There are two types of cross-sensitivity. Reactions that depend on a pharmacologic interaction may occur with all drugs that target the same pathway, whether they are structurally similar or not. This is the case with angioedema caused by NSAIDs and ACE inhibitors. In this situation, the risk of recurrence varies from drug to drug in a particular class; however, avoidance of all drugs in the class is usually recommended. Immune recognition of structurally related drugs is the second mechanism by which cross-sensitivity occurs. A classic example is hypersensitivity to aromatic antiepileptics (barbiturates, phenytoin, carbamazepine) with up to 50% reaction to a second drug in patients who reacted to one. For other drugs, in vitro as well as in vivo data have suggested that cross-reactivity existed only between compounds with very similar chemical structures. Sulfamethoxazole-specific lymphocytes may be activated by other antibacterial sulfonamides but not diuretics, antidiabetic drugs, or anti-COX2 NSAIDs with a sulfonamide group. Approximately 10% of patients with penicillin allergies will also develop allergic reactions to cephalosporin class antibiotics.

Recent data suggest that although the risk of a drug eruption to another drug was increased in persons with a prior reaction, "cross-sensitivity" was probably not the explanation. As an example, persons with a history of an allergic-like reaction to penicillin were at higher risk to develop a reaction to antibacterial sulfonamides than to cephalosporins.

These data suggest that the list of drugs to avoid after a drug reaction should be limited to the causative one(s) and to a few very similar medications.

Because of growing evidence that some severe cutaneous reactions to drugs are associated with HLA genes, it is recommended that first-degree family members of patients with severe cutaneous reactions also should avoid these causative medications. This may be most relevant to sulfonamides and antiseizure medications.

Desensitization can be considered in those with a history of reaction to a medication that must be used again. Efficacy of such procedures has been demonstrated in cases of immediate reaction to penicillin and positive skin tests, anaphylactic reactions to platinum chemotherapy, and delayed reactions to sulfonamides in patients with AIDS. Various protocols are available, including oral and parenteral approaches. Oral desensitization appears to have a lower risk of serious anaphylactic reactions. However, desensitization carries the risk of anaphylaxis regardless of how it is performed and should be performed in monitored clinical settings such as an intensive care unit. After desensitization, many patients experience non-life-threatening reactions during therapy with the culprit drug.

REPORTING

Any severe reaction to drugs should be reported to a regulatory agency or to pharmaceutical companies (e.g., MedWatch, *http://www.fda.gov/Safety/MedWatch/default.htm*). Because severe reactions are too rare to be detected in premarketing clinical trials, spontaneous reports are of critical importance for early detection of unexpected life-threatening events. To be useful, the report should contain enough details to permit ascertainment of severity and drug causality. This enables recognition of similar cases that may be reported from several different sources.

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75 Photosensitivity and Other Reactions to Light

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SOLAR RADIATION

Sunlight is the most visible and obvious source of comfort in the environment. The sun provides the beneficial effects of warmth and vitamin D synthesis. However, acute and chronic sun exposure also has pathologic consequences. Few effects of sun exposure beyond those affecting the skin have been identified, but cutaneous exposure to sunlight is the major cause of human skin cancer and can have immunosuppressive effects as well.

The sun's energy reaching the earth's surface is limited to components of the ultraviolet (UV) spectrum, the visible spectrum, and portions of the infrared spectrum. The cutoff at the short end of the UV spectrum at ~290 nm is due primarily to stratospheric ozone—formed by highly energetic ionizing radiation—that prevents penetration to the earth's surface of the shorter, more energetic, potentially more harmful wavelengths of solar radiation. Indeed, concern about destruction of the ozone layer by chlorofluorocarbons released into the atmosphere has led to international agreements to reduce production of those chemicals.

Measurements of solar flux showed a twentyfold regional variation in the amount of energy at 300 nm that reaches the earth's surface. This variability relates to seasonal effects, the path that sunlight traverses through ozone and air, the altitude (a 4% increase for each 300 m of elevation), the latitude (increasing intensity with decreasing latitude), and the amount of cloud cover, fog, and pollution.

The major components of the photobiologic action spectrum that are capable of affecting human skin include the UV and visible wavelengths between 290 and 700 nm. In addition, the wavelengths beyond 700 nm in the infrared spectrum primarily emit heat and in certain circumstances may exacerbate the pathologic effects of energy in the UV and visible spectra.

The UV spectrum reaching the earth represents <10% of total incident solar energy and is arbitrarily divided into two major segments, UV-B and UV-A, which constitute the wavelengths from 290 to 400 nm. UV-B consists of wavelengths between 290 and 320 nm. This portion of the photobiologic action spectrum is the most efficient in producing redness or erythema in human skin and thus is sometimes known as the "sunburn spectrum." UV-A includes wavelengths between 320 and 400 nm and is ~1000-fold less efficient in producing skin redness than is UV-B.

The wavelengths between 400 and 700 nm are visible to the human eye. The photon energy in the visible spectrum is not capable of damaging human skin in the absence of a photosensitizing chemical. Without the absorption of energy by a molecule, there can be no photosensitivity. Thus, the *absorption spectrum* of a molecule is defined as the range of wavelengths it absorbs, whereas the *action spectrum* for an effect of incident radiation is defined as the range of wavelengths that evoke the response.

Photosensitivity occurs when a photon-absorbing chemical (*chromophore*) present in the skin absorbs incident energy, becomes excited, and transfers the absorbed energy to various structures or to molecular oxygen.

UV RADIATION (UVR) AND SKIN STRUCTURE AND FUNCTION

Human skin consists of two major compartments: the outer epidermis, which is a stratified squamous epithelium, and the underlying dermis, which is rich in matrix proteins such as collagens and elastin. Both compartments are susceptible to damage from sun exposure. The epidermis and the dermis contain several chromophores capable of absorbing incident solar energy, including nucleic acids, proteins, and lipids. The outermost epidermal layer, the stratum corneum, is a major absorber of UV-B, and <10% of incident UV-B wavelengths penetrate through the epidermis to the dermis. Approximately 3% of radiation