CHAPTER 1
Introduction

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Skin cancer, the most common cancer worldwide, has an incidence doubling every 15 to 20 years! The principle factor inducing most of the primary skin cancers discussed in this book is ultraviolet light–induced carcinogenesis. However, as we will stress, other parts of the electromagnetic spectrum, such as x-rays and infrared rays (heat), may also be carcinogenic (Table 1.1). In addition, viral and chemical carcinogenesis may be very important. Details of ultraviolet light–induced carcinogenesis are delineated within the respective chapters on basal cell carcinoma, squamous cell carcinoma, actinic keratosis, melanoma, and the deadliest of all skin cancers: Merkel cell carcinoma [1]. The increased risks for five additional cancer types (prostate, breast, and colon cancers, non-Hodgkin's lymphoma, and multiple myeloma) in first-degree relatives of melanoma cases suggest that individuals with a family history of melanoma should strictly adhere to recommended screenings for all cancers [2].

There are two major challenges in dealing with cancer, the first being prevention. The use of sunscreens has been emphasized and needs to be stressed. Actual skin protection chiefly depends on the way sunscreens are used and the quantity applied [3]. Skin cancer prevention is facilitated by explicit labeling and free provision of sunscreen. Prevention should begin early in childhood [4]. Proper young ladies and men should be seen with bonnets or hats and long sleeves, not photoaging themselves unnecessarily. Certainly, the structural and functional changes of normal cutaneous aging include decreased growth of the epidermis, hair, and nails; delayed wound healing; and impaired cutaneous immune responses. Photoaging, however, is a different process [5]. Evidence suggests that topical retinoids not only may decelerate the photoaging process but also are capable of repairing photoaged skin at both the clinical and biochemical levels and may prevent photoaging [6]. In addition, topical retinoids could be beneficial in the treatment of intrinsically aged skin. Antioxidants may also be employed, particularly in combination, to reduce and neutralize free radicals [7]. Importantly, for every light-complexioned individual (Fig. 1.1), protection from the premature and unsightly effects of sun exposure is mandatory (Table 1.2). As both melanocytic nevi and sunburn are risk factors for the development of melanoma, we should target fair-skinned transplant recipients with melanocytic nevi for sun avoidance education [8]. The goal should be the prevention of both photoaging and photocarcinogensis [9]. Risk assessment is a good idea [10].

A secondary challenge is detection, because most cancers are curable if caught early. This point is emphasized by the "developing epidemic of melanoma" in Hispanic men in California [11]. A statistically significant 1.8% per year increase in incidence of invasive melanomas among Hispanic males has been observed between 1988 and 2001. Among them, melanomas thicker than 1.5 mm at presentation increased at 11.6% per year. This increase in melanoma in Hispanics, confined to thicker tumors with a poor prognosis, emphasizes the need for both prevention and early detection.

The worldwide scourge of AIDS, beginning for us in Europe and America in the early 1980s, is an epidemic that is not abating [12–16]. Kaposi's sarcoma has been an intrinsic part of this epidemic, as delineated in the Kaposi's sarcoma chapter. Since the

Table 1.1 Electromagnetic spectrum

Type of Radiation	Wavelength
Gamma rays, x-rays, Grenz rays	Below 1 nm (10 angstroms)
Ultraviolet light (UV)	
UV "C" range	1–290 nm
UV B	290–320 nm (through ozone layer)
UV A	320–400 nm (through window glass)
Visible light	400–700 nm
Infrared radiation (heat)	700–1,000,000 nm
Radio waves	1,000,000 nm and above

Table 1.2 Preventing skin cancers and premature aging (photoaging)

Avoid sun exposure
Use sunscreen preparations and cover body with clothing
Consider topical retinoid use

first edition of this book was published, the etiologic agent of Kaposi's sarcoma has been identified [17]. Although the incidence of Kaposi's sarcoma has declined dramatically in areas with access to highly active antiretroviral therapy, it remains the most common AIDS-associated malignancy in the developed world and is one of the most common malignancies in developing nations. Current treatment options are ineffective, unavailable, or toxic to many affected persons. A growing body of basic science, preclinical, and observational data suggests that antiviral medications may play an important role in the prevention and treatment of Kaposi's sarcoma–associated herpesvirus, providing hope for the future [18]. The skin may serve as an important organ for study in these patients and often manifests the first signs of AIDS.

Some cutaneous tumors remain an enigma. A good example, one even better than melanoma, is perhaps the deadliest of all skin cancers—Merkel cell carcinoma—which appears to have tripled in incidence from 1986 to 2001 in the United States and Canada [1]. Often appearing as an asymptomatic nodule on sun-exposed skin, it may resemble a basal cell carcinoma, a common misdiagnosis both clinically and histologically that may have fatal consequences. Its origin from the normal epidermal Merkel cell remains controversial, because this neoplasm originates in the dermis and only rarely

Fig. 1.1 The author's light-complexioned 10-year-old son, Edmund, exhibiting evidence of skin cancer prevention at a New Jersey beach.

Table 1.3 Cancers mimicking dermatitis

Erythroplasia of Queyrat and other sites
Paget's disease of the breast
Extramammary Paget's disease
Inflammatory metastatic carcinoma
Bowen's disease
Amelanotic lentigo maligna melanoma
Scar carcinoma

demonstrates epidermal involvement. It may be derived from the haarscheibe or hair disc (touch corpuscles), composed predominantly of Merkel cells. Advances in our understanding of it are moving forward [19].

Viral oncogenesis has taken large leaps ahead through exciting technologic advances that have allowed the typing of human papillomaviruses and have linked them with a variety of skin cancers [20]. In the chapters that follow, some of the probable associations of human papillomavirus infections and cancer are discussed. Through the study of model diseases, such as epidermodysplasia verruciformis and xeroderma pigmentosum, much has been and will continue to be learned about skin cancer. The topical application of the bacterial DNA repair enzyme T4 endonuclease V to sun-damaged skin of patients with xeroderma pigmentosum has promise in lowering the rate of development of actinic keratoses and basal cell carcinoma [21,22].

As the chapters on recognition of skin cancer note, diagnosing skin cancers may at times be difficult. It is amazing how often skin cancer may mimic dermatitis (eczema; Table 1.3). Conversely, worrisome skin tumors may represent benign cutaneous processes or cutaneous infections, especially in immunocompromised persons. The ability to immunosuppress transplant recipients and the AIDS epidemic bring dermatology to the forefront of medicine.

Modern molecular biology has led to much progress. There are important genetic changes contributing to the development of melanoma, basal cell carcinoma and squamous cell carcinoma, and other less common skin cancers [23]. Although our understanding of oncogenes and tumor suppressor genes involved in the development and progression of skin tumors remains fragmentary, recent advances have shown alterations affecting conserved signaling pathways that control cellular proliferation and viability. The *BRAF* oncogene is a good example [24,25]. There have been more than 30 distinct *BRAF* mutations in melanomas described, varying in biological activity. Some may be predictive of clinically relevant tumor differences. *BRAF* somatic mutations are often found in primary and metastatic melanomas and melanocytic nevi. *BRAF*-mutant melanomas appear to be linked with host phenotype, tumor location, and pigmentation, with this somatic mutation sometimes associated with a germline one [26].

All of our modern advancements are of particular advantage in studying patients with genetic cancer syndromes, such as the dysplastic nevus syndrome, the basal cell nevus syndrome, xeroderma pigmentosum, and the Muir-Torre syndrome—all of which are also covered in the chapters to follow.

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