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Online chapter – see www.scionpublishing.com/NCG4

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Case notes – Summary of cases and their page references

CASE 1 ASHTON FAMILY

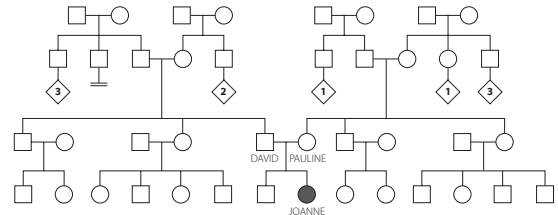
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- John, healthy 28-year-old son of Alfred Ashton – *Chapter 1*
- Family history of ? Huntington disease
- Autosomal dominant inheritance
- Need for diagnostic PCR test – *Chapter 3*
- PCR test confirms diagnosis in John's father – *Chapter 4*
- Pros and cons of predictive test
- Molecular pathology – *Chapter 6*
- Possibilities for therapy – *Chapter 14*

CASE 2 BROWN FAMILY

2 10 67 132 154 313 395

- Baby Joanne, recurrent infections, poor growth – *Chapter 1*
- Sweat test confirms she has cystic fibrosis
- Autosomal recessive inheritance
- Need for molecular test – *Chapter 3*
- *CFTR* variants identified – *Chapter 5*
- Molecular pathology – *Chapter 6*
- Approaches to screening – *Chapter 12*
- Possibilities for therapy – *Chapter 14*



CASE 3 KOWALSKI FAMILY

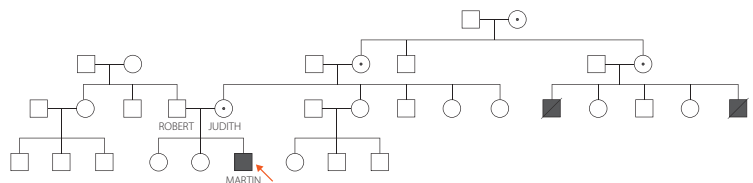
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- Karol, first son of Kamil and Klaudia – *Chapter 1*
- Developmental delay, hypotonic, severe intellectual disability
- Difficulties of genetic testing in such cases
- Likely need for exome sequencing – *Chapter 3*
- Negative SNP chip test for microdeletions – *Chapter 4*
- Exome sequencing – *Chapter 5*
- *De novo ARID1B* variant identified – *Chapter 6*
- Possibilities for therapy – *Chapter 14*

CASE 4 DAVIES FAMILY

4 11 68 98 156 285 315 395

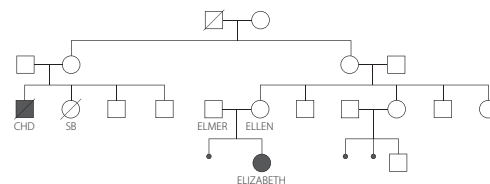
- Martin, aged 24 months, clumsy and slow to walk – *Chapter 1*
- Family history of muscular dystrophy
- X-linked recessive inheritance
- Problems of testing dystrophin gene – *Chapter 3*
- Exon 44–48 deletion identified by MLPA – *Chapter 4*
- Molecular pathology – *Chapter 6*
- Implications of X-inactivation – *Chapter 11*
- Screen all newborn boys? – *Chapter 12*
- Possibilities for therapy – *Chapter 14*



CASE 5 ELLIOT FAMILY

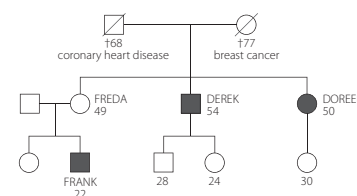
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- Baby girl Elizabeth, parents Elmer and Ellen – *Chapter 1*
- Multiple congenital abnormalities
- Family history of reproductive problems
- ? Chromosome abnormality
- Ellen – balanced 1:22 translocation – *Chapter 2*
- Elizabeth – unbalanced segregation product
- Reciprocal translocation – *Chapter 3*
- Translocation identified by array-CGH – *Chapter 4*
- Possibilities for therapy – *Chapter 14*

**CASE 6 FLETCHER FAMILY**

5 13 69 130 157 395

- Frank, aged 22, with increasingly blurred vision – *Chapter 1*
- Family history of visual problems
- Possible mitochondrial inheritance
- ? Leber hereditary optic neuropathy
- Test mitochondrial genome – *Chapter 3*
- m.G3460A mutation identified – *Chapter 5*
- Molecular pathology – *Chapter 6*
- Possibilities for therapy – *Chapter 14*

**CASE 7 GREEN FAMILY**

25 39 70 97 395

- George, aged 3 years – *Chapter 2*
- Developmental delay, mildly dysmorphic
- Normal 46,XY karyotype but suspect microdeletion
- Test for microdeletions – *Chapter 3*
- 22q11 deletion identified by FISH – *Chapter 4*
- Possibilities for therapy – *Chapter 14*

CASE 8 HOWARD FAMILY

26 39 70 315 395

- Helen, newborn daughter of young parents – *Chapter 2*
- Down syndrome confirmed
- 47,XX,+21 karyotype
- Options for prenatal testing – *Chapter 3*
- Non-invasive prenatal test – *Chapter 12*
- Possibilities for therapy – *Chapter 14*

CASE 9 INGRAM FAMILY

26 42 70 103 285 395

- Isabel, 10 years old with small stature and possibly delayed puberty – *Chapter 2*
- ? Turner syndrome
- 45,X karyotype
- Risk of Y-chromosome DNA – *Chapter 3*
- PCR test for Y sequences negative – *Chapter 4*
- Questions around X-inactivation – *Chapter 11*
- Possibilities for therapy – *Chapter 14*

CASE 10 O'REILLY FAMILY

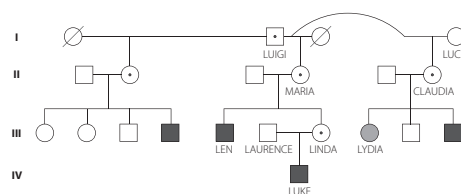
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- Orla has severe myopia, short stature and hip problems – *Chapter 3*
- Family history of similar problems
- ? Stickler syndrome
- Test collagen II genes
- Sequencing identifies *COL2A1* variant – *Chapter 5*
- Molecular pathology – *Chapter 6*
- Possibilities for therapy – *Chapter 14*

CASE 11 LIPTON FAMILY

83 105 395

- Baby boy, Luke, with developmental delay – *Chapter 4*
- Family history of learning difficulties
- Unusual features of Fragile-X pedigrees
- Caused by unstable repeat expansion
- Premutations, full mutations and normal transmitting males
- Measuring repeat expansions
- Possibilities for therapy – *Chapter 14*

**CASE 12 MEINHARDT FAMILY**

84 101 395

- Madelena, baby daughter of Margareta and Manfred – *Chapter 4*
- Multiple congenital abnormalities and developmental delay
- Normal 46,XX karyotype under the microscope
- 16p microdeletion identified by SNP chip
- Is this microdeletion pathogenic?
- ? Recurrence risk
- Possibilities for therapy – *Chapter 14*

CASE 13 NICOLAIDES FAMILY

117 129 159 316 395

- Spiros and Elena both carriers of β -thalassaemia – *Chapter 5*
- Need to define mutations for prenatal diagnosis
- Allele-specific PCR shows Spiros carries the p.Gln39X variant
- Restriction digest shows Elena carries the c.316–106C>G variant
- Molecular pathology – *Chapter 6*
- Population screening for carriers – *Chapter 12*
- Possibilities for therapy – *Chapter 14*

CASE 14 JENKINS FAMILY

143 160 395

- James Jenkins, achondroplasia diagnosed in infancy – *Chapter 6*
- No family history
- Father was 58 years old when James conceived
- James's wife Joanne also has achondroplasia
- Obstetric problems and risks to children
- All cases have same *FGFR3* mutation
- Reasons for apparent high mutation rate
- Possibilities for therapy – *Chapter 14*

CASE 15 TIERNEY FAMILY

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- 4-year-old boy, Jason – *Chapter 7*
- Pale with extensive bruising and tachycardia
- ? Acute lymphocytic leukemia
- Diagnosis of ALL confirmed with *TEL-AML1* fusion gene
- TPMT test prior to chemotherapy – *Chapter 10*
- Severe adverse reaction after false negative TPMT result – *Chapter 10*
- Possibilities for therapy – *Chapter 14*

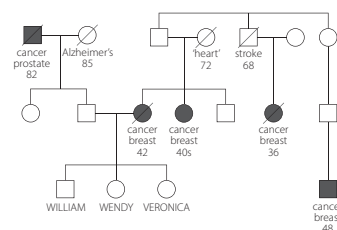
CASE 16 WILSON FAMILY

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- Family history of breast cancer – *Chapter 7*
- Options for genetic testing
- Family *BRCA2* mutation identified
- Implications for relatives
- Possibilities for therapy – *Chapter 14*



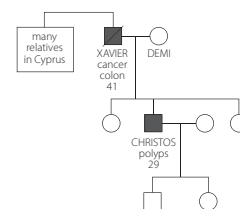
CASE 17 XENAKIS FAMILY

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- Family history of bowel problems – *Chapter 7*
- ? Familial adenomatous polyposis
- *APC* mutation identified
- Risk to relatives
- How to manage his children?
- Possibilities for therapy – *Chapter 14*



CASE 18 CHOUDHARY FAMILY

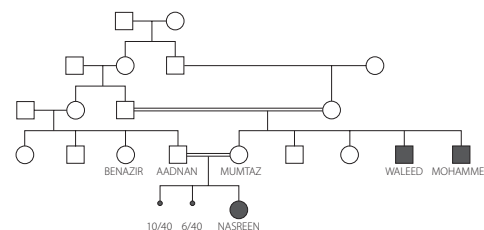
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- Baby girl Nasreen, healthy but deaf – *Chapter 8*
- Multiply consanguineous family
- Autozygosity mapping
- Exome sequencing
- A second recessive condition?
- Calculate coefficient of inbreeding – *Chapter 9*
- Possibilities for therapy – *Chapter 14*



CASE 19 ULMER FAMILY

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- Hannah, 6-month-old baby girl, Ashkenazi Jewish background – *Chapter 9*
- Normal at birth but then increasing problems
- ? Tay–Sachs disease
- Enzyme test confirms diagnosis
- Test the sibs?
- Carrier screening – *Chapter 12*
- Possibilities for therapy – *Chapter 14*

CASE 20 VLASI FAMILY

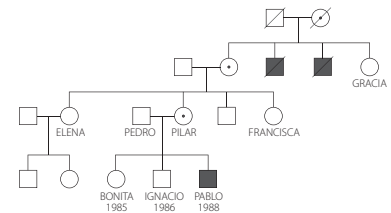
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- Valon, 6-year-old boy with serious learning problems – *Chapter 10*
- Small, microcephalic, blue eyes, fair skin and hair, eczema; hyperactive
- ? Phenylketonuria
- Testing for subsequent baby?
- Newborn screening – *Chapter 12*
- Possibilities for therapy – *Chapter 14*

CASE 21 PORTILLO FAMILY

252 263 286 395

- Sickly boy, Pablo – *Chapter 10*
- Family history of similar problems – *Chapter 10*
- X-linked severe combined immunodeficiency
- Bone marrow transplantation
- Genetic cause defined
- Carrier tests for female relatives
- Implications of X-inactivation – *Chapter 11*
- Possibilities for therapy – *Chapter 14*



CASE 22 QIAN FAMILY

277 287 395

- Girl, Kai, aged 2 years – *Chapter 11*
- Developmental delay, seizures
- ? Angelman syndrome
- Causes and genetic tests
- Possibilities for therapy – *Chapter 14*

CASE 23 ROGERS FAMILY

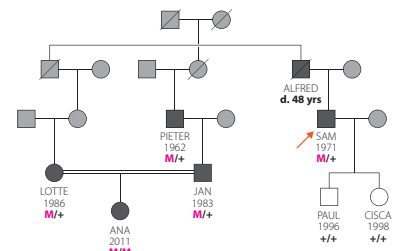
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- Baby boy, Robert, born to older parents – *Chapter 11*
- Normal 46,XY karyotype and pregnancy tests
- Severely hypotonic
- ? Prader–Willi syndrome
- Causes and genetic tests
- Possibilities for therapy – *Chapter 14*

CASE 24 SMIT FAMILY

305 318 395

- Sam Smit, familial hypercholesterolemia – *Chapter 12*
- Identified through cascade screening
- LDLR mutation detected, treatment started
- Affected relatives, including a homozygote
- Conflict between privacy and cascade screening
- Possibilities for therapy – *Chapter 14*



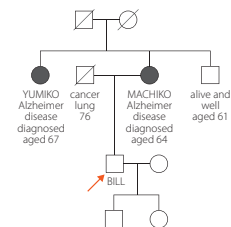
CASE 25 YAMOMOTO FAMILY

333

344

395

- Family history of dementia – *Chapter 13*
- Alzheimer disease
- Test for ApoE4?
- Genetic susceptibility to Alzheimer disease
- Possibilities for therapy – *Chapter 14*



CASE 26 ZUABI FAMILY

334

349

395

- Zafira, woman aged 52 years – *Chapter 13*
- Overweight, sedentary lifestyle, insatiable thirst
- Type 2 diabetes
- Son's lifestyle and heredity put him at high risk
- Management of family
- Genetic susceptibility to Type 2 diabetes
- Possibilities for therapy – *Chapter 14*

