Velo-cardio-facial syndrome (VCFS) is a genetic disorder associated with a deletion of the long arm of chromosome 22. It is the most common interstitial deletion disorder found in man and affects every major system in the body with more than 100 physical and behavioural phenotypic features reported. This book, written by leading international VCFS clinicians and scientists, attempts to summarise the rapid progress that has recently been made in understanding and treating people with VCFS. The focus is on clinical issues with chapters devoted to psychiatric disorders (with particular reference to the high rates of schizophrenia reported), neuroimaging, speech and language disorders, as well as cardiac, ENT, gastrointestinal, ophthalmic, and urological manifestations. Molecular genetics, immunodeficiency, and genetic counselling are also covered, and practical approaches to diagnosis and treatment described. As VCFS is seen as a paradigm for other microdeletion disorders, this book will appeal not just to clinicians who see VCFS patients, but also to those with interests in other genetic disorders.

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Velo-Cardio-Facial Syndrome

A Model for Understanding Microdeletion Disorders

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Abbreviations

AAA anomalies of the aortic arch
CCTCC cortico-cerebellar-thalamic-circuit
COMT catechol-O-methyltransferase
DTI diffusion tensor imaging
FISH fluorescence in situ hybridization
fMRI functional MRI
FSIQ full-scale IQ
IAA interrupted aortic arch
MAPCA major aorto-pulmonary collateral arteries
MRA magnetic resonance angiography
NMDA N-methyl-D-aspartate
NVLD nonverbal learning disability
OSMCP occult submucous cleft palate
PA-VSD pulmonary atresia with ventricular septal defect
PTA (persistent) truncus arteriosus
SLI specific language impairment
SMG supramarginal gyrus
TF tetralogy of Fallot
VCFS velo-cardio-facial syndrome
VDWS van der Woude syndrome
VPI velopharyngeal insufficiency
WMHI white matter hyperintensities
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Foreword

The term velo-cardio-facial syndrome (VCFS) was coined almost 30 years ago and at that time VCFS was thought to be a very rare congenital malformation. Molecular analysis subsequently revealed that VCFS is associated with deletions encompassing genes mapping to chromosome 22q11, and since that discovery VCFS has been studied intensively by clinicians, geneticists and developmental biologists. Part of this interest is sparked by the relative frequency of the deletion; at 1 in 4000 live births VCFS is the most common microdeletion syndrome known in man.

VCFS patients may present at many different clinics given the protean nature of the condition – over 100 different manifestations have been described in the literature. This book attempts to summarise the rapid progress that has recently been made in understanding and treating people with VCFS. We hope that publication of this book will be useful for several reasons: (1) professionals studying or treating one aspect of VCFS are often relatively unaware of the involvement of other systems and this book will assist them in obtaining a more holistic view of people with VCFS; (2) VCFS may be seen as a paradigm for other less common microdeletion disorders and experience with VCFS may help to direct research and treatment strategies across a range of other microdeletion disorders; (3) while this book emphasises the clinical issues relevant to VCFS, it also reflects the increasing recognition that an understanding of relatively rare disorders such as VCFS can tell us much about more common conditions, such as predisposition to psychiatric illness; (4) the study of the embryological basis for the structural malformations observed in VCFS is helping to uncover some basic mechanisms of developmental biology.

There has recently been considerable excitement at how rapidly our understanding of VCFS has evolved and we have sought to convey this excitement in this book. In addition, we have been privileged to meet numerous people with VCFS and their families over the past decade and have been inspired by the courage and dedication of affected individuals and their families. We dedicate this book to them.