
Different biologic effectiveness of blacklight fluorescent lamps available for therapy with psoralens plus ultraviolet A

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In 1976 we reported a change in spectral distribution of "blacklight" fluorescent lamps. It was not possible to determine the spectral composition of these lamps by any codes or packaging materials. Phototherapy booths utilizing standard BL-HO lamps will accept lamps of at least two spectral distributions; both types are commercially available. This study was conducted to determine the biologic efficacy of these two lamp types that we refer to as BL-O and BL-N. The BL-O spectrum had a peak emission at approximately 350 nm with 98% of the energy between 320 and 400 nm. The BL-N spectrum had its peak emission at 365 nm with a range from 340 to 400 nm. The BL-O spectrum was at least 2.5 to 4 times as effective as BL-N in causing minimally perceptible phototoxicity in albino hairless mice given oral doses of 8 mg/kg of 8-methoxypsoralen. Food and Drug Administration (FDA)-approved specifications imply that the BL-O spectrum is to be used for psoralens and ultraviolet A (PUVA) phototherapy. If lamps with the BL-N spectrum are replaced by lamps with the BL-O spectrum, the metered dose must be reduced to no more than one-fourth of the previous dose or the patient may suffer serious phototoxic reactions. (J AM ACAD DERMATOL 11:599-606, 1984.)

Some of the oldest available medical records suggest that plant extracts were used to sensitize the skin prior to sunlight exposure, in an effort to stimulate repigmentation of vitiliginous spots. The photosensitizing materials have been identified as several psoralens (substituted furocoumarins), found in the fruits, leaves, or seeds of several plant varieties (e.g., fig, citrus, *Ammi majus*,

Psoralea corylifolia). More recently it has been found that topically¹ or orally² administered 8-methoxypsoralen (8-MOP) followed by long-wave ultraviolet radiation (UVA; >320 nm) is an effective treatment for psoriasis. Orally administered 8-MOP followed with ultraviolet A (UVA) radiation (PUVA) therapy has been studied over the past decade and found to be valuable for treatment of severely affected psoriatic patients³; PUVA therapy is beneficial also in treatment of mycosis fungoides.⁴

Clinically, PUVA involves treatment of sensitized skin for therapeutic purposes at the risk of causing undesirable phototoxic responses. The physician must regulate UVA and 8-MOP dosage to maximize therapeutic benefit while minimizing the damaging phototoxic side effects. It has been

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fairly well accepted³ that repeated near erythemogenic treatments are necessary for effective therapeutic result; thus the phototoxic response is used to index treatment dosages.

The number of phototherapy booths and sources of replacement lamps has rapidly proliferated as this treatment has become accepted into medical practice and approved by the American Food and Drug Administration (FDA). Part of the standard operating procedure for maintenance of phototherapy booths is the periodic replacement of fluorescent lamps in the booths (the output of the lamps deteriorates with use). Our institution recently requisitioned lamps for one of our phototherapy booths, referring to the lamp "model" number as inscribed on the lamps, F72T12 BL-HO, and indicating the booth manufacturer as preferred vendor. The purchasing department, following their standard procedure, requested bids, received a lower bid from a second lamp vendor, and subsequently purchased them from the lower bidder. These newly purchased lamps were checked to determine their spectral distribution. They were found to have a narrow and long-wave shifted UVA distribution relative to the lamps installed originally by the phototherapy booth manufacturer. Both sets of lamps were coded as F72T12 BL-HO.

In 1976 our laboratory noted a shift of spectral distribution in blacklight lamps.⁵ The coding on the lamps was identical, making it impossible to distinguish two spectrally different sources based on labeling or on packaging materials. We used the designations BL-O (old style) and BL-N (new style) to refer to the two spectra observed. The spectra of originally supplied PUVA lamps and of the replacement lamps, respectively, corresponded exactly to these two spectra. The impact of this change of spectral distribution on biologic systems, and in particular on 8-MOP-sensitized systems, was at that time uncertain.

The recent proliferation of PUVA therapy installations has made identification of lamp spectra a crucial issue in terms of therapeutic application. This concern is compounded by the fact that some commercial phototherapy units will accept lamps of different types. This has restimulated our concern about the relative biologic impact of these two spectral distributions.

This report indicates that currently available

"blacklight" fluorescent lamps do differ in spectral distribution and also in biologic effectiveness without being easily distinguished otherwise.

METHODS AND MATERIALS

Radiometric studies

Spectral irradiance was measured with an Optronics 741 spectroradiometer having a 2 nm bandwidth, calibrated with an NBS traceable 1,000 W DXW standard lamp. This spectroradiometer is interfaced with a Hewlett-Packard 9815 desk-top calculator/controller and a Hewlett-Packard 9872B plotter/digitizer. Data were stored on magnetic tape for calculation and graphic data presentation.

Broad-band irradiance measurements were made with an International Light Model 700 radiometer with a UVA detector assembly (W1503 quartz diffuser, UVA-pass filter, SEE015 detector) that has a peak sensitivity at 360 nm with a bandwidth of 50 nm, the same spectral sensitivity as most phototherapy booth monitors.

An action spectrum for psoralen-sensitized phototoxicity⁶ was used to predict the efficacy of the two sources. Calculations for weighting were completed using this spectrum and the spectral irradiance of the lamps. Spectral irradiance of the two lamps was first normalized to represent equal total UVA irradiance as measured with the UVA radiometer. The spectral distribution of each lamp was then multiplied by the action spectrum at each wavelength to yield the predicted spectral distribution of efficacy. The integrals under these efficacy distribution curves provided predictions of the relative efficacy of the two sources.

The possibility of differentiating the two spectral distributions without the aid of a spectroradiometer was examined with the use of a Schott WG360 cutoff filter (Schott Optical Glass, Inc., Duryea, PA), 2 mm in thickness, placed over the UVA detector head of the IL 700 radiometer. Measurements of the two source types were made with and without the filter in place.

In vivo studies

To determine the biologic effectiveness of the two lamps, we conducted an experiment utilizing 8-MOP-sensitized Skh Hairless-1 mice. This strain of mouse has been shown to react similarly to human skin in dose requirements and action spectrum for acute unsensitized damage.⁷ While this mouse is explicitly not an appropriate model for psoriasis therapy, it is an appropriate model for human erythema and exhibits a similar psoralen-sensitized phototoxicity.

Fasted mice (12 animals per group) were gavaged

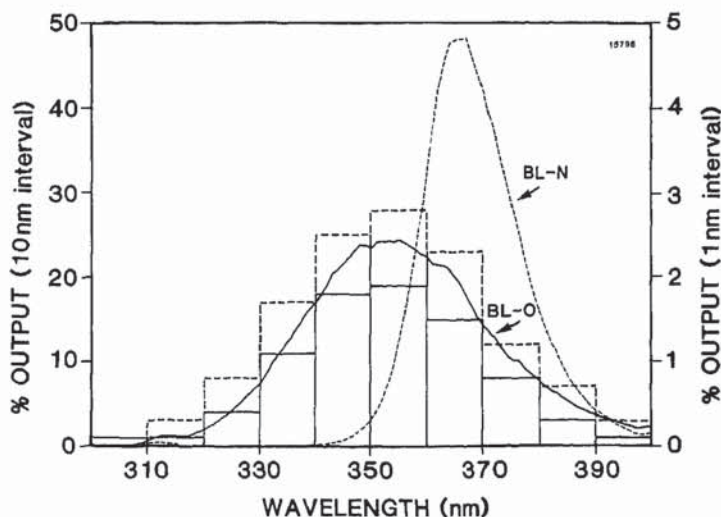


Fig. 1. Spectral distribution of BL-O and BL-N blacklight lamps plotted in relative output per nanometer (*right ordinate*). The histogram represents the limits of the FDA-approved spectral distribution of the irradiation source for PUVA therapy (from Oxsoralen package insert), presented in relative output per 10-nm interval (*left ordinate*).

Table I. UVA doses for minimally perceptible phototoxic response

	Days after irradiation					
	1		2		3	
	BL-N	BL-O	BL-N	BL-O	BL-N	BL-O
Median UVA dose (joules/cm ²)	9.2	3.1	7.7	2.65	7.7	1.9
Confidence interval (95%)	5.5-10.7	1.6-4.3	3.9-10.7	1.6-4.3	3.9-7.7	1.6-4.3
Relative effectiveness* (BL-N dose/BL-O dose)	3.0		2.9		4.1	

*The BL-N lamp spectrum requires 2.9 to 4.1 times the UV dose required by the BL-O lamp spectrum to yield comparable phototoxic reactions.

with 8-MOP (Elder Pharmaceuticals, Bryan, OH) in corn oil (8 mg/kg body weight). A period of 1½ hours elapsed between 8-MOP dosing and exposure to the UV lamps. The animals were restrained without anesthesia, using masking tape. Aluminum foil occlusive masks were placed over the backs of the animals. Each mask had a series of six punched holes 5 mm in diameter to define the test exposure areas. Ear swelling, a quantitative measure of cutaneous damage,⁸ was also used to determine the extent of the phototoxic damage from both light sources. The thickness of the tip of each ear was measured prior to UV treatment.

The light source used for the irradiation of the mice consisted of a custom fixture holding eleven lamps in a "close pack" arrangement (adjacent tubes touching).

Sylvania F40T12 PUVA lamps (BL-O) and Westinghouse F40BL lamps (BL-N) were used, one type for each treatment group.

A preliminary range-finding study was conducted to determine the approximate UVA doses required to cause a minimally perceptible phototoxic response with each source. Based on these data, exposure doses were designed to bracket the minimal phototoxic UVA dose in 40% increments.

The intensity of the lamps at the site of irradiation was 4.1 mW/cm² UVA for the BL-N lamps and 4.0 mW/cm² for the BL-O lamps, as measured with an International Light UVA photodetector. Comparable measurements were made with a Solar Light UVA detector head coupled to a rate meter and integrator. The

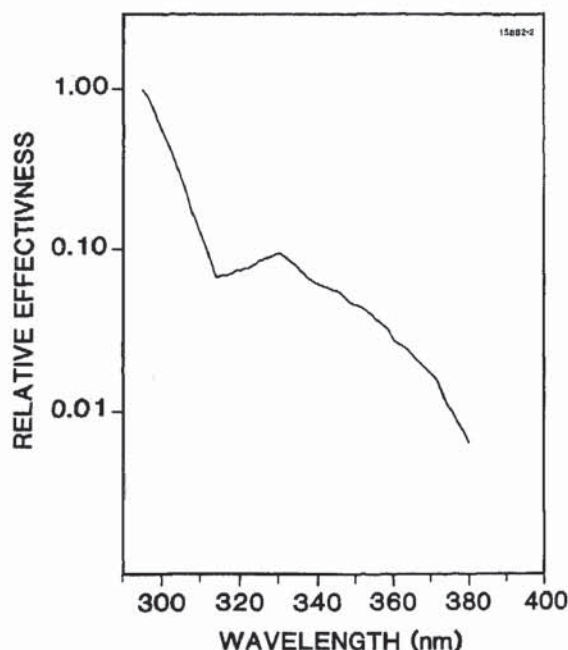


Fig. 2. Action spectrum for phototoxicity for topically applied 8-MOP on human skin. This action spectrum was used to weight the output of the two lamp spectral distributions to yield the effective spectral distribution as presented in Fig. 3. (Drawn from Cripps D, Lowe N, Lerner A: *Br J Dermatol* 107:77-82, 1982.)

integrator was used to monitor and terminate the dosing intervals for the six exposure sites. The six doses delivered for the animals irradiated with the BL-O lamps were 0.8, 1.1, 1.6, 2.2, 3.1, and 4.3 joules/cm² UVA. The doses delivered to the animals irradiated with the BL-N lamps were 2.0, 2.8, 3.9, 5.5, 7.7, and 10.7 joules/cm² UVA. At the end of dose delivery for each irradiation site, the hole in the mask was covered with opaque white adhesive tape. The ears were exposed for the entire irradiation period and received 4.3 joules/cm² on the BL-O group and 10.7 joules/cm² on the BL-N group.

Determination of the lowest dose required for the minimal phototoxic (edema and erythema) response was at 24, 48, and 72 hours after irradiation. At these same observation periods, ear thickness was measured with a Mitutoyo pocket thickness gauge, model 7309. Differences between thickness at the three observation times and the thickness prior to irradiation were recorded.

RESULTS

Fig. 1 shows the two lamp spectra superimposed over the recommended spectral distribution

Table II. Mean increases in ear thickness (μ m)

	Days after irradiation					
	1		2		3	
	BL-N	BL-O	BL-N	BL-O	BL-N	BL-O
\bar{X}	12.1	15.0	36.3	31.3	58.8	56.7
SD	9.27	13.2	23.7	16.8	59.2	51.2
p > 0.50		p > 0.50		p > 0.50		

n = 24; radiation dose: BL-N, 10.7 joules/cm²; BL-O, 4.3 joules/cm².

for 8-MOP phototherapy lamps as described in the FDA-approved Oxoralen package insert. Clearly the BL-O lamp falls within these guidelines, while the BL-N lamp does not.

The original lamps in our phototherapy booth, manufactured by Voltarc for Elder Pharmaceuticals, emitted the spectrum identified in Fig. 1 as BL-O. The replacement lamps purchased by our purchasing department, and manufactured by General Electric Company, Cleveland, OH, had a spectral distribution identical to that labeled BL-N.

Table I gives data from the biologic study of relative effectiveness of these two spectra. Effectiveness was determined by finding the lowest UVA dose required to cause a phototoxic response in each animal. The data indicate relative effectiveness ranging from 2.9:1 to 4.1:1 in favor of the BL-O spectrum compared with the BL-N spectrum, as measured by the IL phototherapy UVA detector.

The data for ear swelling are presented in Table II. Ear swelling was equivalent in both groups; the animals irradiated with the BL-N spectrum had received 2.5 times as much energy as the corresponding group irradiated with the BL-O spectrum. Based on these data, the BL-O lamp type has 2.5 to 4 times the effectiveness of the BL-N lamp type, at the same measured dose.

To determine if this difference in effectiveness was predictable from currently available action spectra, the output of each of the two lamps was weighted by the action spectrum⁶ presented in Fig. 2. This action spectrum was derived by digitizing and replottting the published data of Cripps et al.⁶ The weighted "effective" irradiance of each source is presented in Fig. 3. Integrating the energy beneath the curves yields a 2.2 to 1 ratio of estimated effectiveness of the BL-O compared to

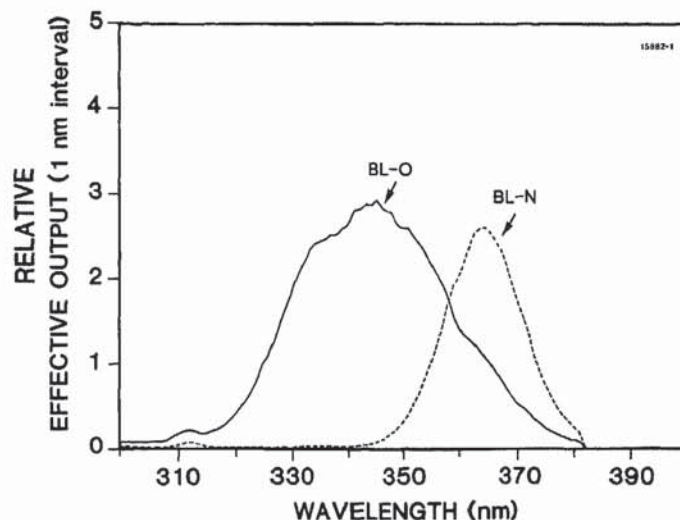


Fig. 3. Effective spectral distribution of BL-O and BL-N lamps for equivalent measured UVA dose as weighted by the action spectrum in Fig. 2. Area integrals yield a 2.2:1 ratio of the BL-O:BL-N lamps in predicted effectiveness.

BL-N. This corresponds in direction to the biologic data presented here.

Measurement of the lamps with the IL 700 UVA detector, utilizing a Schott WG 360/2 mm filter, made it possible to differentiate the two lamp types. This filter absorbs sharply below 360 nm, thus reducing relatively more of the total output of the BL-O lamp. Irradiance of the BL-O lamp through the filter dropped to 45% of the irradiance with no filter over the detector. Similar measurements of a BL-N lamp yielded a drop to only 74% of the original measurement. Thus it should be possible to distinguish between these two lamp spectral distributions without needing a spectroradiometer.

DISCUSSION

The experimental data indicate a difference in efficacy of between 2.5 to 1 and 4 to 1 for the two lamp spectra, to produce a minimal phototoxic response as measured with an International Light UVA phototherapy radiometer. While this does not necessarily mean that this same difference holds for therapeutic efficacy of psoriatic clearing, it has been established that near phototoxic (erythemogenic) doses are desirable for clinical treatment.³ The exact numeric ratio of effectiveness may also depend on the dose of 8-MOP, since

the shapes of dose-response curves for drug and radiation are not identical.*

Weighting the output of these lamp spectra with currently available action spectra for psoralen-sensitized skin gives supporting evidence for our experimental findings. The Cripps et al⁶ action spectrum was based on topically applied 8-MOP on human skin. An action spectrum for orally sensitized or topically 8-MOP-sensitized guinea pigs⁹ was also used to weight the two lamp spectra, yielding similar results. In view of our data, 8-MOP-sensitized hairless albino mice may be somewhat less sensitive than humans or guinea pigs to the longer UVA wavelengths where the BL-N lamp has most of its output.

Given the demonstrated difference in effectiveness of these two lamp types, it becomes very important that clinicians receive the appropriate lamp spectral distribution for their phototherapy booths. Unfortunately, lamp manufacturers do not necessarily use any distinguishing code to denote the spectral type of blacklight lamp. There is some indication that even the choice of vendor will not necessarily guarantee the spectral type of lamp supplied. Verification of spectral distribution of lamps is of greatest concern clinically when lamps

*Forbes PD, Cole CA: Unpublished observations, 1982.

are being changed and should be performed whenever new lamps are received. It is advisable that all lamps within a phototherapy box be changed simultaneously and that replacements be obtained as single batches to avoid having "mixed" spectral sources within a booth.

Clinically, two possibilities exist if lamp styles are changed:

1. *BL-O lamps replaced with BL-N:* As indicated by our data, treatment may require from 2.5 to 4 times the UVA dose used previously to achieve the same therapeutic result. This would compromise the feasibility of treatment due to the extended irradiation time necessary.
2. *BL-N lamps replaced with BL-O:* This possible exchange of lamps is of great danger to the patient if equivalent metered UVA doses are delivered for both lamp styles. Two to four times the minimally perceptible phototoxic dose of UVA to an 8-MOP-sensitized individual could result in severe sunburn, blistering, and possibly painful ulceration.

Institutions or practitioners having UVA phototherapy booths need first to ascertain the spectral type of lamps currently in use. If these are found to be BL-O, then purchase of replacement lamps should specify the spectral distribution of the BL-O lamp. Spectral distribution of these replacement lamps should be verified prior to installation.

If currently utilized lamps are found to be BL-N, replacement lamps should be of the BL-O spectral distribution. Delivered doses as measured with a UVA phototherapy radiometer *must* be reduced by at least a factor of 4 and increased slowly until a therapeutic UVA dosage is ascertained in each patient. It is important to emphasize that spectral distribution cannot be determined by measurement of intensity alone. Both lamp spectra will give approximately equivalent intensities as measured by phototherapy UVA radiometers. Somewhat coincidentally, the total (unweighted) UVA dose supplied by these two spectra corresponds to the dose measured by the IL 700 UVA detector system.

Lamp spectral distribution may be differentiated utilizing the phototherapy booth radiometer and a Schott WG360/2 mm cutoff filter. Placing the

filter over the detector should reduce the output of BL-O lamps to about 45% of the original measurement, and to only about 75% of original output for BL-N lamps. These reductions only hold for single sources or a single type of source. If lamps of these two types are mixed in a phototherapy box, or if there are lamps of other spectral distribution in the box at the time of measurement, this relationship will not hold. Some phototherapy boxes have more than one radiometric sensor, which may not be readily accessible. Nevertheless, each sensor must have a WG360 cutoff filter taped over it to determine the spectral distribution type as described above. Measurement of lamp output with a spectroradiometer is the most accurate means of assessing the spectral distribution of lamps.

It would be beneficial if lamp manufacturers would specifically mark lamps of the BL-O spectral distribution suitable for PUVA therapy with a distinguishing code. We would suggest the use of the code mnemonic "PUVA" after the coding (see "Appendix") for lamp length, diameter, spectral region, and ballast configuration (e.g., F72T12 BL-HO-PUVA) to prevent future danger to patients from change of lamp spectra.

Morrison and Pike¹⁰ recently reported the spectral power distribution of a variety of sources that are or could be used in PUVA phototherapy. Their study, which does not directly examine changes in efficacy, includes examples of both source types considered in the present report.

Authors' note added in proof

A product release from the Westinghouse Lamp Division describes two 72-inch fluorescent blacklight lamps for use in tanning beds or tanning booths. Both lamps are high-output types with recessed double-contact base. One, designated F72T12/BL-S/HO, is rated at 85 watts; the other, designated F72T12/BL-S/S/O, is rated at 162 watts. Although we have not examined these lamps, the manufacturer's specifications suggest that the 85-watt lamp emits spectrum type BL-O, whereas the 162-watt lamp emits spectrum type BL-N. Both lamps are labeled "UVA sunlamp," which should not be confused with the UVB-rich "fluorescent sunlamp" (designation FS) from the same manufacturer, nor with the "RS sunlamp" (mercury doped tungsten lamp) produced by several American

manufacturers (similar to the European Osram Ultravitalux).

Westinghouse Lamp Division is now a subsidiary of North American Philips (Norelco), which generally uses quite different Philips-type lamp designations. Norelco literature lists two lamps, F72T12/BLHO and F72T12/BLVHO, which appear to correspond physically to the Westinghouse "UVA sunlamps" above. The Norelco literature, however, implies that both lamps have a phosphor designated "09" in Philips terminology; Philips type 09 and 10 phosphors appear to correspond to BL-O and BL-N, respectively.

Small lamps (F15T8) are employed in PUVA units for limited exposure areas. Our lamps of this size from General Electric contain the BL-N phosphor. According to the manufacturer's literature, Sylvania lamps of this size employ a phosphor different from either BL-O or BL-N, with a maximum near 370 nm and a broad emission spectrum.

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APPENDIX

Commercially available fluorescent lamps can differ in several characteristics. The following discussion relates to North American practice and considers both physically possible substitutions and detectable differences. Manufacturers' descriptions of lamp configurations make extensive use of terms such as "often," "typically," and "usually."

The primary dimensional characteristics of a fluorescent lamp are its *length* and its cross-sectional *diameter*. These are specified in the first six or seven code characters embossed on each tube as *Fnn Tmm*, where *F* represents a fluorescent source, where *nn* refers to nominal lamp length in inches for most lamps greater than 48 inches long, or to rated watts for shorter lamps (actual length of 72-96 inch lamps is about 2 inches less than nominal), *T* represents a tubular source, and *mm* indicates diameter in units of one-eighth inch (note that *FS* and *FR* have special meanings). In some cases the "T mm" designation is omitted from the label. Lamps of different lengths cannot be substituted; most PUVA applications utilize 72-inch tubes (F72). Different diameters could be substituted in some cases, but all likely sources are presently 1½ inches in diameter (T12).

Spectral emission characteristics are implied in the next set of letters (e.g., *CW* for Cool White lamps, etc.). The designation *BL* refers to "blacklight" and implies a UVA source, which is the only appropriate category for PUVA therapy. As reported above, however, the BL designation is not unambiguous, and differences among BL spectra can have important biologic consequences.

Emission intensity per unit length is affected by the *operating current*. Sources designated *HO* or *VHO* ("high output" or "very high output") are designed to operate at higher current levels than "standard" (implied by absence of the special designation). To operate correctly these lamps require ballasts designed to supply the appropriate current levels. It is not clear whether the terms *HO* and *VHO* have fully standardized definitions, although specific ballasts are generally labeled to indicate the type, length, and number of lamps they are designed to operate. It is possible in principle to operate lamps with ballasts other than those for which they are intended, with effects on output intensity and operating life.

Lamps also differ in the type of *end fitting*. Three commonly used types of fittings in the North American market are the medium bipin (two pins on each end, ½ inch apart), the recessed double-contact fitting, and the "slimline" single-contact fitting. Lamps with different

end fittings are not interchangeable, but the type of end fitting is not usually specified directly in the lamp designation. In some cases specific combinations of end fittings and operating current are jointly implied in a designation (e.g., slimline) used by a particular manufacturer. It is not clear, however, whether such combinations are regarded as invariant by different manufacturers, and current practice indicates that at least spectral changes by a single manufacturer are not necessarily accompanied by designation changes.

Sylvania (GTE) manufactures lamps specifically for their prototype phototherapy booths. These lamps contain internal reflectors that increase the directional emission intensity. They are designated as FR74T12-PUVA and have special end fittings and "slimline" electrical characteristics. Note the nonstandard length (74 inches), the absence of the BL designation, the use of the PUVA description, and the use of *R* to indicate the reflector. These lamps (type BL-O) are not interchangeable with any other available type. It is physi-

cally possible to mount reflector-containing lamps with the reflecting side toward the patient, with obvious loss of output.

Fluorescent lamps may be designed for "preheat," "rapid-start," or "instant-start" operation. Typically preheat lamps exhibit a delay between switching on and firing and may require that the switch be held for 1 or 2 seconds. Certain ballasts, however, permit preheat lamps to operate like rapid-start lamps, and some lamps are designed to be used in either preheat or rapid-start circuits. Operationally, rapid-start and instant-start lamps are indistinguishable but require different ballasts. A single-contact lamp is necessarily of the instant-start type. However, some double-contact lamps are also instant-start; they will fit in preheat or rapid-start fixtures but cannot be operated by ballasts designed for such circuits. It is believed that most available lamps over four feet long suited for PUVA applications are of either the instant-start or the rapid-start type.

Hypersensitivity to rat saliva

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A patient who rapidly developed impressive local edema around a rat bite site is described. An interesting differential diagnosis was presented since the offending rat was experiencing an opiate withdrawal syndrome. A discussion of the possibilities of animal product allergy, local infection, and edema produced by opiate histamine releasers was considered. (*J AM ACAD DERMATOL* 11:606-608, 1984.)

Hypersensitivity to allergens of mammalian origin is a difficult problem among researchers in contact with experimental animals. It is estimated that more than 10% of laboratory workers will exhibit symptoms when exposed to these aller-

gens. The major sources of research animal allergens are urine and urine and dander. No previous report of hypersensitivity to animal saliva has been published. In this report such a case is described.

CASE REPORT

A healthy 28-year-old white man, who had been a medical research laboratory employee for over a year, noticed occasional bronchospasm and local contact urticaria when exposed to albino mice or rats. In March 1983, he was bitten on the left lateral proximal portion of the thumb by a rat that was experiencing a drug

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