Alloimmune disorders of pregnancy

Anaemia, thrombocytopenia and neutropenia in the fetus and newborn

Collectively known as the alloimmune cytopenias, haemolytic disease of the fetus and newborn, alloimmune thrombocytopenia and alloimmune neutropenia are all consequences of maternal immunization to fetal blood cells. The effective prevention, diagnosis and management of these disorders has become a team effort involving haematologists, obstetricians, paediatricians, immunologists, laboratory technicians, midwives and research scientists. This book has been written by experts in their respective fields to bring together the issues of pathogenesis, epidemiology, prevention, diagnosis and clinical management. This comprehensive but accessible account is extensively cross-referenced to emphasize the links between pathogenesis and clinical sequelae, between epidemiology and the rationale for screening programmes, and between diagnosis and therapeutic intervention.

This is an authoritative overview suitable for trainees in obstetrics, maternal and fetal medicine, transfusion medicine and clinical immunology.

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Preface

Definitions and terminology

The alloimmune cytopenias are a group of conditions in which the life span of fetal blood cells or their precursors is shortened by the action of antibodies derived from the mother by placental transfer. Three conditions are recognized: antibodies to fetal red cells, platelets or neutrophils, or their precursors, cause alloimmune anaemia, thrombocytopenia or neutropenia, respectively. Various terms are in common usage for these disorders, many of them inappropriate. For example, alloimmune anaemia is sometimes referred to as Rhesus disease, erythroblastosis fetalis or haemolytic disease of the newborn and all three are misnomers. It is incorrect to use 'Rhesus' to refer to the Rh system, fetal haemolysis may be caused by antibodies outside the Rh system, anaemia is not always associated with erythroblastosis and, finally, the disorder primarily affects the fetus rather than the newborn. Therefore, throughout this book, alloimmune anaemia (perhaps the best term) will be referred to as haemolytic disease of the fetus and newborn (HDFN). For similar reasons, alloimmune thrombocytopenia and alloimmune neutropenia will be used in preference to other terms, such as neonatal alloimmune thrombocytopenia, fetomaternal alloimmune thrombocytopenia and neonatal alloimmune neutropenia, while, at the same time, acknowledging that these terms are also commonly used.

The multidisciplinary approach to the management of the alloimmune cytopenias

The last 10 years of the 20th century saw significant advances in the management of alloimmunized pregnant women; immunologists made progress characterizing the molecular basis of the alloimmune response; molecular biologists solved the genetic basis for all the clinically important blood groups and developed DNA-based fetal typing assays; epidemiologists and health care economists developed a better understanding of the natural history of the alloimmune cytopenias and the

cost-effectiveness of preventative programmes; obstetricians and fetal medicine specialists progressed the use of noninvasive fetal monitoring techniques; and haematologists improved the safety and efficacy of the various fetal transfusion therapies. With significant advances being made on so many fronts, the optimal prevention, diagnosis and management of alloimmunized pregnant women has become a team effort involving haematologists, obstetricians, paediatricians, immunologists, laboratory technicians in hospitals and transfusion centres, midwives and research scientists. However, it is rare for the individuals who contribute to this team effort to have a comprehensive overview of all the laboratory and clinical aspects associated with the alloimmune cytopenias.

Our intention in producing this book has been to bring the issues of pathogenesis, epidemiology, prevention, diagnosis and management together in a way which is both comprehensive and relevant to the various professionals involved. To this end, we have tried to avoid subspecialty jargon and to limit the use of abbreviations as far as possible because those used daily by laboratory scientists may be less familiar to clinicians and vice versa.

Andrew G Hadley
Peter Soothill

Foreword

This book is a very good idea. It brings together all the different aspects of the alloimmune cytopenias that are needed to understand them. The two most important are the red cell and the platelet cytopenias and they have features in common as well as characteristics that sharply differentiate them. For each condition, consideration is given to the genetics, the pathophysiology, the evidence for the efficacy and cost-effectiveness of screening and prevention, and to the management of the affected fetus and neonate. To have authoritative chapters on all these topics within the covers of one book is extremely helpful both for those who are new to these clinical problems and for those who, like the author of this foreword, have been grappling with them for over 20 years. The editors and their multidisciplinary team are to be congratulated and thanked for producing this valuable synthesis.

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Abbreviations

ADCC	Antibody-dependent cell-mediated cytotoxicity
AMIS	Antibody-mediated immune suppression
ARMS	Amplification refractory mutation system
ASPA	Allele-specific primer amplification
C3	Third component of complement
CD	Cluster of differentiation
CLT	Chemiluminescence test
CMV	Cytomegalovirus
CTG	Cardiotocography
DAGT	Direct antiglobulin test
ELISA	Enzyme-linked immunosorbent assay
FBS	Fetal blood sampling
FcγR	Fc gamma receptor (receptor for the Fc domain of IgG)
GAT	Granulocyte agglutination test
GIFT	Granulocyte immunofluorescence test
HbsAg	Hepatitis B surface antigen
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HPA	Human platelet antigen
HTLV	Human lymphotropic virus
IAGT	Indirect antiglobulin test
ICH	Intracranial haemorrhage
IL	Interleukin
Ig	Immunoglobulin
im	Intramuscularly
IU	International Units
IUT	Intrauterine transfusion
iv	Intravenously
IVIG	Intravenous immunoglobulin
Hb	Haemoglobin

HDFN	Haemolytic disease of the fetus and newborn
HLA	Human leukocyte antigen or histocompatibility locus antigen
HPA	Human platelet antigen
HNA	Human neutrophil antigen
kD	Kilodalton
LISS	Low ionic strength saline
MAIGA	Monoclonal antibody immobilization of granulocyte antigens assay
MAIPA	Monoclonal antibody immobilization of platelet antigens assay
MMA	Monocyte monolayer assay
ΔOD_{450}	Optical density at a wavelength of 450 nm
PCR	Polymerase chain reaction
PEG	Polyethyleneglycol
PIFT	Platelet immunofluorescence test
RFLP	Restriction fragment length polymorphism
SNP	Single nucleotide polymorphism
TAV	Time-averaged mean velocity
TPH	Transplacental haemorrhage