Reflux Aspiration and Lung Disease

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Foreword

Anatomically, the GI track and the respiratory system briefly share common space on their journey to their respective end organs. The clinical relevance of this relationship was emphasised over a century ago in 1892 by Sir William Osler in his elegant medicine textbook when he observed that asthma patients frequently have their largest meal in the middle of the day to avoid an asthma attack. Today we are reminded that "the devil is in the details" as we explore the depths of this relationship in the enclosed international multi-authored, multi-specialty text.

As a clinically active gastroenterologist with a career-long interest in gastroesophageal reflux and its relation to all manner of associated pulmonary disorders, this book is a most welcome addition to this field. Doctors Dettmar and Morice have approached this topic with a most welcome intensity by enlisting input for individual chapters from the correct experts. This text belongs in the personal library of all of us who see patients who likely suffer from a lung disease likely related to aspiration of refluxed gastric contents.

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Preface

Reflux and aspiration is the Cinderella of medicine. The conjunction of the aerodigestive tract has devolved to three specialities: respiratory medicine, gastroenterology and otolaryngology. Whilst each speciality brings its own expertise to the table, a synthesis is urgently required. Our ambition in this book has been to bring together a disparate collection of world renowned experts to provide the reader with a comprehensive overview in areas which they may not have previously considered in dealing with the patient. Indeed, this dichotomy or rather 'trichotomy' is a source of much frustration with patients bouncing between individual specialities, each denying that the patient's symptoms lie within their area of expertise. Holistic medicine is absent from this paradigm.

The pathological basis of inflammation in the upper and lower airways has moved on from purely acidic damage to a greater understanding of the aggressive factors which are causative factors.

Modern diagnostic techniques have revealed previously unrecognised aetiological mechanisms and are pointing to targeted therapy.

The conventional paradigm of individual lung disease, such as asthma and pulmonary fibrosis, becomes blurred when the aetiological role of aspiration in the pathogenesis of these syndromes is considered. Indeed, we operate a Joint Airways clinic where individual patients are not pigeonholed but have personalised therapy related to the pathological processes determined by the specific investigations. Perhaps the most important innovations have occurred in the area of therapeutics. The realisation that aspiration was not treated by proton pump inhibitors (however effective they are in classical peptic symptoms) has led to an exploration of alternative therapeutic strategies based on the amelioration of reflux rather than acid.

We hope that the reader will dip into this text and find gems which are relevant to them from other specialities.

Cottingham, UK — Alyn H. Morice
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Acknowledgement

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Contents

Abbreviations[1]

α-SMA	α-Smooth muscle actin
ACE	Angiotensin-converting enzyme
ACG	American College of Gastroenterology
ADL	Activities of daily living
AGA	American Gastroenterological Association
AHR	Airway hyper-responsiveness
ALI	Acute lung injury
AMs	Alveolar macrophages
AR	Anti-regurgitation
ARS	Anti-reflux surgery
ATP	Adenosine triphosphate
AUC	Area under curve
b.i.d.	Twice daily
BAL	Broncho-alveolar lavage
BALF	Broncho-alveolar lavage fluid
BHR	Bronchial hyper-responsiveness
BMI	Body mass index
BO	Barrett's oesophagus
BOS	Bronchiolitis obliterans syndrome
BSG	British Society of Gastroenterology
CC	Chronic cough
CDCA	Chenodeoxycholic acid
CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
COPD	Chronic obstructive pulmonary disease

[1]Churchill said Britain and the USA were two peoples divided by a common language. This was never truer than in the field of (o)esophageal disease. It would have been nice to agree a common language for this volume; however the literature extensively reviewed by our authors uses both UK and US spelling. To change these and the extensive list of abbreviations to fit a common schema would make location of these references difficult if not impossible. We have decided therefore to leave the choice of GORD or GERD, LOS or LES, etc. to the individual contributor and apologise here to the reader for any confusion that arises.

CPAP	Continuous positive airway pressure
CPG	Central pattern generator
CQLQ	Cough-specific quality of life questionnaire
CReSS	Comprehensive Reflux Symptom Scale
CV	Cardiovascular
CYP	Cytochrome P_{450}
DDIs	Drug to drug interactions
DIOS	Distal intestinal obstruction syndrome
DNase	Deoxyribonuclease
EBC	Exhaled breath condensate
ECL	Enterochromaffin-like cells
ECLIPSE	Evaluation of COPD longitudinally to identify predictive surrogate endpoints
EER	Extra-esophageal reflux
EGD	Esophagogastroduodenoscopy
ELISA	Enzyme-linked immunosorbent assay
ENT	Ear, nose and throat
ESLD	End-stage lung disease
FAK	Focal adhesion kinase
FDA	Food and Drug Administration
FDG	18F-Fluorodeoxyglucose
FEES	Fibreoptic endoscopic evaluation of swallowing
FEV-1	Forced expiratory volume in 1 second
FH	Functional heartburn
FVC	Forced vital capacity
GABA	γ-aminobutyric acid
GABAB	GABA type B receptor
GER	Gastroesophageal reflux
GERD	Gastroesophageal reflux disease
GI	Gastrointestinal
GJ	Gastro-jejunal
GMP	Guanosine monophosphate
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GOPG	Gastro-oesophageal pressure gradient
GOR	Gastro-oesophageal reflux
GORD	Gastro-oesophageal reflux disease
GSAS	Gastroesophageal Symptoms Assessment Scale
H2	Histamine2
H2RAs	Histamine2-receptor antagonists
HARQ	Hull airways reflux questionnaire
HCl	Hydrochloric acid
HE	Hypersensitive esophagus
HH	Hiatal hernia
HOB	Head of bed
HP	Helicobacter pylori

HR	Hazards ratio
HRCT	High-resolution computed tomography
HRIM	High-resolution oesophageal manometry combined with impedance
HRM	High-resolution oesophageal manometry
HRQL	Health-related quality of life questionnaire
HSCT	Haematopoietic stem cell transplant
5-HTR4	5-Hydroxytryptamine receptor 4
ICS	Inhaled corticosteroids
ICU	Intensive care unit
IIP	Idiopathic interstitial pneumonia
IL-8	Interleukin 8
IPF	Idiopathic pulmonary fibrosis
IV	Intravenous
LARS	Laparoscopic anti-reflux surgery
LBP	Lipopolysaccharide binding protein
LCM	Leicester Cough Monitor
LCQ	Leicester cough questionnaire
LDH	Lactic dehydrogenase
LES	Lower esophageal sphincter
LFD	Lateral flow device
LLM	Lipid-laden alveolar macrophages
LOS	Lower oesophageal sphincter
LPR	Laryngopharyngeal reflux
LPR-HRQL	Laryngopharyngeal reflux health related quality of life questionnaire
LPS	Lipopolysaccharide
LRTI	Lower respiratory tract infection
LTRAs	Leukotriene antagonists
MAC	Mycobacterium avium complex
MCC	Mucociliary clearance
MCP	Monocyte chemoattractant protein
MDT	Multi-disciplinary team
mGluR5	Metabotropic glutamate receptor 5
MII	Multiple intraluminal impedance
MMP	Matrix metalloproteinases
MPO	Myeloperoxidase
MRI	Magnetic resonance imaging
mRNA	Messenger ribonucleic acid
MRSA	Methicillin-resistant *Staphylococcus aureus*
MTT	An assay
NAB	Nocturnal acid breakthrough
NAC	N-acetylcysteine
NASPGHAN	North American Society of Gastroenterology, Hepatology and Nutrition

NCCP	Non-cardiac chest pain
NCFB	Non-cystic fibrosis bronchiectasis
NERD	Non-erosive reflux disease
nGERD	Nocturnal GERD
NNT	Number needed to treat
NNTB	Number needed to treat for an additional beneficial outcome
NO	Nitric oxide
NPV	Negative predictive value
NSAIDs	Non-steroidal anti-inflammatory drug
NTM	Non-tuberculous mycobacteria
OB	Obliterative bronchiolitis
OR	Odds ratio
OSA	Obstructive sleep apnea
OTC	Over-the-counter
OVA	Ovalbumin
PAR	Protease-activated receptor
P-CABs	Potassium-competitive acid blockers
PCR	Polymerase chain reaction
PDE	Phospho-di-esterases
PET	Positron emission tomography
PGE2	Prostaglandin E2
PHD	Prolylhydroxylase domain proteins
pH-MII	Multiple intraluminal impedance with pH
PP	Post-prandial
PPI	Proton pump inhibitor
PPV	Positive predictive value
PRSQ	Pharyngeal reflux symptom questionnaire
PVFM	Paradoxical vocal fold movement
QoL	Quality of life
QT	Electrocardiogram QT interval
RCTs	Randomized control trials
RESULT	Reflux Surgery in Lung Transplantation
RFS	Reflux finding score
rhDNase	Recombinant human DNase
RI	Reflux index
RNA	Ribonucleic acid
ROC	Receiver operating characteristic
RSI	Reflux symptom index
RSS	Reflux symptom score
SAP	Symptom association probability
SD	Standard deviation
SER	Supraesophageal reflux
SERQ	Supraesophageal reflux questionnaire
SF-36	Short form 36-item questionnaire
SGRQ	St Georges respiratory questionnaire

SI	Symptom index
SIDS	Sudden infant death syndrome
SLP	Speech-language pathologists
SMC	Smooth muscle cells
SPECT	Single photon emission computed tomography
SRMD	Stress-related mucosal damage
SSI	Symptom sensitivity index
TER	Transepithelial resistance
TLESR	Transient lower esophageal sphincter relaxation
TLOSR	Transient lower oesophageal sphincter relaxation
TLOSRs	Transient LOS relaxations
TLR	Toll-like receptor
TNF	Tumour necrosis factor
TNFα	Tumour necrosis factorα
TRP	Transient receptor potential
TRPV-1	Transient receptor potential vanilloid-1
UCSF	University of California, San Francisco
UES	Upper esophageal sphincter
UK	United Kingdom
UOS	Upper oesophageal sphincter
VAEs	Ventilator-associated events
VAP	Ventilator-associated pneumonia
VAS	Visual Analogue Scale
VATS	Video-assisted thoracoscopic surgery
VCD	Vocal cord dysfunction
VFSS	Video Fluoroscopic Swallow Study
WRAP-IPF	Weighing Risks and Benefits of Laparoscopic Anti-reflux Surgery in Patients with Idiopathic Pulmonary Fibrosis
ZO-1	Zonula occludens-1