Advanced Nutrition and Dietetics in Gastroenterology

Advanced Nutrition and Dietetics in Gastroenterology provides informative and broad-ranging coverage of the relation between nutrition and diet and gastrointestinal health and disease. It explores dietary factors involved in causation of a variety of gastrointestinal disorders, as well as the effects of these on nutritional status and the dietary treatments available. It also provides an overview of anatomy and physiology, measurement and assessment of function, and dietary components relevant to gastrointestinal health.

About the Editor
Miranda Lomer is a Senior Consultant Dietitian in Gastroenterology at Guy’s and St Thomas’ NHS Foundation Trust, London, and an Honorary Senior Lecturer in Nutritional Sciences at King’s College London, UK. She was formerly the Chairperson of the Gastroenterology Specialist Group of the British Dietetic Association.

About the Series Editor
Kevin Whelan is Professor of Dietetics at King’s College London. He is also Associate Editor-in-Chief of the Journal of Human Nutrition and Dietetics.
Dietary recommendations need to be based on solid evidence, but where can you find this information? The British Dietetic Association and the publishers of the *Manual of Dietetic Practice* present an essential and authoritative reference series on the evidence base relating to advanced aspects of nutrition and dietetics in selected clinical specialties. Each book provides a comprehensive and critical review of key literature in the area. Each covers established areas of understanding, current controversies and areas of future development and investigation, and is oriented around six key themes:

- Disease processes, including metabolism, physiology and genetics
- Disease consequences, including morbidity, mortality and patient perspectives
- Clinical investigation and management
- Nutritional consequences of disease
- Nutritional assessment, including anthropometric, biochemical, clinical, dietary, economic and social approaches
- Nutritional and dietary management of disease
Contents

Preface vii
Foreword ix
Editor biographies x
Contributors xi

SECTION 1 Physiology and function of the gastrointestinal and hepatobiliary tract 1

1.1 Physiology and function of the mouth 3
1.2 Physiology and function of the oesophagus 8
1.3 Physiology and function of the stomach 15
1.4 Physiology and function of the small intestine 21
1.5 Physiology and function of the colon 28
1.6 Physiology and function of the pancreas 33
1.7 Physiology and function of the hepatobiliary tract 36
1.8 Gastrointestinal microbiota 41
1.9 Gastrointestinal tract and appetite control 48

SECTION 2 Dietary components relevant to gastrointestinal health 55

2.1 Fibre and gastrointestinal health 57
2.2 Short-chain fermentable carbohydrates 72
2.3 Probiotics and the gastrointestinal microbiota 81
2.4 Prebiotics and gastrointestinal health 87

SECTION 3 Gastrointestinal disorders 93

3.1 Orofacial granulomatosis and nutrition 95
3.2 Eosinophilic oesophagitis and nutrition 101
3.3 Gastro-oesophageal reflux disease and nutrition 105
3.4 Oesophageal cancer and nutrition 111
3.5 Gastric cancer and nutrition 118
3.6 Gastroparesis and nutrition 127
3.7 Pancreatitis and nutrition 132
3.8 Pancreatic cancer and nutrition 140
3.9 Cystic fibrosis and nutrition 147
3.10 Lymphangiectasia and nutrition 155
3.11 Coeliac disease and nutrition 160
3.12 Inflammatory bowel disease pathogenesis 169
3.13 Inflammatory bowel disease nutritional consequences 180
3.14 Inflammatory bowel disease dietary management 191
3.15 Lactose malabsorption and nutrition 202
3.16 Intestinal failure and nutrition 210
3.17 Stomas and nutrition 218
3.18 Irritable bowel syndrome pathogenesis 226
3.19 Irritable bowel syndrome dietary management 233
3.20 Diverticular disease and nutrition 243
3.21 Constipation and nutrition 249
3.22 Colorectal cancer and nutrition 255

**SECTION 4**  Hepatobiliary disorders 263

4.1 Gallbladder disease and nutrition 265
4.2 Primary biliary cirrhosis and primary sclerosing cholangitis and nutrition 273
4.3 Alcohol-related liver disease and nutrition 280
4.4 Autoimmune hepatitis and viral hepatitis and nutrition 284
4.5 Non-alcoholic fatty liver disease and hereditary haemochromatosis and nutrition 290
4.6 Decompensated liver disease and nutrition 296
4.7 Hepatocellular carcinoma and nutrition 309
4.8 Liver transplantation and nutrition 311

Index 317
Preface

In recent years there has been an overwhelming interest in the role of diet and nutrition in gastrointestinal health and disease. There are a number of general books that focus on combining these topics but not specifically at an advanced level. The aim of this book is to be an essential and authoritative reference and review for an international audience of health professionals involved in the management or research of patients with gastrointestinal disorders.

The book is divided into four main sections:

- The first section is devoted to the physiology and function of the gastrointestinal and hepatobiliary tract including all the major organs, the gastrointestinal microbiota and the role of the gut neuroendocrine system in appetite regulation.
- The second section covers specific dietary components including fibre, short-chain fermentable carbohydrates, probiotics and the gastrointestinal microbiota and prebiotics in relation to gastrointestinal health.
- The third and fourth sections focus on gastrointestinal and hepatobiliary disorders respectively. These are comprehensive sections reviewing the evidence base relating to the pathogenesis, nutritional consequences and dietary management of disease.

The book provides a cutting-edge review of the evidence base relating to the basic aspects (for example, mechanistic aspects of physiology, immunology, microbiology, etc.) and applied aspects (for example, dietary impact and intervention) of diet and nutrition in gastrointestinal health and extensive focus on diet in the causation and treatment of gastrointestinal disease.

Each chapter provides a critical review of the key literature in each area, focussing on established areas of understanding and also on current controversies and areas of current and future development and investigation. The chapters extensively draw upon the literature with a focus on mechanisms as well as critical reviews of the efficacy of interventions and, where available, reference systematic reviews and meta-analyses.

The book is pitched at an advanced level to reflect the expertise of the readership. The intended readership is practitioners, researchers and educators in the area of gastrointestinal health and disease. This will include an interprofessional mix of dietitians, gastroenterologists, hepatologists, nutritionists, specialist nurses and surgeons. Due to the advanced level of the book, it may also be an invaluable resource for students in the final year of a Bachelors or Masters Degree in dietetics, nutrition, medicine or nursing, especially those undertaking relevant course units or research projects. It will also be of interest to those doing applied research in the areas of gastrointestinal immunology or microbiology. The book will also be of use for university educators preparing teaching materials in the above areas.

Miranda Lomer PhD RD
Senior Consultant Dietitian
Guy’s and St Thomas’ NHS Foundation Trust

Honorary Senior Lecturer
King’s College London
Editor
Advanced Nutrition and Dietetics in Gastroenterology
This book is the first title in a series commissioned as part of a major initiative between the British Dietetic Association and the publisher, Wiley. Each book in the series provides a comprehensive and critical review of the key literature in each clinical area. Each book is edited by one or more experts who have themselves undertaken extensive research and published widely in the relevant topic area. Each book chapter is written by experts drawn from an international audience and from a variety of disciplines as required of the relevant chapter (for example, dietetics, medicine, public health, basic sciences). We are proud to present the first title in the series: *Advanced Nutrition and Dietetics in Gastroenterology*. We hope that it impacts on health professionals’ understanding and application of nutrition and dietetics in the management of people with gastrointestinal disease and improves outcomes for such patients.

Kevin Whelan PhD RD  
Professor of Dietetics  
King’s College London  
Series Editor  
*Advanced Nutrition and Dietetics Book Series*
It is an honour and a privilege to write a foreword for this exceptional book devoted to nutrition and dietetics in gastrointestinal health and disease. Nutrition is a major discipline in gastroenterology and is often overlooked.

The first question a patient asks when faced with gastrointestinal problems is regarding diet. Up to now gastroenterologists have been poorly informed in answering this question. Nutrition should be an integral part of the undergraduate curriculum. It should also be included as a module for trainees in gastroenterology. This is largely ignored. Dietitians have a key role in the multidisciplinary team that cares for patients with gastrointestinal conditions and are experts in food and nutrition.

This book is very welcome as it has contributions from key opinion leaders in gastroenterology who have contributed significantly to the field of nutrition. *Advanced Nutrition and Dietetics in Gastroenterology* is edited by Miranda Lomer who has extensive knowledge and an enviable Curriculum Vitae in both research and clinical management of dietary challenges.

This book is a comprehensive text, and reviews concisely and succinctly, carefully annotated sections relating to the physiology and function of the gastrointestinal and hepatobiliary tract; dietary components relevant to gastrointestinal health; and the role diet plays in gastrointestinal and hepatology disorders. It is logical that diet has an effect on the microenvironment of the gut. Diet can affect the gastrointestinal mucosa directly and indirectly by altering the gastrointestinal microbiota. Nutrition in gastroenterology is a vast area to cover and in addition to practical aspects, this book thoroughly reviews the evidence base and proposes new areas for research.

This book is the result of close collaboration between dietitians, gastroenterologists and scientists dedicated to gastroenterology. It highlights the importance of diet in the multidisciplinary management of patients with gastrointestinal and hepatobiliary disease. It explores the therapeutic dietary strategies required and will improve patient care.

I would recommend *Advanced Nutrition and Dietetics in Gastroenterology* as essential reading for dietitians, physicians, surgeons and scientists with an enquiring mind on the role of diet in health and disease, and it should be mandatory for trainees in gastroenterology.

Professor Colm O’Morain
Emeritus Professor of Medicine
Trinity College Dublin
President of the United European Gastroenterology Federation 2011–2013
Editor biographies

Miranda Lomer PhD RD
Miranda Lomer is a Senior Consultant Dietitian for Gastroenterology at Guy’s and St Thomas’ NHS Foundation Trust and an Honorary Senior Lecturer in the Diabetes and Nutritional Sciences Division at King’s College London. Her clinical speciality and research interests include the dietary management of functional gastrointestinal disorders and inflammatory bowel diseases. Dr Lomer was formerly chairperson of the Gastroenterology Specialist Group of the British Dietetic Association and led the writing of the British Dietetic Association evidence-based guidelines for the dietary management of irritable bowel syndrome in adults and the British Dietetic Association evidence-based guidelines for the dietary management of Crohn’s disease in adults. Dr Lomer is on the panel of the National IBD Standards Group and represented the British Dietetic Association on a National Institute for Health and Clinical Excellence guideline for the diagnosis and management of irritable bowel syndrome in primary care. For her contribution to clinical practice, education and research, Dr Lomer was awarded the British Dietetic Association Elsie Widdowson prestigious annual lecture in 2014.

Kevin Whelan PhD RD
Kevin Whelan is the Professor of Dietetics in the Diabetes and Nutritional Sciences Division at King’s College London. He is a Principal Investigator leading a research programme exploring the interaction between the gastrointestinal microbiota, diet and health and disease. Professor Whelan undertakes clinical trials of probiotics, prebiotics, fibre and fermentable carbohydrates, together with molecular microbiology to measure their impact on the microbiota. In 2012 he was awarded the Nutrition Society Cuthbertson Medal for research in clinical nutrition. Professor Whelan is the Associate Editor-in-Chief for the Journal of Human Nutrition and Dietetics and is on the International Editorial Board for Alimentary Pharmacology and Therapeutics.
Contributors

**Stuart Allan MBBS MRCS**
Northumbria NHS Trust  
North Shields, UK

**Simran Arora MSc RD**
Specialist Hepatology and Liver Transplant Dietitian  
Royal Free London NHS Foundation Trust  
London, UK

**Stephen E. Attwood MD FRCS**
Consultant Surgeon  
Northumbria NHS Trust  
North Shields, UK

**Imran Aziz MBChB MRCP**
Gastroenterology Clinical Research Fellow  
Royal Hallamshire Hospital  
Sheffield, UK

**Qasim Aziz PhD FRCP**
Professor of Neurogastroenterology  
Wingate Institute of Neurogastroenterology  
Queen Mary University of London  
London, UK

**Paul A. Blaker BSc MRCP**
Clinical Fellow in Gastroenterology  
Guy’s and St Thomas’ NHS Foundation Trust  
London, UK

**Stephen R. Bloom FRS**
Head of Division of Diabetes, Endocrinology and Metabolism  
Imperial College London  
London, UK

**Gudrun De Bock PhD**
Professor  
University of Antwerp  
Antwer, Belgium

**Sorrel Burden PhD RD**
Lead Dietitian  
Central Manchester NHS Foundation Trust  
Manchester, UK

**Helen Campbell PhD RD**
Research Dietitian  
Guy’s and St Thomas’ NHS Foundation Trust and King’s College London  
London, UK

**Emma V. Carrington MSc MRCS**
Clinical Research Fellow  
Wingate Institute of Neurogastroenterology, Queen Mary University of London  
London, UK

**Yolande M. Causebrook BSc RNutr**
Nutritionist  
Newcastle University  
Newcastle upon Tyne, UK

**Jaimini Cegla MSc MRCP**
Wellcome Trust Clinical Research Fellow  
Imperial College London  
London, UK

**Saira Chowdhury BSc RD**
Highly Specialist Upper Gastrointestinal GI Surgery Dietitian  
Guy’s and St Thomas’ NHS Foundation Trust  
London, UK
Contributors

Alison Culkin PhD RD
Research Dietitian
St Mark’s Hospital
Harrow, UK

Emma Currie MSc RD
Specialist Gastroenterology Dietitian
Addenbrooke’s Hospital
Cambridge, UK

Barbara Davidson RD
Lead Specialist Dietitian Nutrition Support
Freeman Hospital
Newcastle upon Tyne, UK

Ashish P. Desai FRCS
Consultant Paediatric Surgeon
King’s College Hospital NHS Foundation Trust
London, UK

Frances Dorman BSc RD
Specialist Hepatology Dietitian
King’s College Hospital NHS Foundation Trust
London, UK

Michael P. Escudier MD FDSRCS
Reader and Consultant in Oral Medicine
King’s College London and Guy’s and St Thomas’ NHS Foundation Trust
London, UK

Adam D. Farmer PhD MRCP
Clinical Research Fellow
Wingate Institute of Neurogastroenterology,
Queen Mary University of London
London, UK

Lynnette R. Ferguson DPhil DSc
Professor and Head of Department of Nutrition
University of Auckland
Auckland, New Zealand

Mark Fox MD MRCP
Professor of Gastroenterology
University Hospital Zürich
Zürich, Switzerland
University of Nottingham
Nottingham, UK

Gillian Gatiss MSc RD
Specialist Hepatology and Liver Transplant Dietitian
Cambridge University Hospitals NHS Trust
Cambridge, UK

Liljana Gentschew MSc
Genetic Scientist
University of Kiel
Kiel, Germany

Konstantinos Gerasimidis PhD APHNutr
Lecturer in Clinical Nutrition
University of Glasgow and Glasgow Royal Hospital for Sick Children
Glasgow, UK

Pascale Gerbault PhD
Research Associate
University College London
London, UK

Glenn R. Gibson PhD
Professor of Food Microbiology
University of Reading
Reading, UK

Henriette Heinrich MD
Clinical Research Fellow
University Hospital Zürich
Zürich, Switzerland

Mary Hickson PhD RD
Research Dietitian and Honorary Senior Lecturer
Imperial College Healthcare NHS Trust and Imperial College London,
London, UK

Orla Hynes BSc RD
Highly Specialist Upper GI Surgery Dietitian
Guy’s and St Thomas’ NHS Foundation Trust
London, UK

Peter Irving MD FRCP
Consultant Gastroenterologist
Guy’s and St Thomas’ NHS Foundation Trust and King’s College London
London, UK
Contributors

Santhini Jeyarajah MD FRCS
Clinical Research Fellow
King’s College Hospital NHS Foundation Trust
London, UK

Yiannis N. Kallis PhD MRCP
Consultant Hepatologist
Barts Health NHS Trust, Royal London Hospital,
London, UK

Regina Keenan BSc
Senior Dietitian in Hepatobiliary Surgery
St Vincent’s University Hospital
Dublin, Ireland

Richard Keld MD MRCP
Consultant Gastroenterologist
Wrightington, Wigan and Leigh NHS Foundation Trust
Wigan, UK

Tanya Klopper M Nutr RD
Head of Dietetics, Macmillan Oncology Dietitian
Royal Surrey County Hospital
Guildford, UK

Vikas Kumar PhD
Postdoctoral Researcher
Ohio State University
Ohio, USA

Simon Lal PhD FRCP
Consultant Gastroenterologist
Salford Royal NHS Foundation Trust
Salford, UK

Rachel Lewis BSc RD
Clinical Lead Dietitian Critical Care
Glangwili Hospital
Carmarthen, UK

Anke Liebert PhD
Research Fellow
University College London
London, UK

Miranda C. E. Lomer PhD RD
Senior Consultant Dietitian in Gastroenterology
Guy’s and St Thomas’ NHS Foundation Trust and
King’s College London
London, UK

Angela M. Madden PhD RD
Principal Lecturer in Nutrition and Dietetics
University of Hertfordshire
Hatfield, UK

Luca Marciani PhD
Lecturer in Gastrointestinal MRI
Nottingham University Hospitals and University of Nottingham
Nottingham, UK

Catherine McAneney BSc RD
Clinical Specialist Dietitian Liver Transplantation
Royal Infirmary of Edinburgh
Edinburgh, UK

Laura M. McGeeney MSc RD
Specialist Hepatology and Liver Transplant Dietitian
Cambridge University Hospitals NHS Trust
Cambridge, UK

Alison Morton BSc RD
Clinical Specialist Dietitian
Leeds Teaching Hospital NHS Trust
Leeds, UK

Maria O'Sullivan PhD MINDI
Associate Professor in Human Nutrition
Trinity College Dublin
Dublin, Ireland

Niamh O’Sullivan BSc MINDI
Clinical Specialist Dietitian in Liver Disease
St Vincent’s University Hospital
Dublin, Ireland

Gareth Parkes PhD MRCP
Consultant Gastroenterologist
Barts Health NHS Trust
London, UK
Contributors

Anu Paul MS FRCS
Clinical Fellow in Paediatric Surgery
King’s College Hospital NHS Foundation Trust
London, UK

Mary Phillips BSc RD
Hepato-pancreaticobiliary Specialist Dietitian
Royal Surrey County Hospital
Guildford, UK

Nina C. Powell MSc RD
Specialist Hepatology and Liver Transplant Dietitian
Cambridge University Hospitals NHS Foundation Trust
Cambridge, UK

Tara Raftery BSc MINDI
Research Fellow
Trinity College Dublin
Dublin, Ireland

David S. Sanders MD FRCP
Consultant Gastroenterologist
Royal Hallamshire Hospital
Sheffield, UK

Jeremy D. Sanderson MD FRCP
Consultant Gastroenterologist
Guy’s and St Thomas’ NHS Foundation Trust and
King’s College London
London, UK

S. Mark Scott PhD
Co-Director, Gastrointestinal Physiology Unit
Wingate Institute of Neurogastroenterology,
Queen Mary University of London
London, UK

Clare Shaw PhD RD
Consultant Dietitian
Royal Marsden NHS Foundation Trust
London, UK

Sue Shepherd PhD AdvAPD
Senior Lecturer in Nutrition and Dietetics
La Trobe University
Melbourne, Australia

Amit Kumar Sinha PhD
Postdoctoral Fellow
University of Antwerp
Antwerp, Belgium

Chris Speed BSc
Senior Trial Manager
Newcastle University
Newcastle upon Tyne, UK

Heidi Staudacher M Nutr Diet RD
NIHR Doctoral Research Fellow
King’s College London and Guy’s and
St Thomas’ NHS Foundation Trust
London, UK

Katherine Stephens BSc
Research Fellow
University of Reading
Reading, UK

Dallas M. Swallow PhD
Professor of Human Genetics
University College London
London, UK

Rami Sweis PhD MRCP
Consultant Gastroenterologist
University College London Hospital
London, UK

Mark G. Thomas PhD
Professor of Evolutionary Genetics
University College London
London, UK

Natasha A. Vidas BSc RD
Specialist Hepatology Dietitian
King’s College Hospital NHS Foundation Trust
London, UK

Gemma E. Walton PhD
Postdoctoral Research Fellow
University of Reading
Reading, UK
Han-ping Wang PhD
Principal Scientist
Ohio State University
Ohio, USA

Kevin Whelan PhD RD
Professor of Dietetics
King’s College London
London, UK

David Westaby MA FRCP
Lead Clinician for Pancreatobiliary Services
Imperial College Healthcare NHS Foundation Trust
London, UK
SECTION 1

Physiology and function of the gastrointestinal and hepatobiliary tract
Chapter 1.1

Physiology and function of the mouth

Michael P. Escudier
King’s College London and Guy’s and St Thomas’ NHS Foundation Trust London, UK

1.1.1 Physiology

The mouth is an important organ as it is the entry point into the gastrointestinal (GI) tract and damage and disease can compromise dietary intake. Even very minor disorders can have a profound impact on nutritional status.

Anatomy

The oral cavity consists of a number of structures.

The lips surround the mouth and comprise skin externally and a mucous membrane (which has many minor salivary glands) internally, which together with saliva ensure adequate lubrication for the purposes of speech and mastication.

The cheeks make up the sides of the mouth and are similar in structure to the lips with which they are continuous but differ in containing a fat pad in the subcutaneous tissue. On the inner surface of each cheek, opposite the upper second molar tooth, is an elevation that denotes the opening of the parotid duct which leads back to the parotid gland located in front of the ear.

The palate (roof of the mouth) is concave and formed by the hard and soft palate. The hard palate is formed by the horizontal portions of the two palatine bones and the palatine portions of the maxillae (upper jaws). The hard palate is covered by thick mucous membrane that is continuous with that of the gingivae. The soft palate is continuous with the hard palate anteriorly and with the mucous membrane covering the floor of the nasal cavity posteriorly. The soft palate is made up of a fibrous sheet together with the glossopalatine and pharyngopalatine muscles and the uvula hangs freely from its posterior border.

The floor of the mouth can only be seen when the tongue is raised and is formed by the mucosa overlying the mylohyoid muscle. In the midline is the lingual frenum (a fold of mucous membrane), on either side of which is the opening of the submandibular duct from the associated submandibular gland.

The gingivae form a collar around the neck of the teeth and consist of mucous membranes connected by thick fibrous tissue to the periosteum surrounding the bones of the jaw. The gingivae are highly vascular and well innervated.

The teeth are important in mastication and in humans, who are omnivores, they enable both plant and animal tissue to be chewed effectively. Each tooth consists of a crown, which varies in shape dependent on the position in the mouth, and one or more roots. There are eight permanent teeth in each quadrant, consisting of two incisors, a canine, two premolars and three molars, resulting in a total of 32 permanent teeth.

The tongue is a highly mobile, muscular organ in the floor of the mouth which is important in speech, chewing and swallowing. In conjunction with the cheeks, it guides food between the upper and lower teeth until mastication is complete. The taste buds situated on the tongue are responsible for the sensation of taste (salt, bitter, sweet and sour).
Function

The main role of the mouth is to prepare food for swallowing via the oesophagus and its subsequent passage to the stomach. The first phase of this process is mastication (chewing) which requires activity in the muscles of mastication (masseter, temporalis, medial and lateral pterygoids and buccinator). Chewing helps digestion by reducing food to small particles and mixing it with the saliva secreted by the salivary glands. The saliva lubricates and moistens dry food whilst the movement of the tongue against the hard palate produces a rounded mass (bolus) of food which can be swallowed.

The saliva required for this process is produced by the three paired major salivary glands (parotid, submandibular and sublingual), together with the many minor salivary glands throughout the oropharynx. The total daily production of saliva is around 500 mL, with the rate of production around 0.35 mL/min at rest which increases to 2.0 mL/min during eating and falls to 0.1 mL/min during sleep. The contribution of the various glands varies at rest and during eating (Table 1.1.1).

In addition to its role in digestion and taste, saliva produces a film which coats the teeth and mucosa and helps to cleanse and lubricate the oral cavity. It also prevents dessication of the oral mucosa and acts as a barrier to oral microbiota [1], both physically and through its antimicrobial activity. The buffers within it also help to maintain optimal pH for the action of the salivary amylase and maintain the structure of the teeth.

Role in digestion

Very little digestion of food occurs in the oral cavity. However, saliva does contain the enzyme amylase which begins the chemical process of digestion by catalysing the breakdown of starch into sugars.

### Table 1.1.1 Contribution of groups of salivary glands to overall saliva production at rest and during eating

<table>
<thead>
<tr>
<th></th>
<th>Resting %</th>
<th>Stimulated %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Submandibular</td>
<td>65</td>
<td>49</td>
</tr>
<tr>
<td>Sublingual</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

1.1.2 Measurement and assessment of function

Salivary function is the most commonly assessed measure of oral function and can be achieved clinically by using the Challacombe dry mouth scale (Box 1.1.1).

A reasonable indication of salivary function may be obtained by measuring the resting (unstimulated) salivary flow over a period of 10 min. In health, the rate will normally be around 0.35 mL/min with a range of 0.2–0.5 mL/min. However, this will be reduced in the presence of xerostomic medications or underlying conditions such as Sjögren’s syndrome and a value below 0.2 mL/min requires further investigation and below 0.1 mL/min is indicative of an underlying condition or disease process. Whilst the stimulated parotid flow rate may also be determined, neither is particularly reliable and hence both should only be viewed as indicative rather than diagnostic.

1.1.3 Dental disease

The oral cavity is home to around 500 different microbial species. These bacteria together with saliva and other particles constantly form a sticky, colourless ‘plaque’ on the surface of teeth. Brushing and flossing help to remove this layer which is intimately involved in the development of dental caries and gingivitis. Plaque that is not removed can harden...
and form calculus which requires professional cleaning by a dentist or dental hygienist to prevent the development of periodontal disease which can lead to the destruction of the dental support structures and eventually loss of the affected tooth or teeth.

Whilst both dental caries and periodontal disease have been common for many years, non-carious tooth surface loss, particularly in the form of erosion, is a more recent development and is associated with modern lifestyle and dietary intake.

Dental caries

Dental caries can occur at any stage throughout life and is one of the most common preventable diseases in childhood [2]. In developed countries there has been a fall in the lifetime experience of dental caries by at least 75% since the 1960s but it still remains a concern in children from low socioeconomic groups and immigrants from outside Western Europe.

The occurrence of decay requires the presence of teeth, oral microbiota, carbohydrate and time. Following a meal, oral microbiota in plaque on the tooth surface ferment carbohydrate to organic acids. This rapid acid production lowers the pH at the enamel surface below the level (the critical pH) at which enamel will dissolve. When the carbohydrate supply is exhausted, the pH within plaque rises, due to the outward diffusion of the acids and their metabolism and neutralisation, and remineralisation of enamel can occur. Dental caries only progresses when demineralisation is greater than remineralisation.

As a result, the risk of dental decay is greatly increased by the intake of fermentable carbohydrate, e.g. sugars, at a frequency which results in the pH remaining below the critical level (the highest pH at which there is a net loss of enamel from the teeth, which is generally accepted to be about 5.5 for enamel). This risk can be negated by the total avoidance of sugar or at least minimised by limiting the frequency of intake, e.g. no between-meals consumption.

Periodontal disease

The presence of bacteria on the gingiva causes inflammation (gingivitis), resulting in the gums becoming red and swollen and often bleeding easily. Gingivitis is a mild form of gum disease that can usually be reversed with regular tooth brushing and flossing. This form of gum disease does not include any loss of bone or support tissue.

If gingivitis is not treated, the inflammation can spread and result in the loss of attachment of the gum to the tooth and the development of ‘pockets’ that are colonised by bacteria. The body’s immune system fights these bacteria and as a by-product the body’s natural response and bacterial toxins break down the bone and connective tissue that support the teeth. If this condition remains untreated, the teeth may eventually become mobile and require removal.

While some people are more susceptible than others to periodontal disease, smoking is one of the most significant risk factors and also reduces the chances of successful treatment. Periodontal disease has been reported as a potential risk factor for cardiovascular disease, poorly controlled diabetes and preterm low birth weight [3].

Non-carious tooth surface loss

Regular consumption of acidic foods and drinks can reduce the pH below the critical level and the surface layer of enamel is then lost through a combination of erosion, attrition (action of teeth on teeth) and abrasion (by foodstuffs). Over time, the full thickness of the enamel may be lost in this way, leaving exposed dentine which is often associated with sensitivity to temperature changes. This situation may be avoided by limiting the intake of acidic food and drink, e.g. carbonated drinks.

1.1.4 Oral manifestations of gastrointestinal disease

Oral manifestations can arise either as a direct presentation of the condition itself or secondary to the effects of the condition or its treatment.

Malabsorption may lead to iron, vitamin B12 or folate deficiency whilst blood loss is most commonly associated with iron deficiency. In all cases, a deficiency state may occur, resulting in anaemia. This can present with depapillation of the tongue (glossitis), a burning sensation affecting the oral mucosa, angular cheilitis or oral ulceration. Correction of the underlying deficiency state will
therefore be associated with their improvement and resolution.

Medical therapy commonly involves the use of corticosteroids or other immunosuppressive medications. Both of these increase the risk of opportunistic infections and hence oral candidosis [4] is frequently seen in the form of angular cheilitis (redness, crusting and splitting of the corners of the mouth), denture stomatitis (erythema of the mucosa in contact with the fit surface of a denture), acute pseudomembranous candidosis or oral soreness/burning affecting the tongue or oral mucosa. Some medications, e.g. methotrexate, may also cause oral ulceration which will only resolve on cessation of the treatment.

In contrast, disease-specific presentations vary and are discussed below.

Gastro-oesophageal reflux disease

Due to the high acidity of the gastric contents (pH 1), chronic gastro-oesophageal reflux disease may result in erosion of the teeth [5]. This classically affects the palatal aspect of the upper anterior teeth but may extend further to affect the upper premolar and molar teeth.

Coeliac disease

Coeliac disease may present with oral ulceration or dental enamel defects and, less commonly, atrophic glossitis. In addition, whilst the caries indexes are often lower than in unaffected individuals, they may experience delay in tooth eruption [6].

Crohn’s disease and orofacial granulomatosis

The precise relationship between Crohn’s disease and orofacial granulomatosis remains unclear [7]. They share many orofacial manifestations including cervical lymphadenopathy, lip swelling, angular cheilitis, mucosal tags, full-thickness gingivitis, submandibular duct ‘staghorning’, fibrous banding and oral ulceration [8].

The oral ulceration seen may arise in relation to an associated deficiency state or medical therapy when it takes a linear form and occurs in the sulci, it is suggestive of underlying GI involvement requiring further investigation [8].

Crohn’s disease may also rarely present with pyostomatitis gangrenosum (chronic ulceration) affecting the tongue or oral mucosa [9].

Ulcerative colitis

Oral features of ulcerative colitis are generally secondary to the underlying condition or its treatment. Rarely, pyostomatitis vegetans (a generalised ulceration of the oral mucosa) may be the initial presentation of previously occult ulcerative colitis [10].

Irritable bowel syndrome (IBS)

A significant number of patients with IBS also have orofacial pain such as facial arthromyalgia (16%, [11]) or persistent orofacial pain (atypical facial pain, atypical odontalgia) [12]. Conversely, IBS has been shown to be present in many (64%) patients diagnosed with facial arthromyalgia [11].

References


Chapter 1.2

Physiology and function of the oesophagus

Rami Sweis
University College London Hospital, London, UK

The oesophagus co-ordinates the transport of food and fluid from the mouth to the stomach. The oesophagogastric junction (OGJ) is a physiological barrier which reduces reflux of gastric contents. In harmony, these processes limit contact of the swallowed bolus, refluxed acid and other chemicals with oesophageal mucosa. Disruption of function can interrupt bolus delivery or induce gastro-oesophageal reflux. Symptoms produced may range in severity from heartburn and regurgitation to dysphagia and pain.

1.2.1 Anatomy

Oesophagus

The oesophagus is a muscular tube connecting the pharynx to the stomach. The cervical oesophagus extends distally from the cricopharyngeus and the thoracic oesophagus terminates at the hiatal canal before it flares into the gastric fundus. The muscularis propria consists of the outer longitudinal and inner circular muscle layers. The musculature is divided into the proximal striated and mid-distal smooth muscle. This proximal ‘transition zone’ is located one-third of the distance from the pharynx and is the site with the weakest force of peristaltic contractions [1].

Histologically, the oesophageal wall is composed of the mucosa, submucosa and muscularis mucosa. The oesophageal body is lined by non-keratinised stratified squamous epithelium which abruptly joins with the glandular gastric columnar epithelium at the squamocolumnar junction. This can be the site of mucosal change associated oesophagitis and Barrett’s oesophagus.

The antireflux barrier

The OGJ is not a clearly identifiable sphincter but its sphincter-like properties can be defined functionally as a high-pressure zone between the stomach and oesophagus. Sphincter competence is dependent on the integrity and overlap of the intrinsic lower oesophageal sphincter (LOS) and diaphragmatic crura. A separation, hiatus hernia, is associated with disruption of LOS integrity, loss of the intra-abdominal LOS segment and an increased susceptibility to gastro-oesophageal reflux.

1.2.2 Physiology and function

Voluntary swallowing initiates with ‘deglutitive inhibition’ of the smooth muscle oesophagus and LOS. This reflex relaxation is nitric oxide mediated and permits passage of the bolus with minimal resistance. The subsequent excitatory, predominantly cholinergic, activity produces a progressive wave of smooth muscle excitation. A co-ordinated peristalsis clears the bolus from the oesophagus.

The LOS exhibits a continuous resting (basal) tone which relaxes on stimulation of the intramural nerves such as during deglutitive inhibition (swallowing). Disruption of this physiological process may impact on bolus transport and induce symptoms
1.2 Physiology and function of the oesophagus

A representative normal swallow using high-resolution manometry is presented in Figure 1.2.1.

Spontaneous LOS relaxations normally occur as a response to gastric postprandial distension and bloating: ‘transient lower oesophageal sphincter relaxation’ (TLOSR). LOS relaxation can also follow peristaltic activity: ‘swallow-induced lower oesophageal sphincter relaxation’ (SLOSR). Gastro-oesophageal reflux and belch occur when there is equalisation of pressure between the stomach and oesophagus (common cavity) (Figure 1.2.2). Patients with gastro-oesophageal reflux disease (GORD) do not have an increased frequency of TLOSRs; rather, the tendency of reflux to occur during these events is greater [2]. The effectiveness of oesophageal clearance of refluxed material is an important contributor to the severity of GORD [3–5]. Other determinants of GORD include the presence and size of a hiatus hernia, increasing age and obesity as well as the calorie and fat content of the diet [6,7].

**Box 1.2.1 Co-ordinated peristaltic activity**

Co-ordinated peristaltic activity is a multistep process which usually requires:

- a pharyngeal ‘pump’ – to push food and fluid through the oesophagus
- gravity – whereby bolus weight contributes to its aboral progress
- appropriate relaxation and opening of the oesophagogastric junction
- effective oesophageal motor function – deglutitive inhibition followed by co-ordinated peristaltic contraction
- a positive oesophagogastric pressure drop.

Measurement and assessment of function

In the absence of disease on endoscopy and failure to respond to empirical therapy, guidelines recommend manometry and ambulatory reflux testing [8,9]. Recent advances in technology provide better insight into the assessment of oesophageal function and disease.

**Manometry**

Peristalsis and OGJ activity can be measured with manometry. Conventional manometry (4–8 sensors) measures the circumferential contraction, pressure wave duration and peristaltic velocity of single water swallows. High-resolution manometry (HRM; 21–36 sensors) is an advance on conventional systems as it provides a compact, spatiotemporal representation of oesophageal pressure activity. In addition, it can measure the forces that drive movement of food and fluid through the oesophagus and OGJ [10]. An uninterrupted well-co-ordinated peristalsis defines oesophageal motility while the presence of a positive pressure gradient in the absence of obstruction describes whether this motility is effective and likely to clear the bolus [11] (see Figure 1.2.1). Thus HRM improves diagnostic sensitivity to peristaltic dysfunction as symptoms and mucosal damage are more likely to occur as a result of disturbed bolus transport and poor clearance [5]. Furthermore, recent advances in methodology have shown how HRM can also facilitate the assessment of swallowing behaviour (eating and drinking) when symptoms are more likely to be triggered [5,12,13] (Box 1.2.2).

**Ambulatory reflux studies**

Gastro-oesophageal reflux disease (GORD) occurs when gastric contents pass into the oesophagus at an increased frequency, are not effectively cleared or are perceived in an exaggerated manner. This can lead to mucosal damage and/or symptoms with varying degrees of severity. Presenting symptoms alone are an unreliable guide to identifying oesophageal dysfunction [14,15]. Objective testing is required to avoid inappropriate medical and surgical therapy. Ambulatory pH monitoring provides an assessment of oesophageal acid exposure and symptoms. Standard testing is performed using a 24-hour nasopharyngeal pH catheter (with or without impedance, see next section). Diagnosis is made based on measurements of oesophageal acid exposure (e.g. total number of reflux events and percent time reflux events cause a pH drop below a threshold of 4) as well as the association of reflux events with symptoms. Measurements can
be further subdivided into upright and supine. However, intolerance to the nasal catheter can influence the result.

**Multiple intraluminal impedance with pH monitoring (MII-pH)**

Oesophageal symptoms are often related to disturbed bolus transport rather than acid reflux [16]. Also symptoms may persist despite effective acid suppression as acid-reducing medications do not influence the frequency or volume of non-acid reflux episodes [17,18]. Multiple intraluminal impedance (MII) can determine the direction of bolus movement, the success or failure of bolus transit and the proximal extent of the refluxate. Furthermore, it can discriminate between liquid and gas reflux. When combined with a pH sensor (MII-pH), it can differentiate between acid (pH <4), weakly acid (pH 4–7) or weakly alkaline (pH >7) reflux [19]. Therefore, MII-pH is considered to be more sensitive than standard pH testing, with up
Figure 1.2.2  Transient lower oesophageal sphincter relaxation followed shortly afterwards by a common cavity during which there is equalisation of pressure between the stomach and oesophagus when reflux is most likely to occur. The event is terminated and the oesophagus is cleared of refluxed contents with the arrival of a well-coordinated primary peristalsis. Oesophageal and lower oesophageal sphincter pressures return to baseline levels following completion of peristalsis. TLOSR, transient lower oesophageal sphincter relaxation.

Box 1.2.2  Hierarchical analysis of high-resolution manometry
Hierarchical analysis of high-resolution manometry studies according to the Chicago Classification whereby pathology in the OGJ is considered first. Major motility disorders (achalasia, absent peristalsis, diffuse oesophageal spasm and extreme hypertensive disorders) are never found in healthy individuals, are commonly associated with impaired bolus transport and, in turn, often lead to symptoms. The significance of peristalsis abnormalities described in ‘Other motility disorders’ is not clear as these can also be found in asymptomatic individuals [20].

I. Oesophagogastric junction (OGJ) obstruction
Achalasia
Classic (non-relaxing LOS + aperistalsis + dilated oesophagus)
Compression (non-relaxing LOS + aperistalsis + oesophageal pressurisation)
Vigorous (non-relaxing LOS + oesophageal spasm)

Other obstruction
Eosinophilic oesophagitis
Benign or malignant stricture
Post surgery (e.g. antireflux procedure)

II. Major motility disorder
Absent peristalsis
Diffuse spasm
Jackhammer oesophagus (nutcracker with extreme pressures)

III. Other motility disorders
Weak peristalsis
Frequent failed peristalsis
Hypertensive peristalsis
Rapid contractility
to 20% improvement in diagnostic yield [21]. Indications for its use are the same as for standard ambulatory pH studies. In those with established GORD but ongoing symptoms despite optimal medical therapy, MII-pH can be performed while on acid reducing medication in order to identify if (non-acid) reflux is the culprit or to exclude breakthrough acid reflux. In addition, in the assessment of atypical disease (e.g. laryngopharyngeal reflux, aerophagia, supragastric belching, cough).

**Wireless pH monitoring (Bravo®)**

Wireless pH monitoring (Bravo®, Given Imaging) is an endoscopically placed, catheter-free, ambulatory pH monitoring system (Figure 1.2.3). Bravo® is a viable option for those who are intolerant to the nasal catheter [6]. It can measure for prolonged periods (at least 48 h) [22,23] and is especially suitable for patients with intermittent symptoms [22,24] or those with persistent typical symptoms whose catheter-based study was inconclusive [25]. However, Bravo® cannot discriminate between liquid and gas reflux nor can it differentiate between acid and nonacid reflux.

### 1.2.3 Pathology

#### Motility

An important advance of the modern HRM-based classification (the Chicago Classification) [26–28] is that it is hierarchical; the OGI is considered first because pathology within the OGI will influence oesophageal function above [20]...