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Minimal Erythema Dose (MED) Testing

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Abstract:	Ultraviolet radiation (UV) therapy is sometimes used as a treatment for various common skin conditions, including psoriasis, acne, and eczema. The dosage of UV light is prescribed according to an individual's skin sensitivity. Thus, to establish the proper dosage of UV light to administer to a patient, the patient is sometimes screened to determine a minimal erythema dose (MED), which is the amount of UV radiation that will produce minimal erythema (sunburn or redness caused by engorgement of capillaries) of an individual's skin within a few hours following exposure. This article describes how to conduct minimal erythema dose (MED) testing. There is currently no easy way to determine an appropriate UV dose for clinical or research purposes without conducting formal MED testing, requiring observation hours after testing, or informal trial and error testing with the risks of under- or over-dosing. However, some alternative methods are discussed.
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TITLE

Minimal Erythema Dose (MED) Testing

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Short Abstract: This article describes how to conduct minimal erythema dose (MED) testing in order to determine the lowest dose of ultraviolet radiation that will cause erythema (burning) when administered to an individual.

Long Abstract: Ultraviolet radiation (UV) therapy is sometimes used as a treatment for various common skin conditions, including psoriasis, acne, and eczema. The dosage of UV light is prescribed according to an individual's skin sensitivity. Thus, to establish the proper dosage of UV light to administer to a patient, the patient is sometimes screened to determine a minimal erythema dose (MED), which is the amount of UV radiation that will produce minimal erythema (sunburn or redness caused by engorgement of capillaries) ~~in the average Caucasian~~of an individual's skin within a few hours following exposure. This article describes how to conduct minimal erythema dose (MED) testing. There is currently no easy way to determine an appropriate UV dose for clinical or research purposes without conducting formal MED testing, requiring observation hours after testing, or informal trial and error testing with the risks of under- or over-dosing. However, some alternative methods are discussed.

Protocol Text*:*

1) Preparing for UV exposure

1. Explain to the participant how MED testing works ("I'm going to expose some skin on your arm to UV light over the course of about 20 minutes, and tomorrow, we're going to check that section of your skin in order to determine how sensitive you are to the light. You may experience a sunburn in the small areas that we expose to UV. If the sunburn is painful or bothers you, you can treat it like you would any other sunburn.")

2. Staff and participant should wear UV protective glasses.

3. The participant should be wearing a short-sleeved shirt or roll her sleeve up.

4. Have the participant put on a glove to protect the skin on her hand.

5. Remove the Daavlin patch[1] backing on the left and right sides of the patch, and place it on the inner lower arm just adjacent to the glove, avoiding any existing skin blemishes.

6. Cover any additional skin on the arm with the participant's shirt or other material.

7. Place the arm so that the holes in the patch will be exposed to the UV light source. No other skin should be exposed to the UV light.

8. Tell the participant she ~~can take her arm out if she feels~~will feel warmth but her arm will not be burning during the test.

2) Conducting UV exposure

1. Patch holes (e.g., 6) should be exposed to UV at intervals throughout the exposure period.

2. Start with hole 1 open.

3. Select the total duration of the exposure based on the manufacturer specifications for the light source and the participant's Fitzpatrick skin type I-VI (very fair to very dark; Fitzpatrick, 1988).[2] Fairer skin is more likely to burn.

4. Set a timer for the total duration of exposure (e.g., 20 minutes). A second backup timer may also be used. Start the timer(s).

5. For example, open hole 2 after ~~4~~ 2 minutes, open hole 3 after ~~8~~ 4 minutes, open hole 4 after ~~12~~ 8 minutes, open hole 5 after ~~16~~ 12 minutes, and open hole 6 after ~~18~~ 16 minutes. Thus, the skin UV exposure times will be 20 minutes for hole 1,

18 minutes for hole 2, 16 minutes for hole 3, 12 minutes for hole 4, 8 minutes for hole 5, and 4 minutes for hole 6.

6. In order to more easily identify the exposed areas after 24-48 hours, mark the skin exposed on the far edge of the first and last holes of the patch and ask the participant to not wash off the marks until after the skin is examined.

7. Have the participant remove the glove and patch.

8. Reiterate to the participant that the skin must be reexamined in 24-48 hours.

3) Assessing the MED

1. After 24-48 hours, examine the exposed areas of skin. Red or pink skin indicates erythema or burning. Erythemetous skin exposed to the shortest duration of UV is defined as the minimal erythema dose or MED.

2. Future exposures to UV should be for durations shorter than the MED to avoid burning.

3. If the areas of exposure are difficult to identify, you may want to put the patch back on using the marks to align with the exposed skin. This is also helpful if using a skin color measurement device such as a spectrophotometer.

4. Spectrophotometers provide measures of L* (darkness) and b* (hue). a* refers to the redness of the skin. A higher a* value indicates redder skin.

5. If using a skin color measurement device such as a spectrophotometer, place the spectrophotometer aperture in the center of the hole to be measured.

6. Measure each of the 6 exposure areas in numerical order and one unexposed area near the others for comparison. Try to measure the center of each hole but not a freckle or mole or other non-UV discolorations. Label each of the measurements. The measurement from the unexposed area should be labeled 0 minutes and be listed next to area 6 (the shortest exposure area - 4 minutes).

7. Increases in a* values should correspond with increases in UV exposure duration. Try re-measuring values that are not in corresponding order.

8. A 2.5 point difference in the a* of unexposed skin compared to exposed skin indicates a significant difference in redness, suggesting potential burning.

9. Add 2.5 to the lowest a* value. Anything at or above this value would be considered potentially burning. The lowest exposure time above this value is considered the MED.

Representative Results:

[Insert Figure 1 about here]

Figure 1 shows the three steps of conducting MED testing: preparing for UV exposure, conducting UV exposure, and assessing the MED.

[Insert Figure 2 about here]

Figure 2 shows the Daavlin patch on a forearm with one sticker removed for UV exposure. The subsequent five stickers would then be removed at varying time-points to expose the skin to varying durations of UV.

[Insert Table 1 about here]

Table 1 shows sample spectrophotometer a* values and corresponding durations of UV exposure for each of the six patch openings. Note that the a* values increase with increasing exposure to UV. There is also greater than a 2.5 point difference in a* values indicating that the MED has been reached. According to the sample data in Table 1, the lowest skin reading is 6.86. 6.86 + 2.5 = 9.36. Thus, anything at or above 9.36 would be considered potentially burning. The reading at 18 minutes is 9.53, which is above 9.36 and is thus considered the MED.

[Insert Figure 3 about here]

Figure 3 shows visible UV exposure on a forearm. Six squares of skin were exposed to UV in between the two black dots using the Daavlin patch. On the left side of the image are the areas that were exposed the longest (i.e., the lower left square #1 for 20 minutes and the upper left square #2 for 18 minutes). Squares #1 and 2 appear somewhat red, whereas the remainder do not, indicating that the MED is 18 minutes (square #2)

[Insert Table 2 about here]

Table 2 shows sample spectrophotometer a* values, except the MED in this example has not been reached. A lack of a 2.5 point difference in a* values indicates that burning did not occur and that the MED was not met (i.e., the participant did not burn even at the longest UV exposure duration). Thus, we would not expect to see any visible red areas.

[Insert Table 3 about here]

Table 3 shows sample spectrophotometer a* values, but the data for the skin that was not exposed to UV labeled NA do not make sense because the a* value is higher than the 4 through 16 minute exposures. Therefore, one should re-measure the unexposed skin. The expected a* value would be less than 7.2 for which the skin was exposed to UV for the shortest duration of 4 minutes.

Discussion:

Ultraviolet radiation (UV) therapy is sometimes used as a treatment for various common skin conditions, including psoriasis, acne, and eczema. The dosage of UV light is prescribed according to an individual's skin sensitivity, which is determined as a function of the individual's Fitzpatrick skin type I through VI (very fair to very dark).[2] Human skin varies in its sensitivity to UV radiation because of varying degrees of skin pigmentation, thickness, and other factors. Thus, to establish the proper dosage of UV light to administer to a patient, the patient is sometimes screened to determine a minimal erythema dose (MED), which is generally understood as the amount of UV radiation that will produce minimal erythema (sunburn or redness caused by engorgement of capillaries) ~~in the average Caucasian~~of an individual's skin within a few hours following exposure.

There is currently no easy way to determine an appropriate UV dose for clinical or research purposes without conducting formal MED testing, requiring observation hours after testing, or informal trial and error testing with the risks of under- or over-dosing. However, there are various options for several aspects of the MED testing. Options for exposure areas of the body: We chose to expose the inner fore-arm to UV because it is easily accessed for testing and is exposed to less sunlight than some other areas of the body. However, the upper buttocks is another area that typically receives minimal UV exposure. Another option for timing the exposures: A geometric ratio series can be used with a constant ratio between adjacent apertures, such as 1.0, 1.4, 2.0, 2.8, 3.0, 5.6, 8.0, etc. with a ratio of the square root of two between adjacent sites. Better resolution can be achieved with more apertures and a ratio between apertures of the cube-root of two, so that there are two apertures between each doubling of dose. ~~An option for a light source: A solar simulator (e.g., Multiport Model 601, Solar Light Co.)[3] could be used, but they cost over $50,000, and the UV dosing would still need to be converted based on the end UV source. FDA regulations for testing the effectiveness of sunscreen sun protection factors require the use of a solar simulator with a continuous emission spectrum from 290 to 400 nanometers with a limit of 1,500 Watts per square meter on total irradiance for all wavelengths between 150 and 1,400 nanometers.[4]~~ Options for UV exposure templates: Like Daavlin, The Copenhagen company Chromo-Light has an MED patch, but it does not seem to be widely available.[5] Daavlin also has a glove and a fabric patch for larger skin areas.[1] MED testing using these options is similar to using the Daavlin sticker patch. However, one must ensure that the fabric options fit the users properly and stay in place during testing. The H. Waldmann ~~GmbH~~ & Co. KG also has a larger more expensive mechanical template for erythema testing.[6] Options for the assessment of erythema: Some studies use the L* (darkness) value of the spectrophotometer rather than the a* (redness) value.[7,8] A likert-type visual rating scale for erythema can be also used instead of spectrophotometry.[9]

A few investigators have conducted pilot testing establishing ranges of UV doses that produce MEDs by skin type, which would eliminate MED testing per se.[9-12] However, skin typing is inexact. Kwon and colleagues performed a similar study recommending UV doses corresponding to MEDs based on spectrophotometry readings for darker skinned individuals.[7] However, with both of these approaches, one must still convert the UV dose based on the intensity of the device used in the publication to the

device at hand. UV intensity and effects are determined by the nature of the UV emitting device, the lamps used in the device, the skin sensitivity, and the distance of the skin from the device, all of which vary from situation to situation. This is probably the biggest source of error and confusion in using any MED methodology. However, if one wishes to conduct conversions from one device to another, the ~~Durham~~ DURHAM Erythema ~~MED~~ Tester is an all-in-one device that contains both a UV source and a template that delivers ten graded irradiances increasing in 26% intervals in a single exposure, without opening or closing of motorized apertures, by employing graded opaque printed dots or etched small holes in a metal foil, so that in one exposure, all of the desired irradiances are delivered simultaneously~~with holes that open and close that can be used to conduct MED testing~~.[13] For more information about MED testing, dosimetry, and calibration in phototherapy, including how to report MED testing procedures, the authors recommend the guidelines from the British Photo-dermatology Group.[14]

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*Figure
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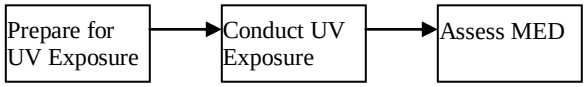
Figure 1: Experiment Schema

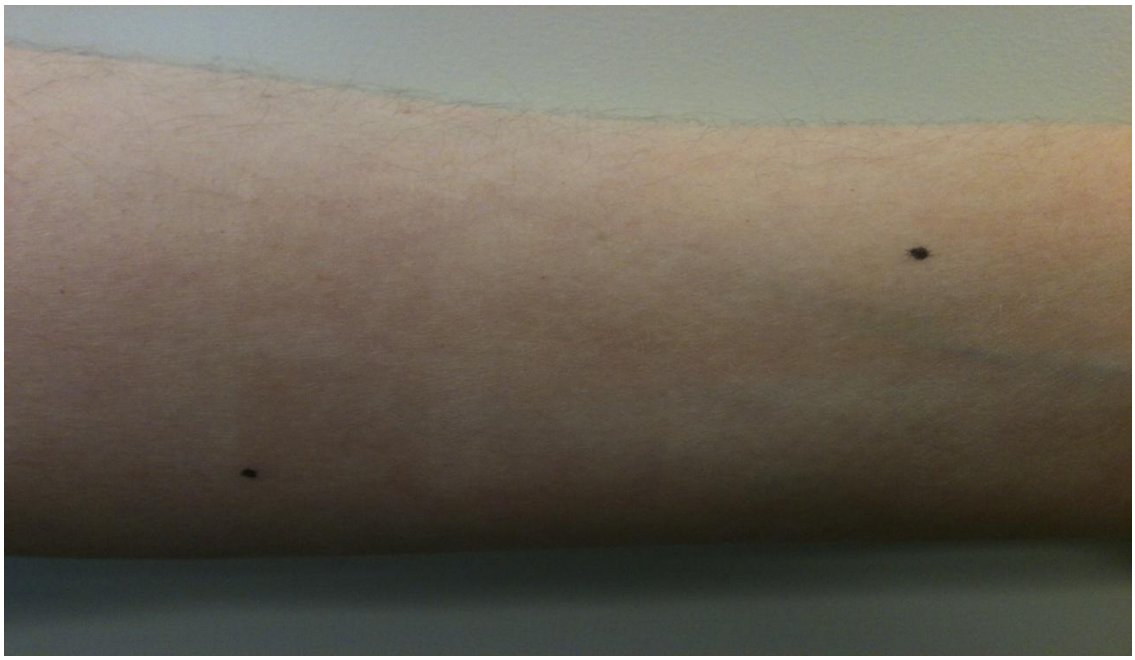


Legend: Figure 1 shows the experimental schema.

Figure 2: Daavlin UV Exposure Patch

Legend: Figure 2 shows the Daavlin patch on a forearm.

Figure 3: Visible UV Exposure of the Arm



Legend: Figure 3 shows visible UV exposure on a forearm.

*Table of Reagents/ Materials Used
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Table 1: Sample Spectrophotometer Data

Patch Opening #	a* Value	Minutes of UV Exposure
1	10.57	20
2	9.53	18
3	8.1	16
4	8.06	12
5	7.75	8
6	7.2	4
NA	6.86	0

Legend: Table 1 shows sample spectrophotometer data in which the MED has been reached.

Table 2: Sample Spectrophotometer Data

Patch Opening #	a* Value	Minutes of UV Exposure
1	9.2	20
2	9.0	18
3	8.1	16
4	8.06	12
5	7.75	8
6	7.2	4
NA	7.0	0

Legend: Table 2 shows sample spectrophotometer data in which the MED has not been reached.

Table 3: Sample Spectrophotometer Data

Patch Opening #	a* Value	Minutes of UV Exposure
1	10.57	20
2	9.53	18
3	8.1	16
4	8.06	12
5	7.75	8
6	7.2	4
NA	9.0	0

Legend: Table 3 shows sample spectrophotometer data in which the data do not make sense because the a* values do not increase consistently with increasing exposure time.

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Major Concerns:
The Long Abstract identifies MED as the minimal erythemal dose to an average Caucasian skin, but the technique described is designed to find the unique MED for an individual. Average values can be estimated by using the Fitzpatrick or Boston skin type method of choosing a start dose.

Response: Individual testing is now specified in the abstract and first paragraph of the discussion.

The Protocol preparation point 1 should include a warning to the patient that some areas of the skin will be burned and may be sore, but that this is expected and normal, in order to 'bracket' the MED area with definitely erythemal and non-erythemal areas.

Response: Warning text was added to point 1.

The fore-arm is not the ideal site, since most people expose the arm to sun. A better choice (though less convenient) is the skin of the upper buttock, which is unlikely to be sun-exposed in most people.

Response: We prefer the inner fore-arm because it is more convenient and gets less UV exposure than some other body parts. However, we now mention the upper buttocks as another good option in the discussion.

The site needs to be chosen carefully to avoid skin blemishes.

Response: We added avoidance of skin blemishes to point 5 of the protocol.

In Point 8, the patient should be warned that the sensation of warmth is not burning during the test, to avoid rendering the test null and void through non-participation.

Response: Point 8 was revised accordingly.

Note that in Protocol 2/5, the exposures are incorrect. After 20 minutes, hole 2 has 16 not 18 minutes, hole 3 gets 12 not 16 mins, hole 4 gets 8 not 12 minutes, hole 5 has 4 not 8 minutes and hole 6 gets 2 not 6 minutes.

Response: These times were corrected.

It's better to use a geometric ratio series with a constant ratio between adjacent apertures, such as 1.0, 1.4, 2.0, 2.8, 3.0, 5.6, 8.0 etc. with a ratio of the square root of 2 between adjacent sites. Better resolution can be achieved with more apertures and a ratio between of the cube-root of 2, so that there are two apertures between each doubling of dose.

Response: These suggestions were added to the discussion.

In the discussion of alternatives at the end, it is not acceptable to use a solar simulator for MED testing, since the spectrum of the metal-halide lamp is completely different from that of a TL-01 or UV6 fluorescent tube, and will give incorrect results.

Response: This was removed.

The Durham tester is a passive device that delivers 8 or 10 graded irradiances in a single exposure, without opening or closing of motorised apertures, by employing graded opaque printed dots or etched small holes in a metal foil, so that in one exposure, all the desired irradiances are delivered simultaneously. Saalmann GmbH (now MedLite) also offer a similar device.

Response: Additional information about the DURHAM tester was added to the last paragraph of the discussion.

Any method of testing which employs a separate UV source from that of the treatment device must have its spectrum and irradiance verified and correlated with the treatment cabin's parameters, as noted in the last paragraph. This is probably the biggest source of error and confusion in using any MED/MPD methodology.

Response: This was emphasized in the last paragraph of the discussion.

Minor Concerns:
Note that Waldmann GmbH is short for Waldmann Gesellschaft mit beschraenkte Haftung (company with limited liability) so that adding '& Co. KG.' is redundant.

Response: This was corrected.

The picture of the post-test result is poor - a better-illuminated photo would make this easier to read and assess.

Response: If the editors would like a new image, we can create one when the video is created.

Further discussion of MED/MPD testing, and the importance of calibration and dosimetry can be found in the British Photodermatology Group Guidelines for dosimetry and calibration in UV radiation therapy (Br J Dermatol 2002, 146: 755-763.

Response: Information about this citation was added.