

Immunohematology

JOURNAL OF BLOOD GROUP SEROLOGY AND EDUCATION

PROCEEDINGS FROM THE
SYMPOSIUM HONORING THE CAREER OF
DR. PETER D. ISSITT
MAY 15, 1998

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PhD, FRCPath, FIBMS, FIBiol
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SYMPOSIUM MODERATORS AND SPEAKERS



Speakers standing left to right:

David Anstee, PhD; Marion E. Reid, PhD; Malcom L. Beck, FIBMS, FIBiol, FRCPath;
Laurence D. Petz, MD; George Garratty, PhD, FRCPath; and W. John Judd, FIBMS,
MIBiol.

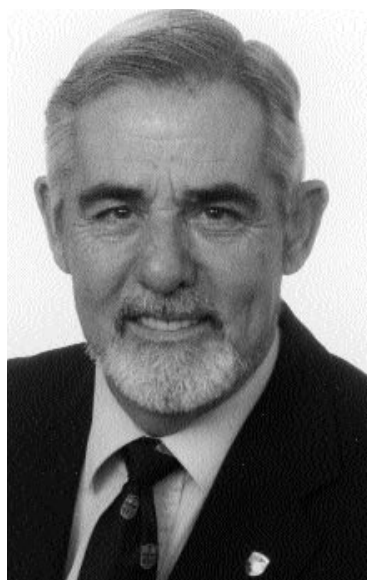
Moderators seated left to right:

Delores Mallory, MT(ASCP)SBB; Edwin A. Steane, PhD; Honoree Peter D. Issitt,
PhD, FRCPath, FIBMS, FIBiol; and John Case, FIBMS, FIMLS.

Photo by Faye Kugele, American Red Cross, River Valley Region, Louisville, Kentucky.

Symposium to honor the career of Peter D. Issitt, PhD, FRCPath, FIBMS, FIBiol

G. GARRATTY AND D. MALLORY



DR. PETER ISSITT

Dr. Peter Issitt received his training in England at the Royal Postgraduate Medical School and at St. Mary's Hospital, London. In 1964, he moved to the United States and was a research fellow at the New York Blood Center. Following that, for 11 years he was an associate professor and the director of laboratories of the Hoxworth Blood Center of the University of Cincinnati and directed the master of science degree program in Immunohematology. In

1981, he moved to Miami to become scientific director of the Red Cross Blood Program, South Florida Region. In 1989, he moved to Duke University Medical Center where he was an associate professor of pathology and the scientific director of the Transfusion Service.

His major research interests were the serology and genetics of the human red cell blood groups. He authored six textbooks on the blood groups, including four editions (1970, 1975, 1985, and 1998) of *Applied Blood Group Serology*. He has published over 300 papers.

Peter has received many prestigious awards. In 1974, he was awarded the Ivor Dunsford Memorial Award, in 1986 the Emily Cooley Memorial Award, and in 1991 the Morton Grove-Rasmussen Memorial Award from the American Association of Blood Banks. In 1987, he received the Zoutendyk Memorial Medal from the South African Institute of Medical Research; in 1991, the Petteway-Shepherd Award of the NCABB; in 1994, the

Eleanor Lloyd Memorial Lectureship of the British Blood Transfusion Society; and in 1995, the Philip Levine Outstanding Research Award of the American Society of Clinical Pathologists.

It is obvious that Peter is one of the giants of immunohematology. His decision to retire at a relatively early age took some of us by surprise. The shock was somewhat tempered by the publication of the 4th edition of his text, *Applied Blood Group Serology*, which was co-authored with Professor David Anstee and will help keep Peter in our minds, as every immunohematologist will have a copy of this book near them for the next 5-10 years!

The symposium we put together in May 1998 was primarily to honor Peter's contributions to science, but it was also to pay tribute to Peter as our friend. The lecturers (authors of the contributions in this issue of *Immunohematology*) and the moderators (Delores Mallory, Edwin Steane, and John Case) have all been friends of Peter for many years. It is no coincidence, and will evoke no apologies, that six of the nine lecturers/moderators were members of the "British Mafia"; one (D.M.) has been an honorary member of this group for some years, one (D.A.) is a true "Brit," and the only lecturer with an American accent (L.D.P.) has been tainted by working closely with this group since 1968. We believe that the symposium was successful in illustrating the many and varied contributions that Peter made to immunohematology during his career, and we hope that you enjoy reading the associated material in this issue of *Immunohematology* as much as we enjoyed hearing it at the symposium.

We know that you will join us in thanking Peter for all his contributions to our field and in wishing him a well-earned and joyful retirement for many years to come.

George Garratty and Delores Mallory

The structure and function of Rh antigens—from monkeys to worms

D.J. ANSTEE

Introduction

The Rh blood group system is often described as the most complex of all the blood group systems. This opinion is probably true, although now that the biochemical basis of the Rh system is understood, it is clear that much of the complexity that made it impenetrable to all but the most dedicated blood groupers (like Peter Issitt) was artificial, and reflected man's lack of understanding rather than its inherent complexity.

related proteins in this organism, which may enhance our future understanding of the role of Rh proteins in human RBCs.

Contribution of MNS to the study of glycoporphin A and glycoporphin B

M. E. REID

Introduction

When the organizers of the symposium for Dr. Peter Issitt asked me to participate, I was delighted and honored. Peter has a long-standing interest in both antigens and antibodies of the MNS blood group system and has made numerous contributions in this area that provided the basis for studies on glycoporphin. He has authored a textbook specifically on the MNS system. Because I also have an interest in this system, it was easy to find areas of mutual interest to discuss. While I still lived and worked in England I was aware of someone called Peter Issitt, but it was not until I first worked at the New York Blood Center that I actually met him and for years was intimidated by his knowledge of both blood groups and the English language. I was fortunate enough to get to know him better and now know that he has a phenomenal memory, is highly organized, is accurate in his terminology, is eloquent, and readily shares his knowledge. I thank Peter for his many contributions throughout his career and value his friendship. I am honored to have known him. This review is based on material presented at the symposium and will focus on selected areas relating to the MNS blood group system of particular interest to Peter.

Vox Sang 1994;67(S2):115.

Monoclonal antibodies as blood grouping reagents

M.L. BECK

Introduction

It is a great privilege to participate in this symposium to honor the career of Dr. Peter Issitt. It has been my good fortune that Peter has been both a personal friend as well as an esteemed professional colleague for more than 30 years. This 30-year period has been highlighted by the many contributions made by Dr. Issitt to the field of immunohematology. It strikes me as especially fitting that he should mark his retirement with the publication of the fourth edition of *Applied Blood Group Serology*, which, like its predecessors, will become the standard text for this field. A significant portion of chapter 7 is a discussion of the impact of monoclonal antibodies, the subject of my presentation.

A relatively seamless transition from human polyclonal to monoclonal sources of blood grouping reagents occurred in the last decade, facilitated largely by two independent events. The first was the declining availability of injectable blood group substance for hyperimmunization programs; the second was the simultaneous emergence of hybridoma technology. The transition to monoclonal sources of routine blood grouping reagents began shortly after the report of Köhler and Milstein in 1975;¹ currently, virtually all commercially prepared ABO grouping reagents are formulated from murine monoclonals. It is clear that reagents for D typing will soon follow suit. Monoclonal reagents have been well accepted although a few unexpected complications have been recorded, mainly during ABO grouping. Other concerns about the restricted specificity of monoclonal anti-D reagents might require a reappraisal of traditional approaches to D typing. These issues will form the basis of this presentation.

Blood transfusion in hemolytic anemias

L.D. PETZ

Introduction

Transfusion of patients with hemolytic anemias has a unique set of potential problems. In autoimmune hemolytic anemia (AIHA), the indications for transfusion must be considered in light of the fact that there is a somewhat increased risk of transfusion due to difficulty in compatibility testing and because the patient's autoantibody can be expected to cause a shortened life span of transfused red blood cells (RBCs). Nevertheless, blood transfusion must never be regarded as contraindicated, even though the results of the compatibility test may be strongly positive. Special care must be taken in performing compatibility tests and, in particular, when serum autoantibodies are present, techniques for selecting donor RBCs should include adsorption tests to exclude the presence of alloantibodies. Transfusion therapy should not be overly aggressive because an increase in RBC mass subjects the patient to an increased amount of autoantibody-mediated hemolysis, which can lead to marked posttransfusion hemoglobinemia and hemoglobinuria. Alloantibody-induced hemolytic transfusion reactions in patients with hemolytic anemia have the potential for adverse effects not found in other patients, particularly a decrease in the hemoglobin to a level below that present prior to transfusion. This finding is well documented in sickle cell anemia and thalassemia but may also occur in patients with acquired hemolytic anemias. The posttransfusion drop in hemoglobin may occur as a result of development or augmentation of autoantibodies following transfusion. Another possible mechanism is bystander immune hemolysis; that is, hemolysis or an increased rate of hemolysis of autologous RBCs ("hyperhemolysis") as a result of the immune destruction of transfused allogeneic RBCs. Still another possible mechanism is the hemolysis of transfused RBCs coupled with suppression of erythropoiesis, which can lead to an acute posttransfusion drop in hemoglobin in patients with an intrinsic short RBC survival, as has been documented in sickle cell anemia.

Dr. Peter Issitt has made extensive contributions to transfusion medicine as well as to our understanding of hemolytic anemias. Accordingly, a discussion of blood transfusion in patients with hemolytic anemia is a particularly pertinent way to honor his work. This paper will review certain aspects of transfusion of patients with autoimmune and hereditary nonimmune hemolytic anemias.

Specificity of autoantibodies reacting optimally at 37°C

G. GARRATTY

Introduction

Because autoantibodies reacting optimally at 37°C (“warm” autoantibodies) reacted with almost all red blood cells (RBCs) tested, they were thought initially to be “nonspecific” (i.e., reacting with an antigen present on all human RBCs). Nevertheless, there were some early indications that this was untrue. In 1947 and 1949, respectively, Denys and van den Broucke¹ and Kuhns and Wagley² reported that 15–37 percent of donor RBCs did not react with sera from patients with autoimmune hemolytic anemia (AIHA).

Modern approaches to pretransfusion testing

W.J. JUDD

Introduction

Approaches to pretransfusion testing have undergone considerable revision in recent decades. Prompted by reductions in operating budgets that started with reforms to health care reimbursement, practices that yield a large number of unwanted positive tests and those generating data not applied to patient management are being abandoned.¹ Past testing strategies are being replaced with streamlined protocols that facilitate timely, cost-effective provision of blood and blood products.² New technologies have emerged, including monoclonal reagents to replace human source antibodies for ABO/Rh typing,³ polyethylene glycol (PEG) as an “enhancement” reagent for use in antibody detection and identification studies,⁴ solid-phase technologies for demonstrating red blood cell (RBC) antigen-antibody interactions,⁵ and column technologies that are beginning to replace conventional test tube procedures for pretransfusion testing.⁶ Furthermore, with the emergence of blood bank information systems, several laboratories now use the integrity of computer software to detect ABO incompatibility between the sample submitted for pretransfusion testing and the donor unit selected for transfusion.⁷

Dr. Peter Issitt’s contributions to the field of immunohematology are without doubt innumerable. In this article, I shall touch on some of the observations and comments he has made that have contributed to the evolution of pretransfusion testing practices. Data generated over the past quarter of a century to support the streamlining of test protocols at the University of Michigan (Table 1) will be reviewed, as will currently required elements of pretransfusion testing. Redundant practices will be discussed and modern testing protocols using newer methods for antibody detection and an electronic crossmatch will be presented.