Cleft Lip and Palate
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Epidemiology, Aetiology and Treatment

Volume Editor

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28 figures and 9 tables, 2012
Cleft lip and palate: epidemiology, aetiology, and treatment / volume editor, Martyn T. Cobourne. p. ; cm. -- (Frontiers of oral biology, ISSN 1420-2433 ; v. 16)
Includes bibliographical references and indexes.
I. Cobourne, Martyn T. II. Series: Frontiers of oral biology ; v. 16. 1420-2433
617.5'22--dc23
2012015056

Bibliographic Indices. This publication is listed in bibliographic services, including Current Contents* and Index Medicus.

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© Copyright 2012 by S. Karger AG, P.O. Box, CH–4009 Basel (Switzerland)
www.karger.com
Printed in Germany on acid-free and non-aging paper (ISO 9706) by Bosch-Druck GmbH, Ergolding
ISSN 1420–2433
e-ISSN 1662–3770
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Foreword

There is some truth in the old adage that ‘an expert is someone who knows more and more about less and less’. Craniofacial biology was simpler when I was a Glasgow dental student in the 1960s. Knowledge of normal and abnormal orofacial development was mainly derived from the histological dissection of animal and human embryos, accompanied by speculation on the growth mechanisms responsible. Understanding of those mechanisms has of course been transformed in the ensuing half century with the advent of new laboratory technologies, animal models, genome-wide sequencing, and so forth.

On the other hand, evidence around clinical care, with some exceptions, has hardly changed. Indeed many of the historical disputes regarding best surgical techniques and the value or otherwise of adjunctive procedures such as presurgical orthopaedics (an even earlier Glasgow export) continue to the present day. But happily, there are signs that we are beginning to dig ourselves out of this mire, with the emergence of well-structured multicentre comparisons and even well-powered randomised trials.

One of the high points of my time in clinical cleft research was participation in a European Commission project known as Eurocran (2000–2005), which forged a research partnership of clinicians, geneticists, laboratory scientists, and epidemiologists, and which continues in various forms today. Almost by osmosis, we began to grasp the importance of each other’s research in the thick mix of initiatives required to advance understanding, care, and prevention.

Accordingly, this book fills a significant gap in the literature, providing an update on the state of the science concerning the aetiology and mechanisms responsible for clefts of the lip and palate, together with an overview of contemporary clinical management.

The first section provides a thorough international review of the epidemiology of orofacial clefting, affirming that non-syndromic, non-chromosomal clefting has a polygenic multifactorial aetiology that exhibits geographic and racial variations. In particular, variations emerging on the basis of sub-phenotype, gender and exposure to environmental factors in themselves raise important research questions about cause and ultimate prevention. Complementing this is a review of the considerable progress in gene identification over the last two decades, alongside the influence of environmental factors. Future advances in these areas will require collaboration between clinicians and scientists.

The second section explores the coordination of different tissues and signalling pathways necessary for palatogenesis, via cutting-edge research involving mouse models. A helpful chapter providing an account of the stages of palatogenesis and the critical cellular and molecular mechanisms that accompany each step provides a clear framework for assimilating the more detailed accounts of individual growth factors that follow.
The last section covers the principal elements in clinical care. Surgical anatomy, primary surgery and major secondary procedures are covered, and the uncertainty in selecting protocols of primary surgery in particular is acknowledged. Orthodontics and speech therapy are presented in a pragmatic way with emphasis on teamwork and a choice of interventions designed to optimise outcome while minimising burden. A full account of alveolar bone grafting, possibly the most important addition to cleft care in recent decades, is included. Finally, the importance of monitoring outcomes and collaborative multicentre working in research are stressed.

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Clefts affecting the lip and palate are a relatively common group of developmental anomalies that occur in many human populations. They are seen in isolation or in combination with more widespread developmental disease, and can contribute towards significant morbidity for affected individuals, particularly in their formative years, which inevitably has an impact throughout their lifetime. These conditions are the focus of research for scientists within many different specialties, and this is reflected in the current volume which is divided into three broad sections describing current concepts in the epidemiology, molecular biology and contemporary management of cleft lip and palate.

In the first section, the etiological basis of human cleft lip and palate is discussed in the broadest sense, with focus on the epidemiology and underlying genetic and environmental contributions to this condition. In the second section, the developmental biology of early lip and palate development is discussed. There is an extensive discussion of the predominant developmental model used to investigate facial development, the mouse, whilst the principle molecular signalling pathways involved in lip and palate development are also described (Hedgehog, Bone Morphogenetic Protein, Fibroblast Growth Factor and WNT), with focus on their role in the aetiology of oro-facial clefting. Finally, in the third section, current concepts and controversies in the management of cleft lip and palate are discussed, including the assessment of treatment outcome, interventions for primary surgical correction, orthodontic treatment, alveolar bone grafting and the management of speech and language development. In the final chapter, the use of molecular tools in the prevention and treatment of cleft lip and palate is discussed, highlighting how translational research might offer possibilities to harness knowledge of the underlying developmental biology of lip and palate formation to prevent or more effectively treat cleft lip and palate in affected human populations. Once again, these experiments are being conducted primarily in the mouse, but they offer exciting possibilities for future strategies aimed at combating this common developmental anomaly.

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