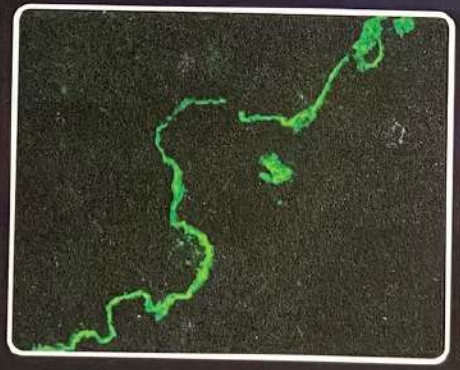
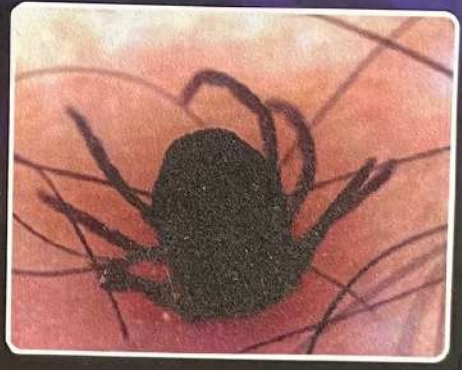
VOLUME 1

IADVL Textbook of Dermatology

FIFTH EDITION

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10 Genodermatoses

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KEY MESSAGES

- Genodermatoses are inherited disorders commonly encountered in dermatology practice.
- The majority of these are life-long, involving multiple systems.
- Diagnosis of these group of disorders is mainly with clinical features, associations and genetic analysis.
- Treatment is multidisciplinary.
- Providing options for prenatal diagnosis to the parents and genetic counseling to prevent future occurrence is very important in these cases.

INTRODUCTION

Patients with genodermatoses constitute a significant section in dermatological practice. The majority of these are life-long, multisystem disorders. Some carry the risks of malignancy and premature death. Many genodermatoses cause cosmetic disfigurement, and patients present to the dermatologist for their unusual appearance. Management of these disorders is not only limited to the diagnosis of the particular patient but also probing into the family tree to know the inheritance pattern, providing options for prenatal diagnosis to their parents and genetic counseling to prevent further such occurrences. With this background, it is understandable that a basic knowledge of genetics is essential to dermatologists. The discussion in the following section includes the principles of genetic transmission of diseases and the terms related to it.

PRINCIPLES OF GENETIC TRANSMISSION

Transmission of characters through generations is determined by genes located on the chromosomes. Such transmission may or may not follow Mendelian laws. As a broad group, these are categorized as inherited disorders. A familial disorder is recognized by the occurrence of a character in a family clearly in excess of its expected occurrence in the same population.[1] A congenital character is one present at or before birth.[1] Congenital and familial conditions do not necessarily imply genetic transmission. Non-Mendelian inherited disorders such as psoriasis and atopic dermatitis are quite common and show familial clustering frequently.[2]

The genotype of an individual indicates the characters transmitted through the genes. The physical expression of these characters is designated as phenotype. Autosomal characters are borne by autosomes (22 pairs of chromosomes) and sex-linked characters are carried by sex chromosomes (X/Y). Genes are located at particular chromosome loci as alleles. Two different alleles at a particular locus of a chromosome pair indicate heterozygosity, whereas identical alleles at a locus indicate homozygosity. Males with the expression of X-linked characters (unpaired alleles) are termed hemizygous.[2] A dominant character is defined as one whose phenotypic expression is possible in the heterozygous state. A recessive character manifests only in the homozygous state.

Four major patterns of genetic transmission are possible— autosomal dominant (AD), autosomal recessive (AR), X-linked dominant (X-L-D), and X-linked recessive (X-L-R). Sex-linked transmission may also occur through Y chromosomes (holandric transmission). The salient features of these are described in **Table 10.1**.[1,2] A schematic representation of the different patterns of genetic transmission is shown in **Fig. 10.1**.

The above inheritance patterns are related to nuclear DNA. Disorders related to mitochondrial DNA show a maternal inheritance simulating X-linked inheritance patterns.[3] Here, all sons and daughters of an affected woman are involved, but father-to-offspring transmission is not possible.[2–4] Palmoplantar keratoderma with sensorineural deafness (mutation of *MTTS1*) follows this type of inheritance pattern.[3,4] Nonspecific characters