

Brief contents

Detailed contents *xi*

System-based contents *xv*

Glossary of terms used in dysmorphology *xix*

Glossary of genetic and genomic terms *xxiv*

Abbreviations *xxxv*

Chapter advisers *xlvi*

Expert advisers *xlix*

Expert advisers to the first edition *liii*

1 Introduction

2 Clinical approach

3 Common consultations

4 Cancer

5 Chromosomes

6 Pregnancy and fertility

Appendix

Index *863*

1

53

333

541

623

703

805

Detailed contents

System-based contents xv
 Glossary of terms used in dysmorphology xix
 Glossary of genetic and genomic terms xxiv
 Abbreviations xxxv
 Chapter advisers xlviii
 Expert advisers xlix
 Expert advisers to the first edition liii

1 Introduction 1

Adoption 2
 Approach to the consultation with a
 child with dysmorphism, congenital
 malformation, or developmental delay 4
 Autosomal dominant (AD) inheritance 8
 Autosomal recessive (AR) inheritance 10
 Communication skills 12
 Complex inheritance 14
 Confidentiality 16
 Confirmation of diagnosis 18
 Consent for genetic testing 20
 Genetic basis of cancer 22
 Genetic code and mutations 24
 Genomes and genomic variation 28
 Genomic imprinting 30
 Genomic sequencing and interpretation of
 data from WES or WGS analyses 32
 Mitochondrial inheritance 34
 Reproductive options 36
 Testing for genetic status 38
 Timing and origin of new dominant
 mutations 42
 Useful resources 44
 X-linked dominant (XLD), semi-dominant,
 pseudoautosomal, and male-sparing
 inheritance 46
 X-linked recessive (XLR) inheritance 50

2 Clinical approach 53

Ambiguous genitalia (including sex
 reversal) 54
 Anal anomalies (atresia, stenosis) 58
 Anterior segment eye malformations 62
 Arthrogryposis 66
 Ataxic adult 70
 Ataxic child 74
 Brachydactyly 78
 Broad thumbs 82

Cardiomyopathy in children under 10 years 84
 Cataract 88
 Cerebellar anomalies 92
 Cerebral palsy 96
 Chondrodysplasia punctata 98
 Cleft lip and palate 102
 Coarse facial features 106
 Coloboma 110
 Congenital heart disease 112
 Congenital hypothyroidism 116
 Corneal clouding 120
 Deafness in early childhood 122
 Developmental delay in the child with
 consanguineous parents 126
 Developmental regression 128
 Duane retraction syndrome 132
 Dysmorphic child 134
 Dystonia 138
 Ear anomalies 142
 Facial asymmetry 146
 Failure to thrive 150
 Floppy infant 154
 Fractures 158
 Generalized disorders of skin pigmentation
 (including albinism) 162
 Hemihypertrophy and limb asymmetry 164
 Holoprosencephaly (HPE) 168
 Hydrocephalus 172
 Hypermobility joints 176
 Hypertrichosis 178
 Hypoglycaemia in the neonate and infant 182
 Hypospadias 186
 Intellectual disability 188
 Intellectual disability with apparent X-linked
 inheritance 194
 Increased bone density 198
 Intracranial calcification 200
 Large fontanelle 204
 Laterality disorders including heterotaxy and
 isomerism 206
 Leukodystrophy/leukoencephalopathy 208
 Limb reduction defects 212
 Lissencephaly, polymicrogyria, and neuronal
 migration disorders 216
 Lumps and bumps 222
 Macrocephaly 224
 Microcephaly 228
 Micrognathia and Robin sequence 232

Microphthalmia and anophthalmia 236
Minor congenital anomalies 240
Nasal anomalies 242
Neonatal encephalopathy and intractable seizures 246
Nystagmus 252
Obesity with and without developmental delay 254
Ocular hypertelorism 258
Oedema—generalized or puffy extremities 260
Oesophageal and intestinal atresia (including tracheo-oesophageal fistula) 266
Optic nerve hypoplasia 270
Overgrowth 272
Patchy hypo- or depigmented skin lesions 276
Patchy pigmented skin lesions (including café-au-lait spots) 278
Plagiocephaly and abnormalities of skull shape 280
Polydactyly 284
Prolonged neonatal jaundice and jaundice in infants below 6 months 288
Ptosis, blepharophimosis, and other eyelid anomalies 292
Radial ray defects and thumb hypoplasia 296
Retinal dysplasia 300
Retinal receptor dystrophies 302
Scalp defects 306
Seizures with developmental delay/intellectual disability 308
Short stature 312
Skeletal dysplasias 316
Structural intracranial anomalies (agenesis of the corpus callosum, septo-optic dysplasia, and arachnoid cysts) 320
Sudden cardiac death 324
Suspected non-accidental injury 326
Syndactyly (other than 2/3 toe syndactyly) 328
Unusual hair, teeth, nails, and skin 330

3 **Common consultations** 333

Achondroplasia 334
Alpha-1 antitrypsin deficiency 338
Alport syndrome 340
Androgen insensitivity syndrome (AIS) 344
Angelman syndrome 346
Autism and autism spectrum disorders 350
Autosomal dominant polycystic kidney disease (ADPKD) 354
Beckwith–Wiedemann syndrome (BWS) 358

Charcot–Marie–Tooth disease (CMT) 362
Ciliopathies 366
Congenital adrenal hyperplasia (CAH) 370
Consanguinity 374
Craniosynostosis 378
Cystic fibrosis (CF) 382
Dementia—early onset and familial forms 386
Diabetes mellitus 390
Dilated cardiomyopathy (DCM) 394
DNA repair disorders 398
Duchenne and Becker muscular dystrophy (DMD and BMD) 402
Ehlers–Danlos syndrome (EDS) 406
Epilepsy in infants and children 410
Epilepsy in adults 416
Facioscapulohumeral muscular dystrophy (FSHD) 420
Fragile X syndrome (FRAX) 424
Glaucoma 428
Haemochromatosis 430
Haemoglobinopathies 436
Haemophilia and other inherited coagulation disorders 442
Hereditary haemorrhagic telangiectasia (HHT) 446
Hereditary spastic paraplegias (HSP) 448
Hirschsprung's disease 452
Huntington disease (HD) 454
Hyperlipidaemia 458
Hypertrophic cardiomyopathy (HCM) 460
Immunodeficiency and recurrent infection 464
Incest 472
Leigh encephalopathy 474
Limb–girdle muscular dystrophies 476
Long QT syndrome and other inherited arrhythmia syndromes 480
Marfan's syndrome 484
Mitochondrial DNA diseases 490
Myotonic dystrophy (DM1) 496
Neural tube defects 500
Neurofibromatosis type 1 (NF1) 506
Noonan syndrome and the Ras/MAPK pathway syndromes: neuro-cardio-facial-cutaneous syndromes 512
Parkinson's disease 516
Retinitis pigmentosa (RP) 518
Rett syndrome 520
Sensitivity to anaesthetic agents 524
Spinal muscular atrophy (SMA) 526
Stickler syndrome 528
Thrombophilia 530

Tuberous sclerosis (TSC) 534

X-linked adrenoleukodystrophy
(X-ALD) 538

4 **Cancer** 541

BRCA1 and BRCA2 542

Breast cancer 546

Cancer surveillance methods 552

Colorectal cancer (CRC) 556

Confirmation of diagnosis of cancer 562

Cowden syndrome (PTEN hamartoma
tumour syndrome (PHTS)) 564

Familial adenomatous polyposis (FAP) and
adenomatous polyposis due to *MUTYH*,
NTHL1, *POLE*, and *POLD1* 568

Gastric cancer 574

Gorlin syndrome 576

Juvenile polyposis syndrome (JPS) 578

Lifestyle factors in cancer: smoking, alcohol,
obesity, diet, and exercise 582

Li-Fraumeni syndrome (LFS) 584

Lynch syndrome (LS) 586

Multiple endocrine neoplasia (MEN) 592

Neurofibromatosis type 2 (NF2) 596

Ovarian cancer 600

Peutz-Jeghers syndrome (PJS) 604

Phaeochromocytoma and paraganglioma 608

Prostate cancer 610

Renal cancer 612

Retinoblastoma 614

von Hippel-Lindau (VHL) disease 618

Wilms tumour 620

5 **Chromosomes** 623

22q11 deletion syndrome 624

47,XXX 628

47,XXY 630

47,YYY 634

Autosomal reciprocal
translocations—background 636

Autosomal reciprocal
translocations—familial 640

Autosomal reciprocal
translocations—postnatal 642

Autosomal reciprocal
translocations—prenatal 644

Cell division—mitosis, meiosis, and
non-disjunction 646

Chromosomal mosaicism—postnatal 652

Chromosomal mosaicism—prenatal 654

Deletions and duplications (including
microdeletions and microduplications) 660

Down's syndrome (trisomy 21) 666

Edwards' syndrome (trisomy 18) 670

Inversions 672

Mosaic trisomy 8 674

Mosaic trisomy 16 676

Patau syndrome (trisomy 13) 678

Prenatal diagnosis of sex chromosome
aneuploidy 680

Ring chromosomes 682

Robertsonian translocations 684

Sex chromosome mosaicism 688

Supernumerary marker chromosomes
(SMCs)—postnatal 690

Supernumerary marker chromosomes
(SMCs)—prenatal 692

Triploidy (69,XXX, 69XXY, or 69,XYY) 694

Turner syndrome, 45,X, and variants 696

X-autosome translocations 700

6 **Pregnancy and fertility** 703

Anterior abdominal wall defects 704

Assisted reproductive technology: *in vitro*
fertilization (IVF), intracytoplasmic sperm
injection (ICSI), and pre-implantation
genetic diagnosis (PGD) 706

Bowed limbs 710

Congenital cystic lung lesions, Currarino
syndrome, and sacrococcygeal
teratoma 712

Congenital diaphragmatic hernia 714

Cytomegalovirus (CMV) 716

Drugs in pregnancy 718

Female infertility and amenorrhoea: genetic
aspects 722

Fetal akinesia 724

Fetal alcohol syndrome (FAS) 728

Fetal anticonvulsant syndrome (FACS) 732

Fetomaternal alloimmunization (rhesus D
and thrombocytopenia) 736

Hyperechogenic bowel 738

Hypoplastic left heart 740

Imaging in prenatal diagnosis 742

Invasive techniques and genetic tests in
prenatal diagnosis 744

Low maternal serum oestriol 748

Male infertility: genetic aspects 750

Maternal age 754

Maternal diabetes mellitus and diabetic
embryopathy 756

Maternal phenylketonuria (PKU) 758

Miscarriage and recurrent miscarriage 760

Neonatal (newborn) screening (NS) 762

Non-invasive prenatal diagnosis/testing
(NIPD/T) 764

Oedema—increased nuchal translucency, cystic hygroma, and hydrops 768
 Oligohydramnios (including Potter/oligohydramnios sequence) 770
 Paternal age 772
 Polyhydramnios 774
 Posterior fossa malformations 776
 Premature ovarian failure (POF) 778
 Radiation exposure, chemotherapy, and landfill sites 780
 Rubella 782
 Short limbs 784
 Talipes (club-foot) 788
 Toxoplasmosis 790
 Twins and twinning 792
 Urinary tract and renal anomalies (congenital anomalies of the kidney and urinary tract—CAKUT) 796
 Varicella 800
 Ventriculomegaly 802

Appendix 805

Antenatal and neonatal screening timelines 806
 Bayes' theorem 807
 Carrier frequency and carrier testing for autosomal recessive disorders 810
 Centile charts for boys' height and weight 815
 Centile charts for girls' height and weight 819

Centile charts for occipital–frontal circumference (OFC) 823
 CK (creatine kinase) levels in carriers of Duchenne muscular dystrophy (DMD) 825
 Conversion charts—imperial to metric 826
 Denver Developmental Screening Test 827
 Distribution of muscle weakness in different types of muscular dystrophy 829
 Dysmorphology examination checklist 830
 Embryonic fetal development (overview) 831
 Family tree sheet and symbols 833
 Haploid autosomal lengths of human chromosomes 835
 Investigation of lethal metabolic disorder or skeletal dysplasia 836
 ISCN nomenclature 837
 Karyotypes 839
 Normal range of aortic root dimensions 841
 Paternity testing 844
 Patterns of cancer 846
 Radiological investigations including magnetic resonance imaging (MRI) 852
 Skeletal dysplasia charts 853
 Staging of puberty 856
 Surveillance for individuals at increased genetic risk of colorectal cancer 857

Index 863