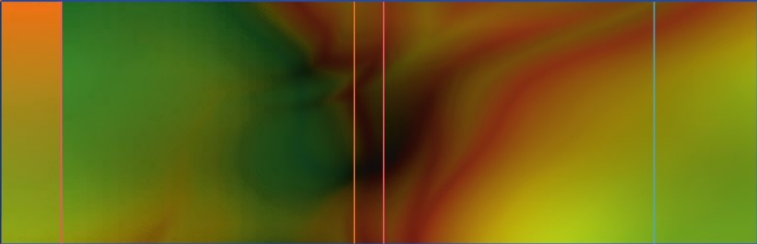


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Neurofibromatoses in Clinical Practice



Springer

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Preface

Over the last 20 years there has been a rapid increase in our understanding of the disease mechanisms underlying neurofibromatosis 1 (NF1) and neurofibromatosis 2 (NF2), and related disorders. The neurofibromatoses are inherited diseases that involve the nervous system predominantly, but are distinct on both clinical and genetic grounds. Advances in molecular biology and mouse models have paved the way for clinical trials to combat benign and malignant tumors that characterize both diseases.

NF1 and NF2 are well documented in the medical literature, but partly due to the nomenclature, the distinction between the two conditions is blurred by clinicians. Furthermore the characterization of related and overlapping disorders has added to the complexity of diagnosis and management. The media has focused inexorably on people with NF1 who have extreme disfigurement, aiming to titillate rather than educate us, while NF2 is largely unknown outside of hospital practice.

In this book we aim to provide an accessible, up-to-date guide for nonspecialists on the diagnosis, management, and long-term care of people with NF1 and NF2. We emphasize the referral pathways to specialist centers for individuals with complex disease and highlight the available support networks. Above all we wish to show that coping with the neurofibromatoses relies on a partnership between patient and clinician, based on mutual trust and an ability to listen to the needs and choice of the individual.

Rosalie E. Ferner

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Contents

1 Neurofibromatosis 1	1
History of Current Terminology	1
Epidemiology	2
Mosaic NF1	2
Genetics of NF1	3
Genetics of Mosaic NF1	3
Skin Manifestations of NF1	4
Café au Lait Patches	4
Freckling	5
Campbell de Morgan Spots	5
Xanthogranulomas	5
Glomus Tumors	5
Bone	8
Pseudarthrosis of the Long Bones	8
Short Stature	9
Reduced Bone Mineral Density	10
Scoliosis	10
Non-ossifying Neurofibromas	11
Vertebral Scalloping	11
Neurological Complications of NF1	11
Neurofibromas	12
Neurofibromatous Neuropathy	23
Cognitive Impairment	24
Brain Tumors	25
Optic Pathway Gliomas (OPG)	27
Presentation of NF1-OPG and Difference from Sporadic OPG	28

Nervous System Malformations	30
Epilepsy	32
Multiple Sclerosis	33
Cerebrovascular Disease	33
The Eye (See Section on Neurological Complications for Optic Pathway Glioma)	34
Cardiovascular Disease	35
Hypertension	35
Respiratory Problems	36
Gastrointestinal Disease	37
Gastrointestinal Stromal Tumor GIST	37
Carcinoid Tumors	37
Gastrointestinal Neurofibromas and Dysplastic Lesions	37
Pregnancy	37
Genetic Diagnosis and Counseling	38
Prenatal Testing	38
Genetic Counseling for Patients with Segmental NF1	39
Accuracy and Cost of NF1 Mutation Testing	39
Assessment and Follow-up of People with NF1	39
Children	39
Young People 16–25 Years	40
Adults	40
Nationally Commissioned “Complex NF1” Service	41
References	43
2 Neurofibromatosis Type 2 (NF2)	47
Terminology	47
Disease Name and Synonyms	47
Diagnosis	48
Epidemiology	49
Mosaicism	49
Clinical Manifestations	50

Screening At-Risk Individuals	55
Surveillance	57
Managing Affected Children.	58
Screening Individuals with Insufficient Criteria for NF2.	58
Genetics	58
Differential Diagnosis.	59
NF2 Management	60
Surgery.	60
Radiotherapy	61
Hearing Rehabilitation	62
New Therapies	62
Genetic Counseling and Prenatal Counseling.	63
Mode of Inheritance	63
Risk to Family Members	63
Predictive Testing	65
Complications That Require Referral to National NF Centers	65
Conclusions	66
References	66
 3 The Neurofibromatoses: Differential	
Diagnosis and Rare Subtypes.	71
Introduction	71
Case History: The Importance of Clinical Diagnosis Prior to Genetic Testing.	74
Clinical Assessment.	75
Past Medical History	75
Family History.	77
Examination	77
Radiology/Histology Review	77
NF Pigmentary Changes: Key Clinical Features	78
Café au Lait Spots	78
Skin Fold Freckling	80
Peripheral Nerve Tumors in NF: Clinical Clues to Diagnosis	81

Neurofibromas Versus Schwannomas	81
NF2 Plaques	82
Eye Features of NF	83
NF1 Differential Diagnosis: The NF1/NF2	
Overlap	83
Case History: Delay in Diagnosis	
in a Child with NF2.....	84
NF1 Subtypes	85
Introduction	85
Segmental/Localized NF1	85
Generalized Mosaic NF1.....	87
The NF1 Microdeletion Syndrome.....	87
Molecular Basis of Deletions	90
The Clinical Phenotype	90
Should All NF1 Patients Be Tested	
for Deletions?	93
Spinal NF1.....	93
Watson Syndrome.....	95
CAL-Only Phenotypes	96
Legius Syndrome	96
NF1 Exon 17 3-bp Inframe Deletion	
(c.2970_2972delAAT).....	100
Neuro-Cardio-Facial Cutaneous (NCFC)	
Syndromes and Their Overlap	
with NF1	101
Introduction	101
Noonan Syndrome	105
Is There a Neurofibromatosis Noonan	
Syndrome?.....	105
LEOPARD Syndrome.....	105
Costello and Cardio-Facio-Cutaneous	
(CFC) Syndromes.....	106
Other Pathway Disorders	107
Constitutional Mismatch Repair Deficiency	
(CMMR-D): A Rare But Important Cause	
of a Phenotype Overlapping with NF1	108

When to Think About CMMR-D in a Child Presenting with Multiple CAL Spots or Segmental NF1	109
CAL in Other Mismatch Repair Disorders	109
NF1: Differential Diagnosis – Other Conditions	110
Introduction	110
Conditions with CAL Spots and Other Patchy Skin Pigmentation Changes	111
Conditions with Skin Lesions Misdiagnosed as CAL Spots	113
Conditions with Tumors	114
NF1 Diagnostic Criteria: Pitfalls	115
NF1 Genetic Testing Indications	118
NF2: Differential Diagnosis and Related Conditions	119
Introduction	119
Schwannomatosis	119
Multiple Meningiomas	121
Misdiagnosis of Other Cerebello-Pontine (CP) Angle Tumors as Vestibular Schwannomas	121
References	122
4 Psychological Impact of the Neurofibromatoses	129
Neurofibromatosis 1	129
Unpredictability of Disease Complications . . .	129
Need for Expert Clinicians	130
Disfigurement	131
Facial Plexiform Neurofibromas	131
Cutaneous and Subcutaneous Neurofibromas	131
Education	133

xiv Contents

Neurofibromatosis 2	134
Measures of Quality of Life in NF2	134
Hearing Rehabilitation	135
Specialist Neurofibromatosis Nurses and Specialist Advisers.	136
The Neuro Foundation	137
The Patient as Educator	137
References	140
 5 Clinical Quiz: Diagnostic and Management Pitfalls of Neurocutaneous Disease.	 141
Quiz Questions.	141
Quiz Answers	145
 Appendix	 149
 Index	 159

Introduction

Rosalie E. Ferner

Definition of Neurofibromatosis 1 and Neurofibromatosis 2

Neurofibromatosis 1 (NF1) and neurofibromatosis 2 (NF2) are inherited neurocutaneous conditions that are clinically and genetically distinct and carry a high risk of tumor formation.¹ NF1 occurs in 1 in 2,500 births while NF2 is rare and has a birth incidence of 1 in 33,000.^{2,3} NF1 and NF2 encode proteins that act as tumor suppressors by controlling cell growth and proliferation. The NF1 gene is on chromosome 17q11.2 and the protein product is neurofibromin; the gene for NF2 is on chromosome 22q 11.2 and encodes a protein known as merlin.⁴⁻⁸ NF1 is characterized by café au lait patches, skin fold freckling, iris Lisch nodules, bony dysplasia, and benign peripheral nerve sheath tumors called neurofibromas.⁹ The complications are variable, unpredictable, and widespread, ranging from learning difficulties, high blood pressure, and gastrointestinal symptoms to disfigurement and malignancy.¹

Bilateral vestibular schwannomas are the hallmark lesion of NF2 and cause hearing and balance disturbances.^{1,10} Schwannomas may develop on other cranial nerves, spinal nerve roots and peripheral nerves. Meningiomas, ependymomas and gliomas are associated with NF2.^{1,10} Skin manifestations are less conspicuous than in NF1, but eye problems including juvenile cataracts are recognized.^{1,10}

Recent Advances

Recent advances in molecular biology, mouse models of disease, and improvements in neuroimaging have permitted the distinction between NF1 and NF2 and the characterization of the many clinical manifestations.¹ They have resulted in the development of clinical trials that are underway to evaluate targeted therapy for disease complications. Conditions can be delineated that overlap with NF1 and NF2 but are distinct genetically and have different clinical outcomes. Legius syndrome is associated with mutations in the tumor suppressor gene *SPRED1* on chromosome 15, and is characterized by café au lait patches, freckling, and mild learning problems, without neurofibromas or Lisch nodules.¹¹ People with schwannomatosis have mutations in the *INI1/SMARCB1* tumor suppressor gene and develop multiple schwannomas in the absence of vestibular schwannomas or other NF2 tumors.^{12,13}

Aims

Neurocutaneous diseases are complex to diagnose and treat and many patients require specialist multidisciplinary management and surveillance. However, due to multiple disease manifestations people with NF1 and NF2 present to different clinicians without specialist expertise in these diseases. Our aim is to provide a succinct accessible guide to the neurofibromatoses for the nonspecialist, including diagnosis, current management protocols, and indications for referral to specialist centers. The goal is optimum provision of care for neurocutaneous disease throughout the UK through partnership between local clinicians, specialist NF centers, and people with NF1 and NF2.

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