436e Atlas of Clinical Manifestations of Metabolic Diseases

J. Larry Jameson

The term *metabolism* is derived from the Greek *metabol,* meaning "to change." This term encompasses the broad array of chemical pathways that are necessary for normal development and homeostasis. In practice, clinicians generally use the term *metabolism* in reference to energy utilization for anabolism or catabolism. Alternatively, intermediary metabolism describes the myriad cellular pathways that convert energy sources from one form to another (e.g., the citric acid cycle). The emerging field of *metabolomics* is based on the premise that the identification and measurement of metabolic products will enhance our understanding of physiology and disease.

Over the years, the classification of metabolic diseases has extended beyond traditional pathways involved in fuel metabolism to include disorders such as lysosomal storage diseases and connective tissue diseases. Thus, metabolic diseases really reflect disorders of cell biology, and many have a well-defined genetic basis. For example, lysosomal storage diseases **(Chap. 432e)** result from a variety of genetic defects, usually in a lysosomal enzyme, causing accumulation of a substrate within the lysosome. Certain lipodystrophies and cardiomyopathies can be caused by mutations in lamin A, a structural protein in the nuclear envelope. Membrane defects **(Chap. 435e)**, usually involving transporters of amino acids, sugars, or ions, cause disorders such as cystinuria, Hartnup's disease, or Wilson's disease **(Chap. 429)**. Connective tissue diseases **(Chap. 427)** frequently involve defects in collagen synthesis or structure (osteogenesis imperfecta, Ehlers-Danlos syndrome, Alport's syndrome) or in other extracellular matrix structural proteins such as fibrillin (Marfan syndrome). Many metabolic disorders originate from defects in enzymes involved in the synthesis or degradation of amino acids, carbohydrates, lipids, purines, or pyrimidines **(Chaps. 431e, 433e, and 434e)**. Lipoprotein disorders **(Chap. 421)** are caused by defects in a wide array of cellular pathways including membrane receptors (the low-density lipoprotein receptor), enzyme defects (lipoprotein lipase), carrier proteins (apolipoprotein B100), or transporters (ATP-binding cassette transporter ABCA1). In some instances, metabolic abnormalities induce compensatory physiologic responses that reflect the interactions of multiple metabolic pathways. For example, the metabolic syndrome **(Chap. 422)**, which includes a constellation of clinical features (central obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol, hyperglycemia, and hypertension), likely has multiple genetic and environmental origins. Cushing's syndrome reflects the metabolic effects of excess cortisol on multiple tissues **(Chap. 406)**.

This broader definition results in a plethora of metabolic diseases, numbering in the thousands. Fortunately, comprehensive reference sources exist, such as the Online Metabolic and Molecular Bases of Inherited Disease (OMMBID) (*http://www.ommbid.com/)* and the Online Mendelian Inheritance in Man (OMIM) (*http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM*). The study of metabolic diseases has been invaluable for advancing our understanding of human genetics by providing insight into principles such as patterns of inheritance, variable expressivity, phenotypic variation, and novel approaches to therapy, including screening programs, blood and organ transplantation, gene therapy, and enzyme replacement **(Chap. 82)**.

This atlas provides a visual survey of selected metabolic disorders with references to the topics elsewhere in the text. The author encourages submission of additional illustrations that might facilitate learning among our peers and thereby enhance the recognition and care of patients with these disorders.

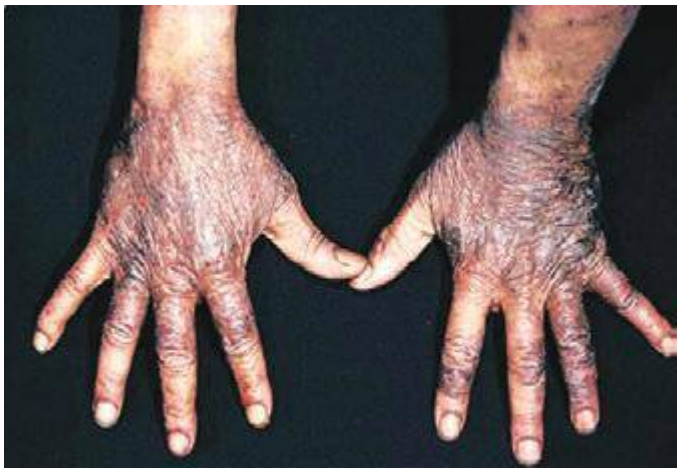

FIGURE 436e-1 "Gauntlet" of pellagra (niacin deficiency). Note indurated, lichenified, pigmented, and scaly skin on the dorsa of the hands. *(Source: K Wolff et al: Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology, 5th ed. New York, McGraw-Hill, 2005.)* **See Chap. 96e.**

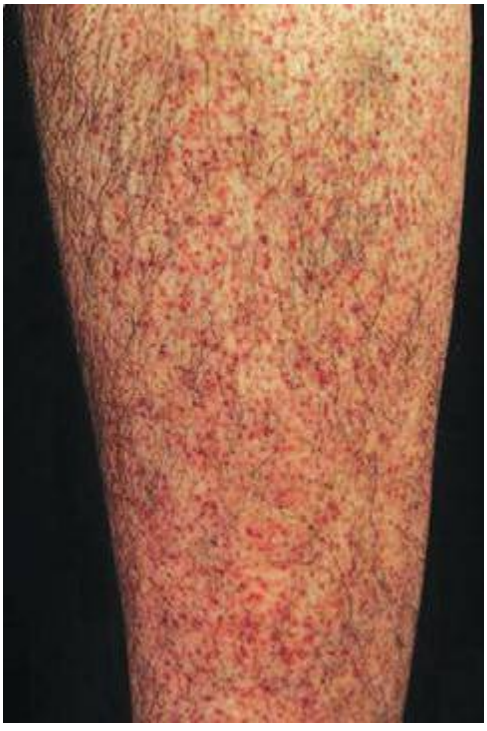

FIGURE 436e-2 Scurvy (vitamin C deficiency). Note perifollicular hemorrhage on the leg. The follicles are often plugged by keratin (perifollicular hyperkeratosis). This eruption occurred in a 46-year-old alcoholic, homeless man who also had bleeding gums and loose teeth. *(Source: K Wolff et al: Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology, 5th ed. New York, McGraw-Hill, 2005.)* **See Chap. 96e.**