

Congenital genetic disorders

Congenital/genetic disorders

Neurofibromatosis There are two distinct neurofibromatosis (NF) syndromes, in which Schwann cells form tumours (Figure 45.3). Each is caused by different genes on different chromosomes: 70% are autosomal dominant and 30% arise from sporadic mutations. NF-1 (von Recklinghausen's disease) is the commoner variant, mutation on chromosome 17. Skin manifestations appear in early life, with the development of more than five smooth-surfaced café-au-lait spots, subcutaneous neurofibromata, armpit or groin freckling and Lisch nodules. NF-2 produces multiple central nervous system tumours. **Naevoid basal cell carcinoma (Gorlin's) syndrome** This is an autosomal dominant inherited condition caused by an abnormal tumour suppressor gene on chromosome 9q 22-31 coding the 'patched' protein; 90% of patients develop multiple basal cell carcinomas (BCCs). Patients may exhibit specific phenotypical characteristics, including overdeveloped supraorbital ridges; broad nasal roots; hypertelorism; bifid ribs; scoliosis; brachymetacarpalism; palmar pits; and molar odontogenic cysts; patients are also prone to other tumours. **Xeroderma pigmentosum** This syndrome is caused by an abnormality on the 'patched' gene of chromosome 9q, resulting in aberrant nucleotide repair during cellular DNA maintenance. It confers a >2000-fold increase in skin cancer risk and has autosomal recessive inheritance. Sufferers are intolerant of UVR, leading to premature skin ageing and development of multiple neoplasms. Most affected individuals die in early adulthood from metastatic disease (60% mortality by 20 years of age). **Gardner's syndrome** This syndrome is an autosomal dominant disease variant of familial adenomatous polyposis (FAP), which is caused by gene mutations on chromosome 5q 22. Gardner's syndrome can cause the development of cutaneous pathology, such as multiple epidermoid cysts and lipomata. **Ferguson-Smith syndrome** A rare autosomal dominant inherited abnormality on chromosome 9q in which affected individuals develop multiple self-healing squamous cell carcinomas (SCCs) without relation to sun exposure. **Congenital/genetic disorders**

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