XV Lancefield International Symposium on Streptococci and Streptococcal Diseases. The Governor of Goa, Mr Mohammed Fazal, spoke of the challenge facing scientists in finding ways to fight against serious diseases by improving methods of prevention and treatment. That scientists are responding to the challenge, I believe, has been demonstrated during the XV Lancefield Symposium.

The opening lecture given by Dr Richard Krause, entitled ‘A Half Century of Streptococcal Research: Then and Now’ focused on landmark research undertaken during the first half of the 20th Century. This research provided the foundations for understanding the pathogenesis and epidemiology of streptococcal diseases. Dr Krause particularly highlighted the work of Rebecca Lancefield after whom the symposia are named. Lancefield identified structural differences in organisms that allowed her to classify streptococci into serogroups and serotypes and led her to define the biologic significance of M protein on group A streptococci. Dr Krause also stressed the importance of studies undertaken by Wannamaker Rammelkamp, and Denny, who by careful epidemiologic study, demonstrated that treatment of a streptococcal sore throat with penicillin could prevent rheumatic fever. The second half of the 20th century saw increasing development of techniques for dissecting the structure and function of streptococci, explaining the pathogenesis of streptococcal disease and describing the epidemiology of disease manifestations.

One of the most striking impressions from the XVth Lancefield Symposium was the apparent explosion of new or advanced technologies being used to progress knowledge. At the time of the XIV Lancefield Symposium in 1999, the Group A Streptococcus had just been sequenced. Now at the XV Symposium Professor Jo Ferretti described the work that his laboratory and others had done in sequencing eight different strains representing a number of streptococcal species. This work opens the door to comparative genomics and to understanding the relationships and distinctions between and within species. It should now be possible to better understand cell physiology and metabolism, identify bacterial virulence factors, determine antimicrobial resistance mechanisms, explore the impact of gene acquisitions and deletions, identify phage determined activities, detect alternative vaccine candidates, and help to explain bacterial evolution.

Additional to progress on bacterial genomic structure, we heard how Dr Pat Cleary was using Lux gene technology to answer questions on the persistence of streptococci in nasal-associated lymphoid tissue. Another new technology, microarray, had been used by Dr Larry McDaniel's group to analyse pneumococcal virulence factors. In a number of presentations amazing photographs were shown of streptococci attaching to, or internalising in, epithelial and endothelial cells. These photographs had been taken using scanning electron microscopy. Dr Manfred Rodhe set a high standard with his extraordinary set of photographs suggesting that host cell caveole initiate invasion by group A streptococci.

An important focus of the Symposium was Rheumatic Fever (RF) and Rheumatic Heart Disease (RHD). Dr Padnavati set the scene by detailing the enormous burden of RF and RHD that occurs globally but particularly in developing countries. In India about six million children are suffering from RHD - a number nearly equivalent to twice the total population of New Zealand. RHD is estimated to cause around 0.5 million deaths per year globally. Dr Ganguly highlighted the challenges facing India to control RF and RHD. He outlined some of the primary prevention strategies that were being implemented at the community level. Dr Ganguly described research already undertaken in India that identified a correlation between RF and HLA antigens involving the HLA-DR locus. He stressed that if an M protein epitope-based vaccine was to be used in India it would need to be tailor-made to take into account the M types of streptococci circulating there.
Dr Madeleine Cunningham's most eloquent keynote address walked the participants through her group's research. They have hypothesised that immune injury is caused by group A streptococci during the development of RF/RHD. She described their experimental evidence that showed B cells activated by the carbohydrate of group A streptococci bind to the surface of the heart valves and T cells activated by myosin-like peptides of M protein cause valvulitis with tissue scarring. Some subsequent presentations addressed the issue of rheumatic carditis from the clinical perspective. Echocardiographic data, pathological findings, and surgical descriptions discussed were considered to support the importance of valvulitis rather than myocarditis in the pathology of RHD. Other presentations and discussions associated with RF included treatment regimen for secondary prophylaxis, the Jones criteria, surgical and non-surgical interventions and immunogenetics of RHD.

A landmark paper was presented by Dr Christine Kirvan from Madeleine Cunningham's laboratory. The paper entitled 'Antibody-mediated neuronal cell signaling in Sydenham's Chorea' demonstrated how anti-streptococcal monoclonal antibodies derived from a patient with Sydenham's Chorea were found to cross-react with ganglioside antigen and human caudate and brain sections. Furthermore, a monoclonal antibody produced a significant increase in calcium/calmodulin-dependent protein kinase (CAM kinase II) in a human neuronal cell line. When acute phase serum from patients with Sydenham's Chorea was tested, there was highly increased CAM kinase activity that was not present in convalescent serum from the same patients. The data suggest that antibody-mediated cell-signaling via CAM kinase II is important in the pathogenesis of Sydenham's Chorea.

In the absence of alternative population-based strategies for prevention of acute RF the focus is on the vaccine technology. The session devoted to vaccines provided fascinating listening. Dr Michael Good described the development of chimeric peptides as potential vaccine candidates. He described how by flanking the chimeric peptides with helical peptides the structure was forced into a helical formation that induced antibodies in a similar fashion to native M protein. In another presentation we heard results from studies that had examined the kinetics of colonisation and elimination of Streptococcus gordonii, an organism being tested for vaccine delivery. A third study reported, identified C5a peptidase as a candidate vaccine antigen following demonstration that C5a peptidase elicits an immune response in children naturally infected with group A streptococci. The high conservation of C5a peptidase across all tested streptococcal serotypes suggests C5a peptidase may be an attractive vaccine candidate.

The production and utilisation of vaccines first requires well developed surveillance systems. Such systems inform on the frequency and distribution of strains causing disease, inform public health intervention strategies and provide the information against which vaccines can be developed and their effectiveness measured. The numbers of papers presented both orally and by poster that encompassed epidemiologic surveillance of clinical disease and/or the serologic or molecular typing of strains was proof that laboratories worldwide are very active in this area. The papers reported from Europe and North America mostly focused on dimensions of invasive disease. In contrast, those from developing countries such as India, or from the Southern Hemisphere, focused more on the surveillance of throat and skin infections and on Rheumatic Fever. It was apparent from the presentations and discussions of data that differences exist in the clinical presenting features of the same disease in different parts of the world. Similarly, predominant group A strain types vary according to geography. Types occurring in the industrialised nations of the Northern Hemisphere are distinct from those causing the same disease in developing countries of the world. Within Australia, a similar dichotomy occurs with differences in disease presentations between the tropical north and the more populated region of southern Australia. Serogroup B streptococcal types and their disease manifestations appear less diverse globally but this observation possibly reflects that information on serogroup B disease and types causing it was not presented from the more tropical regions of the world. The need to understand what strain types are causing disease and where is of paramount importance for both serogroup A and serogroup B streptococci since vaccines based on type-specific polysaccharides or proteins would need to be tailor made to fit the circumstance.

The range of techniques available and now used in epidemiologic studies is providing a wealth of information.
on strains types. However, to what extent the information is internationally comparable because of variations in techniques is uncertain. One typing system that has been standardised and quality controlled by a core of six reference laboratories is M typing. The move to a sequence-based emm typing, while permitting type description of all group A streptococci, is possibly differentiating streptococci that would be recognised as biologically indistinguishable in a functional assay. The need for evidence-based accurate information for determining strategic policies by WHO was stressed by Dr Jonathan Carapetis. As an external consultant to WHO he informed the conference of the current organisational structure at WHO and of the fact that streptococcal disease had no current advocacy or programme in which it comfortably sat. During the conference the heads of national streptococcal laboratories present met to discuss the role for them in addressing the burden of disease internationally. They resolved to make representation to WHO to ensure that recognition is given to the fact that any programme on the control of RF/RHD also requires quality surveillance of disease, including laboratory identification and typing of streptococci.

Finally, the Organising Committee under the leadership of Professor Ganguly and Professor Chhatwal must be congratulated both for the excellent conference and for the venue used. In preparing for the Symposium the Organising Committee had experienced considerable difficulty in planning due to uncertainties of participation and international travel by overseas registrants in the wake of terrorism and cross-border unrest. The fact that many overseas scientists had travelled to India to participate indicated that the committee had made the correct decision to hold the XV LISSSD in Goa as planned. The next meeting is to be held in Australia in September 2005.

_Diana Martin_
President
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