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A Collection of Papers Presented at the Seventh Annual Clinical Conference on Cancer, 1962 at The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas

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Introduction to the Seventh Annual Clinical Conference

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THE ANNUAL Clinical Conference at The University of Texas M. D. Anderson Hospital and Tumor Institute was initiated in order that physicians of Texas and other interested persons might have an opportunity to discuss and evaluate recent advances in diagnostic and therapeutic methods in the management of cancer.

At previous conferences, we have discussed cancer of the breast, melanoma, cancer chemotherapy, head and neck tumors, and carcinoma of the uterus, endometrium, and ovary. The focal topic for this Seventh Annual Clinical Conference is "Tumors of the Skin." Various aspects of this subject are of particular interest to physicians of this geographic region, where skin cancer has an extremely high incidence.

More benign and malignant neoplasms occur on the skin of man than on any other anatomic site. The skin is also the site most amenable to therapeutic measures. However, accurate differential diagnosis of skin cancer is essential and often difficult. Such a differentiation is necessary because of variations in the histologic type, tendency to metastasize, and reaction to therapeutic procedures of the different types of skin cancer.

For example, multiple, small cutaneous tumors of basal cell nevus are histologically indistinguishable from basal cell carcinoma; even more serious, the presence of some multinucleated nevoid giant cells could lead to a diagnosis of malignant melanoma from sections of

benign dermal nevi. To prevent such erroneous diagnoses, the pathologist and clinician must work in close collaboration. The clinician should question the findings of the pathologist when there is a wide discrepancy between the histopathologic observations and the clinical features of the individual lesions. Only a careful estimation of both clinical and pathologic findings can assure a correct diagnosis.

To be effective, improved methods of diagnosis and treatment of patients with skin cancer must be employed at the earliest possible stage. At M. D. Anderson Hospital, patients admitted with an early stage of lip carcinoma showed a 76.1% cumulative proportion survival 5 years after diagnosis; by contrast, those admitted with more advanced stages showed only a 32.2% cumulative proportion survival after the same interval. Patients admitted with malignant melanoma of the skin in an early stage showed a 70.5% cumulative proportion survival 5 years after diagnosis; those who were admitted with more advanced stages showed only an 18.1% cumulative proportion survival after the same interval.

In 1955, 3,638 people in the United States died of skin cancer (1.5% of all cancer deaths). Approximately half (1,806) of these deaths were ascribed to malignant melanomas.

Of the total number of cancer patients admitted to M. D. Anderson Hospital through 1961, 24% had skin cancer. Excluding patients with melanoma, there were 5,840 patients with 14,383 skin lesions. More than 90% of all skin cancers are on surfaces which are habitually exposed to the environment.

The etiology of skin cancer is less nebulous than that of many other types of carcinoma. This is partially because of its unique characteristic of being visible in early stages and accessible to diagnostic and therapeutic procedures. That certain factors, such as actinic radiation, skin pigmentation, environmental conditions, and genetic influences, have a definite bearing on the development of skin cancer in susceptible individuals has been proved. Experimental and epidemiologic data continue to substantiate the relevance of these factors and to test educational and chemotherapeutic means of prevention.

Therapeutic approaches to the management of skin cancer consist of surgery, radiation, and chemotherapy. To determine a definitive method of therapy, each lesion must be evaluated after consideration of its individual and specific indications. The goal of therapy should

be the highest cure rate with the best cosmetic results and minimum expense.

Surgical excision followed by reconstructive surgery is effective in many instances. The adaptability of radiation makes it superior to surgical excision in certain sites; increased tumor size and the radioresistance of certain tumors may limit the therapeutic value of radiation. Also, the prospect of adding irritation to a skin sensitized by exposure to the sun must be taken into account when x-radiation is considered. The objective of the radiation modalities is to distribute uniformly throughout the area of the tumor the optimum radiation dosage to produce necrosis of the malignant cells. In the management of malignant melanoma, the effectiveness of regional perfusion and chemotherapy combined with surgical modalities is being tested.

Reports in this volume have been divided into three sections: etiology and epidemiology, diagnosis, and treatment.

ETIOLOGY
and EPIDEMIOLOGY
of TUMORS of the SKIN

Environment and Skin Cancer

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FEW MEDICAL CONCEPTS have remained unchallenged for the past 60 years, yet the concept of a direct association between excessive solar exposure and skin cancer has not varied significantly during this period. The anatomic, geographic, and occupational relationships observed and recorded before 1900 by Unna (1894), Dubreuilh (1896), and others are still valid. These clinicians were aware of the inherent protection offered by dark skin, the marked susceptibility of fair-skinned outdoor workers, and the increased incidence of skin cancers in geographic regions receiving great amounts of sunlight. Their clinical observations received solid support from Findlay (1928), who produced skin cancer in mice by repeated ultraviolet exposure. In 1933, Roffo induced with natural sunlight cancers in rats and showed that this carcinogenic effect was inhibited by common window glass, which filtered out wave lengths less than 0.32 μ (1933 and 1934). The finding that skin cancers can be readily produced experimentally has resulted in the accumulation of a wealth of valuable information regarding ultraviolet carcinogenesis. The many contributions of Blum (1955 and 1959) are notable.

Few would disagree with Belisario's statement (1959) that carcinogenic wave lengths of the solar spectrum constitute the main predisposing factor known for the initiation of skin cancer. There is, however, considerable controversy over the pathogenic mechanisms

involved and the cellular environment in which actual carcinogenesis occurs.

Sunlight-induced malignant tumors in man are squamous or basal cell carcinomas. According to Blum, all such tumors originate in the epidermis. He suggests that the primary injury is limited to epidermis because of the low penetration of ultraviolet rays and that dermal injury and erythema are caused by the migration of unknown mediators from the injured epidermis. Cancer may be induced by a given amount of ultraviolet light of appropriate wave length, independent of dose rate. Successive doses of radiation progressively accelerate the process, each dose further increasing the rate of cellular proliferation (Blum, 1955).

Blum believes that the principal protective mechanism in Caucasian skin involves thickening of the stratum corneum and that eventually a correlation will be found between transmission by the stratum corneum and cancer incidence which is not related to pigment. He attributes the lower incidence of skin cancer in dark-skinned races to the enhanced absorptive ability of the corneum by virtue of its melanin content (1959). He states that small but significant increases in corneal thickening diminish depth penetration because of the stratum corneum's great scattering effect; thus only a small fraction of the incident dose reaches the viable epidermal cells or dermis. Experimental evidence cited in support of this concept includes studies of excised human and albino mouse skin that demonstrate a significant difference between transmission through normal and through irradiated human and albino mouse skin, the difference being attributed to thickening of the stratum corneum following irradiation (Kirby-Smith, Blum, and Grady, 1942). However, with untanned human skin, approximately 10% of the 0.31 μ ultraviolet wave length penetrated into the dermis. Even in slightly tanned skin, penetration was calculated to be approximately 5%, a significant quantity if the total exposure is large.

The chief disadvantage of these indirect studies of transmission through excised skin is the inability to differentiate ultraviolet absorption by viable cells from attenuation by the stratum corneum. Human epidermis, which is much thicker than mouse skin, was shown to transmit wave lengths of 0.32 μ to a notably lesser extent. This finding probably explains why in irradiated human skin epidermal cancers develop, whereas in irradiated mice both squamous cell carcinomas and sarcomas of dermal origin tend to develop. That penetration is not the only factor involved is indicated by the finding that the ratio