

Veterinary Immunology – Principles and Practice

Second Edition

Michael J. Day

BSc, BVMS(Hons), PhD, DSc, DiplECVP, FASM, FRCPath, FRCVS

Professor of Veterinary Pathology

School of Veterinary Sciences

University of Bristol

Langford, Bristol, UK

in collaboration with

Donald D. Schultz

BS, MS, PhD, DACVM

Professor and Chair

Department of Pathobiological Sciences

School of Veterinary Medicine

University of Wisconsin-Madison

Madison, Wisconsin, USA



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Foreword

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Veterinary immunology is one of the most recent, and the most important, basic and clinical sciences in veterinary medicine. Veterinary immunology became an important part of the veterinary curriculum approximately 40 years ago when most veterinary medical students were introduced to concepts of basic immunology during their first or second year of veterinary school. Clinical immunology was either a minor part of the basic immunology course or it was taught at a later time as part of the medicine courses. During the past 40 years, information regarding basic and clinical immunology in veterinary medicine has increased beyond the scope of a single course. However, this textbook, *Veterinary Immunology – Principles and Practice, Second Edition*, includes both basic and clinical concepts of veterinary immunology.

The author is a veterinary immunologist engaged in both basic and clinical research studies in immunology and immunopathology. The book provides not only the veterinary medical student, but also the graduate veterinarian, with excellent information on the basic and clinical aspects of veterinary immunology. The basic aspects of the science are made easily understandable to those with limited or no knowledge of immunology. At the same time the book provides an excellent insight into the complexity of diseases caused by or prevented via innate and/or adaptive immunity. The book is equally valuable to those with little or no understanding of clinical medicine and to those with an excellent knowledge of basic clinical medicine. This is accomplished through the author's unique presentation style in which the basic concepts of immunology are introduced and explained, often in the context of the mechanism for an immune-mediated disease

or the immunological mechanism for prevention or treatment of a disease. The author has also 'sifted and winnowed' through the complexities of basic medical immunology in order to provide the reader with factual information that applies to most veterinary species. This text, unlike many introductory immunology texts available for medical students and undergraduate or graduate students in the biological sciences, does not focus on the myriad of information on the immunology of the mouse, a favourite species of many immunologists who perform *in-vivo* studies. Ironically, most immunologists are of the opinion that because the mouse's immune system is easily manipulated for *in-vivo* and *ex-vivo* immunological studies, it serves as a model for all other species. Unfortunately, this is often not true and many of the veterinary species differ significantly between each other as well as with the mouse regarding basic and clinical mechanisms of diseases caused by and/or prevented via their immune system. The species differences, when known, are defined in this text. Information on differences among species should make this text a valuable reference for all immunologists, especially those with an interest in real animal studies. Information is included on food animal species, but the focus in the clinical immunology sections is on companion animal species, especially the dog and cat. The author has published a more detailed book, *Clinical Immunology of the Dog and Cat*, which is beautifully illustrated with graphs and figures including histopathology sections of immune-mediated diseases in these species. Similarly, this text is very well illustrated, but for obvious reasons does not contain the detail found in the *Clinical Immunology of the Dog and Cat*.

I especially like this book because the veterinary immunology course taught to second-year veterinary medical students at the University of Wisconsin-Madison first presents the 'Basics of Veterinary Immunology' via eighteen didactic lectures, followed by 'Clinical Immunology' via twelve 'Clinical Correlates'. In addition, there are approximately 50 hours in the course that cover laboratory exercises such as vaccinating calves and puppies, performing clinical immunology tests for the diagnosis of diseases of companion and food animals, and other laboratory procedures (phagocytic tests, lymphocyte function tests

and multiple serological tests). This book provides a very helpful way of understanding these diagnostic tests, animal immunization and immune-mediated diseases.

This second edition of *Veterinary Immunology – Principles and Practice* is a book for veterinary students worldwide. It is also an excellent review and update for veterinarians who graduated five or more years ago and want or need to know more about basic and clinical veterinary immunology.

Ronald D. Schultz

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Preface (First Edition)

xi

Veterinary Immunology – Principles and Practice has the simple aim of providing undergraduate veterinary students with core knowledge of veterinary immunology, while emphasizing the clinical relevance of this subject area. Veterinary students often struggle with the complexity of the immune system and find it difficult to relate immunological concepts to veterinary practice. In many universities, immunology is taught to veterinary undergraduates at a superficial level and the subject is also often delivered by basic scientists with an inappropriate focus on murine or human systems. Despite this, immunology is a key subject in the veterinary curriculum; it links together subject areas such as biochemistry, microbiology, parasitology and pathology with clinical medicine. One of the main clinical applications of immunology is the practice of vaccination, and all graduating veterinarians must have a solid understanding of the principles of vaccinology.

There are relatively few textbooks of veterinary immunology to support the delivery of undergraduate courses in this subject. I hope that *Veterinary Immunology – Principles and Practice* will fill a key niche in providing students with an affordable and practical reference that will also have relevance as they progress through a practice career. The key features of this book include:

- A sufficient level of detail of core knowledge without this being diluted by minutiae.
- Clear definition of learning objectives and bullet-point summaries of key points, with key words highlighted throughout the text in bold font and listed in a glossary.

- An affordable price for a full colour text supported by numerous diagrams and photographic images.
- An emphasis on clinical examples with a series of 15 clinical case studies that present core information related to clinically significant immun-mediated diseases. This aspect is truly unique to this text and is found in no other reference book on this subject. These case studies should very clearly indicate to the student the major clinical relevance of immunology. They provide a bridge between this book and the more practitioner-orientated *Clinical Immunology of the Dog and Cat*. Both of these texts share fundamental aspects of presentation (e.g. diagrammatic symbols), which should make it straightforward to progress from one to the other.

This book is born from the lecture course in veterinary immunology that I have delivered over the past 20 years to students at the University of Bristol. I am delighted to have had the opportunity of working with Professor Ron Schultz on this project. Ron has made insightful suggestions on the text and ensured that the content also covers the curriculum needs of students in North America. I am very grateful to Ron for sharing his vast experience in veterinary immunology and helping shape this major new resource. Both of us share a passion for this subject and the teaching of it to veterinary undergraduates. However, it is our belief that *Veterinary Immunology – Principles and Practice* will not only have relevance to the student market, but should serve as a simple reference for veterinarians already in practice.

I would like to acknowledge the support and enthusiasm for this project from Michael Manson and Commissioning Editor Jill Northcott. This is my fourth book for Manson Publishing, but the first truly undergraduate textbook. My thanks go to the production team of Kate Nardoni (project

manager), Susan Tyler (illustrator) and Peter Beynon (copy editor) for their professional input into the finished product.

M. J. Day
January 2011

Preface (Second Edition)

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I was delighted with the response to publication of the first edition of *Veterinary Immunology – Principles and Practice* in 2011. The book was very well received by veterinary students and has now become the adopted text in numerous veterinary schools throughout the world. The text achieved its goal of providing a concise and affordable book supported by high-quality colour illustration. Many colleagues who teach veterinary immunology were highly complimentary about this new resource and offered constructive suggestions for changes to a second edition. Teachers of the subject were also very pleased with the opportunity, provided by the publishers, to obtain teaching sets of the images and diagrams used in the book.

Immunology is a rapidly developing subject area and in order for this textbook to remain current the text of the second edition has been widely updated with advances in knowledge since 2011. The format and style of the text remains the same, but the second edition contains around 20 new and updated figures, one new table and two new clinical case studies. New developments in fundamental and clinical veterinary immunology

are reported, with expanded information on commonly used diagnostic test procedures and the inclusion of newly arising diseases such as bovine neonatal pancytopenia.

I have been delighted to have the opportunity once more of collaborating with my friend and colleague, Professor Ron Schultz, on this second edition. I would also like to acknowledge my Commissioning Editor, Jill Northcott, and the production team of CRC Press.

It has been over 15 years since I first began working with Manson Publishing on the production of my first book, *Clinical Immunology of the Dog and Cat*. This second edition of *Veterinary Immunology – Principles and Practice* would have been my sixth Manson publication, but as the final manuscript for this edition was submitted, Michael announced his retirement and the transfer of Manson Publishing to CRC Press. I would like to acknowledge my long and fruitful collaboration with Michael and wish him the very best for the future.

M. J. Day
May 2014

Abbreviations

AchR	acetylcholine receptor	CFT	complement fixation test
AD	atopic dermatitis	C_H	constant region of the heavy chain
ADCC	antibody-dependent cell-mediated cytotoxicity	CH₅₀	total haemolytic complement (assay)
AGD	agar gel diffusion	C_L	constant region of the light chain
AIDS	acquired immune deficiency syndrome	CLA	cutaneous lymphocyte antigen
AIHA	autoimmune haemolytic anaemia	CLAD	canine leucocyte adhesion deficiency
AINP	autoimmune neutropenia	CLE	cutaneous lupus erythematosus
AITP	autoimmune thrombocytopenia	CLIP	class II-associated invariant chain peptide
ALL	acute lymphoblastic leukaemia	CLI	chronic lymphoid leukaemia
ALP	alkaline phosphatase	CM	cell-mediated immunity
ANA	antinuclear antibody	CNS	central nervous system
APC	antigen presenting cell	ConA	concanavalin A (mitogen)
APTT	activated partial thromboplastin time	COX	cyclooxygenase
ASIT	allergen-specific immunotherapy	cpm	counts per minute
AST	aspartate aminotransferase	CR	complement receptor
BALT	bronchial-associated lymphoid tissue	CRP	C-reactive protein
BCR	B-cell receptor	CTLA-4	cytotoxic T lymphocyte antigen-4
BLAD	bovine leucocyte adhesion deficiency	DAF	decay accelerating factor
BLV	bovine leukaemia virus	DAMP	damage-associated molecular pattern
BNP	bovine neonatal pancytopenia	DAT	direct antiglobulin test
BoLA	bovine leucocyte antigen	DEA1	dog erythrocyte antigen 1
BSA	bovine serum albumin	DLA	dog leucocyte antigen
BVDV	bovine viral diarrhoea virus	DNA	deoxyribonucleic acid
CADESI	canine atopic dermatitis extent and severity index	DOI	duration of immunity
CALT	conjunctiva-associated lymphoid tissue	DTH	delayed-type hypersensitivity
CAV	canine adenovirus	EAE	experimental autoimmune encephalomyelitis
CD	cluster of differentiation	EBP	eosinophilic bronchopneumopathy
CDR	complementarity determining region	ELA	equine leucocyte antigen
CDV	canine distemper virus	ELISA	enzyme-linked immunosorbent assay
		ELISPOT	enzyme-linked immunospot
		EPI	exocrine pancreatic insufficiency

ER	endoplasmic reticulum	Ig	immunoglobulin
ES	excretory–secretory (proteins)	IGHA	gene encoding the IgA heavy chain
Fab	antigen-binding fragment (of Ig)	IL	interleukin
FAD	flea allergy dermatitis	IMHA	immune-mediated haemolytic anaemia
Fc	crystallizable fragment (of Ig)	IMP	inosine monophosphate
FcR	Fc (Ig heavy chain) receptor	IMNP	immune-mediated neutropenia
FeLV	feline leukaemia virus	IMTP	immune-mediated thrombocytopenia
FHV	feline herpesvirus	iTreg	induced Treg (cell)
FIP	feline infectious peritonitis	IVIG	intravenous immunoglobulin (therapy)
FISS	feline injection site sarcoma	JAK	Janus kinase
FITC	fluorescein isothiocyanate	KCS	keratoconjunctivitis sicca
FIV	feline immunodeficiency virus	KIR	killer cell immunoglobulin-like receptor
FLA	feline leucocyte antigen	KLH	keyhole limpet haemocyanin
FOCMA	feline oncornavirus-associated cell membrane antigen	LAD	leucocyte adhesion deficiency
GALT	gastrointestinal-associated lymphoid tissue	LAK	lymphokine-activated killer (cell)
G-CSF	granulocyte colony-stimulating factor	LFA-1	lymphocyte function-associated antigen-1
GITR	glucocorticoid-induced TNF-receptor-regulated (gene)	LG	large granular lymphocyte
GMCSF	granulocyte–macrophage colony stimulating factor	LPS	lipopolysaccharide
GMP	guanosine monophosphate	M cell	microfold cell
GnRH	gonadotrophin-releasing hormone	M1/M2	subtypes of macrophages
GTP	guanosine triphosphate	MAC	membrane attack complex
GVHD	graft-versus-host disease	MAdCAM	mucosal addressin cell adhesion molecule
GWAS	genome-wide association study	MALT	mucosa-associated lymphoid tissue
HAI	haemagglutination inhibition	MAMP	microorganism-associated molecular pattern
HAT	hypoxanthine, aminopterin and thymidine	MASP	MBL-associated serine protease
HEV	high endothelial venule	MBL	mannan-binding lectin
HGPRT	hypoxanthine–guanine phosphoribosyl transferase	MCH	mean cell haemoglobin
HIV	human immunodeficiency virus	MCHC	mean cell haemoglobin concentration
HLA	human leucocyte antigen (human MHC)	MCP	membrane co-factor protein
IBD	inflammatory bowel disease	MCV	mean cell volume
IBH	insect bite hypersensitivity	MDA	maternally derived antibody
IBR	infectious bovine rhinotracheitis	MHC	major histocompatibility complex
ICAM-1	intercellular adhesion molecule-1	MMP	matrix metalloproteinase
IDST	intra-dermal skin test	mRNA	messenger RNA
IEL	intraepithelial lymphocyte	MS	multiple sclerosis
IEP	immunoelectrophoresis	NADPH	nicotinamide adenine dinucleotide phosphate
IFA	immunofluorescent antibody (test)	NALT	nasal-associated lymphoid tissue
IFN	interferon (e.g. IFN- γ)		

NET	neutrophil extracellular trap	rHuIFN-α	recombinant human IFN- α
NF-AT	nuclear factor of activated T cells	RIG	retinoic acid inducible gene (receptor)
NFκB	nuclear factor κ B	RNA	ribonucleic acid
NI	neonatal isoerythrolysis	ROS	reactive oxygen species
NK	natural killer (cell)	RT-PCR	reverse transcriptase polymerase chain reaction
NKT	natural killer T (cell)	SAA	serum amyloid A
NLR	NOD-like receptor	SCID	severe combined immunodeficiency/immunodeficient
NO	nitric oxide	SI	stimulation index
NOD1/2	nucleotide-binding oligomerization domain 1/2	SLA	swine leucocyte antigen
NOD	non-obese diabetic mouse	SLE	systemic lupus erythematosus
NOS	nitric oxide synthase	SLIT	sublingual immunotherapy
nTreg	natural Treg (cell)	SNP	single nucleotide polymorphism
NZB	New Zealand black mouse	SPC	summary of product characteristics
OLA	ovine leucocyte antigen	SRBC	sheep red blood cell
OSP	outer surface protein	SRID	single radial immunodiffusion
OVA	ovalbumin	STAT	signal transducers and activators of transcription
PALS	periarteriolar lymphoid sheath	TAM	tumour-associated macrophage
PAMP	pathogen-associated molecular pattern	TAP	transporter protein (TAP1/TAP2)
PBMC	peripheral blood mononuclear cell	Tc	T cytotoxic (cell)
PBS	phosphate buffered saline	TCR	T-cell receptor
PCR	polymerase chain reaction	TFh	T follicular helper (cell)
PCV	packed cell volume	Tg	thyroglobulin
PEG	polyethylene glycol	TGF	transforming growth factor
PHA	phytohaemagglutinin	Th	T helper (cell)
PI	persistently infected	TLR	Toll-like receptor
pIgR	polymeric immunoglobulin receptor	TMS	trimethoprim-sulphonamide
PRR	pattern recognition receptor	TNF	tumour necrosis factor
PT	prothrombin time	TNS	trapped neutrophil syndrome
PTH	parathyroid hormone	TPMT	thiopurine methyltransferase
PVDF	polyvinylidene fluoride	Treg	T regulatory (cell)
PWM	pokeweed mitogen	TSH	thyroid-stimulating hormone
PWMS	post-weaning multi-systemic wasting syndrome (of pigs)	UPC	urine protein:creatinine (ratio)
RAG	recombination activating gene	VEGF	vascular endothelial growth factor
RAO	recurrent airway obstruction	V_H	variable region of the heavy chain
RBCs	red blood cells	V_L	variable region of the light chain
RF	rheumatoid factor	VN	virus neutralization
rHuGCSF	recombinant human granulocyte colony-stimulating factor	WHO	World Health Organization
rHuGMCSF	recombinant human granulocyte-monocyte colony-stimulating factor	X-SCID	X-linked severe combined immunodeficiency