# Artificial Reproduction of Lupus Erythematosus by Provocative Phototesting

Young Ho Cho, M.D., Seung Kyung Hann, M.D., Yoon-Kee Park, M.D.,
Min Seok Song, M.D., Sungbin Im, M.D

*Department of Dermatology, Yonsei University College of Medicine, Seoul, Korea*

**Sunlight is one of the well-established factors which play key roles in the induction and exacerbation of lupus erythematosus. In two patients of discoid lupus erythematosus, we have experimentally reproduced skin lesions by provocative phototesting. Both UVA (100 joules/cm$^2$) and UVB (80 millijoules/cm$^2$) radiation induced the skin lesions. The reproduced skin lesions were clinically and histopathologically consistent with lupus erythematosus.**

**(Ann Dermatol 5:(2) 105-108, 1993)**

*Key Words:* Lupus erythematosus, Provocative phototest

Today it is generally accepted that sunlight can induce or exacerbate cutaneous and systemic lupus erythematosus (LE). Furthermore, there is growing evidence that ultraviolet radiation may specifically affect the pathogenesis of LE. Artificial ultraviolet radiation can be equally deleterious. Epstein [1] was the first investigator to introduce the repeated exposure technique, which enabled him to induce LE lesions in 5 out of 25 patients. The action spectrum of LE is generally believed to be confined to UVB radiation. Some investigators[2-3] performed action spectrum studies with monochromatic radiation, and the action spectrum in LE was ascribed to the UVB range. Recently, Lehmann et al.[4] reported that both UVA and UVB radiation can induce reproduction of LE lesions by a provocative phototest of his patients with discoid LE, subacute LE, and systemic LE. We report herein two cases of discoid LE in which we could experimentally reproduce LE lesions by a provocative phototest.

## REPORT OF CASES

**Case 1.** A 45 year-old male visited our clinic with an erythematous keratotic patch and plaque on his face which had been present for about 14 months. On physical examination, a finger-tip sized round erythematous plaque was seen on his nose. In the left preauricular area, a 3×8cm sized, well defined, dull red patch was noted (Fig.1). The patent's past and family history were not contributory. The results of the following laboratory tests were within normal limits or negative:complete blood cell count, urinalysis, liver function test, chest X-ray, LE cell test, and anti-DNA antibody. The anti-nuclear antibody was 1:80 positive, nucleolar type. A skin biopsy was performed from the left preauricular area. Histopathologic sections showed hyperkeratosis, epidermal thinning, and liquefaction degeneration of the basal cell layer. The upper dermis contained heavy perivascular and disseminated lymphohistiocytic infiltrations (Fig. 2). The direct immunofluorescence findings were negative.

**Case 2.** A 58 year-old female visited our clinic with erythematous atrophic patches on her face, neck, and dorsa of hands which had been present for 19 years (Fig. 3). The patient had a history of photosensitivity to sunlight manifested by the aggravation of existing lesions or the development of new ones. Lesions usually became worse during warmer seasons and improved during cooler ones. On physical examination, multiple, va-

Received August 26, 1992
Accepted for publication April 19, 1993
**Reprint request to:** Seung Keung Hann, Department of Dermatology, Yonsei University College of Medicine, Seoul, Korea

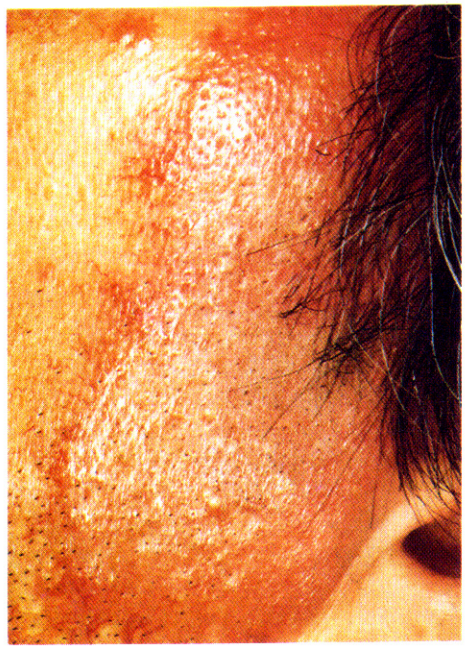

**Fig. 1.** A 3×8cm sized, dull red atrophic patch with patulous follicle and telangiectasia on the preauricular area (case 1).

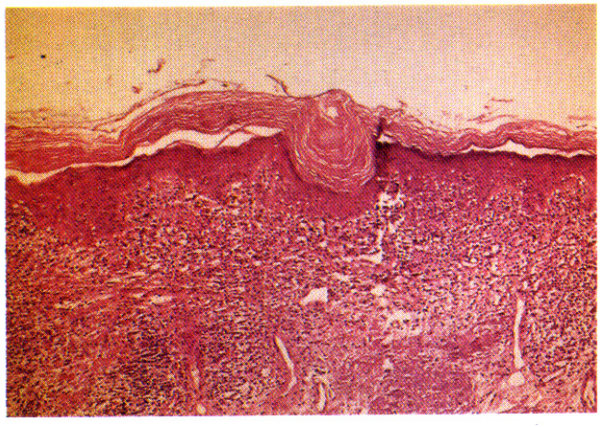

**Fig. 2.** The biopsy specimen from the left preauricular area, showing hyperkeratosis, epidermal thinning, and liquefaction degeneration of basal cells with heavy lymphocytic infiltrates in the dermis (case 1, H&E stain, ×100).

riable sized, erythematous patches together with atrophic scarring and hypopigmentations were seen on her face, ears, neck, and dorsa of hands. The results of the following laboratory tests were within normal limits or negative: complete blood cell count, urinalysis, liver function test, chest X-ray, anti-nuclear antibody, urinary porphobilinogen, coproporphyrin, and uroporphyrin. A skin biopsy specimen from the cheek showed epidermal thinning, liquefaction degeneration of the basal cell layer, and perivascular patchy lymphohistiocytic infiltrations. The direct immunofluorescence findings from the same site showed minimal lgG and C3 deposit along the dermo-epidermal junction with focal fibrinogen deposit at the dermis.

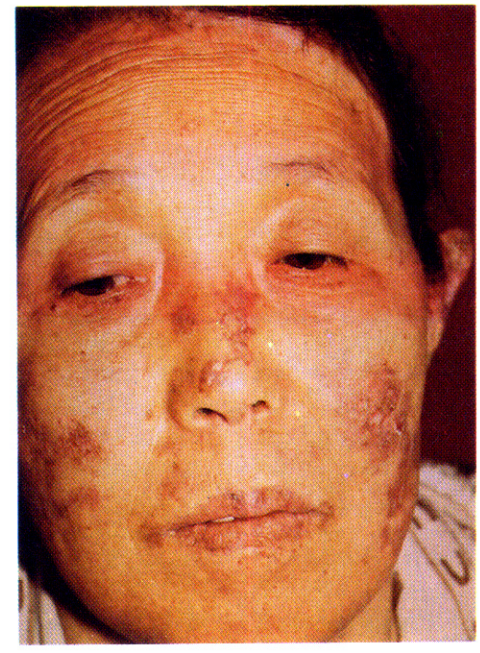

**Fig. 3.** Erythematous atrophic patches with depigmentation on the face (case 2).

## PROVOCATIVE PHOTOTEST

Phototesting was performed with a Sellas sunlight (Dr. sellmeier Co., Dusseldorf, Germany) as the UVA light source and a bank of fluorescent lamps (FST 12-UVB-HOlamp, Elder, Bryan, Ohio) for the UVB light source. In our two patients, the MED was 50 joules/cm$^2$ for UVA and 40 millijoules/cm$^2$ for UVB. Sites on the sun-exposed forearms and the back, which had not been exposed to sun, were irradiated with 100 joules/cm$^2$ of UVA and 80 millijoules/cm$^2$ of UVB, daily for 3 consecutive days. The test areas were evaluated at 24, 48, and 72 hours until specific lesions appeared but no longer than 3 weeks after the last session of irradiation (Table 1). In case 1, twenty-four hours later, erythema was observed at both UVA and UVB irradiated sites. Test sites then remained unchanged for the next 5 days. On day 5, the papules appeared on both

the UVA-and UVB-irradiated forearm and back (Fig. 4). Biopsy specimens were taken. There was no clinical and histopathologic difference between UVA and UVB induced lesions. In case 2, Twenty-four hours later, erythemas were produced at the UVB irradiated sites and pigmentations were observed at the UVA irradiated sites. Five days later, only pigmentation and telangiectasia were observed on both the UVA and UVB irradiated sites. On day 10, the papules appeared only on the UVA irradiated back and persistent pigmentations were observed at the UVB irradiated sites. The lesions lasted 3 weeks after irradiation. On day 17, a biopsy specimen was taken from the papule. Biopsy specimens from papules at the UVA test on the back showed changes consistent with LE: epidermal thinning and flattening, liquefaction degeneration of the basal cell layer, and mild lymphohistiocytic dermal infiltration (Fig.5). The direct immunofluorescence findings were negative.

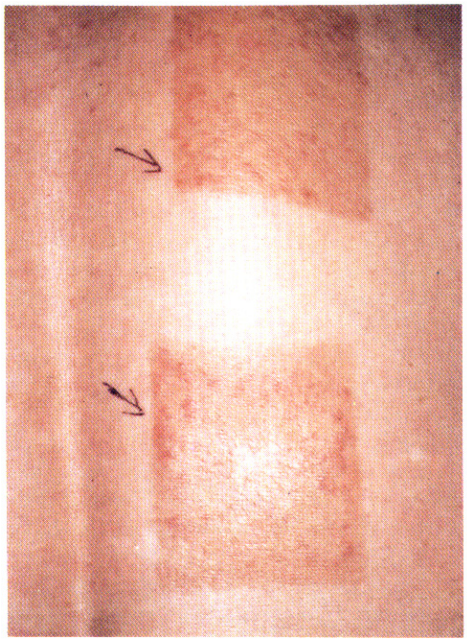

**Fig. 4.** Induction of LE lesion with UVA (lower) and UVB (upper) (case 1)

Table 1. Test protocol for provocative phototesting

| | | |
|---|---|---|
| Test site | : | Back and extensor surface of the arm |
| Dosage | : | 100 J/cm$^2$/day of UVA for 3 days<br>80 mJ/cm$^2$/day of UVB for 3 days |
| Evaluation | : | 24, 48, 72 hour up to 3 weeks after last irradiation |

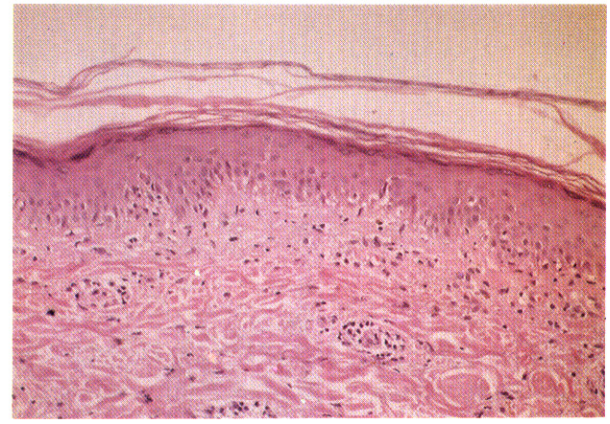

**Fig. 5.** The biopsy specimen of UVA-induced lesions from test area (case 2, H&E stain, ×200).

## DISCUSSION

LE remains a disease of unknown etiology. The role of light as a causative or precipitating factor has been suspected for many years. In 1927, Fiet[5] reported three patients with localized lesions of LE who developed a generalized flare of the disease following exposure to a high pressure mercury vapor lamp. Thus, many investigators have tried to reproduce LE lesions by exposure to artificial sources of ultraviolet radiation. Because of various radiation sources and test protocols and the limited number of patients, conflicting results were obtained in regard to photoactivation or production of LE lesions. Nevertheless, in most studies the action spectrum of LE was confined to wavelengths shorter than 320mm. Wavelengths longer than 320nm, however, have not been adequately evaluated.

Epstein et al.[1] reported that five of nine patients with a history of photosensitivity and lupus erythematosus developed an abnormal reaction consisting of an erythematous follicular papule or plaque at skin sites irradiated with a high pressure mercury arc (hot quartz contact lamp). Baer and Harber[6] performed the same phototests in 29 patients with LE (23 discoid, 5 systemic, 1 subacute cutaneous). An abnormal reaction was observed only in one patient with subacute cutaneous LE. In Everett's study[7], both

involved and uninvolved skin sites were irradiated. In three of the eight patients, the involved skin sites showed extension of the lesions following irradiation. The uninvolved areas of the skin developed no abnormal reactions. Freeman et al.[2] irradiated the skin of 2 subacute and 8 discoid LE patients with monochromatic light of 300nm wave length. In 5 out of 10 patients, persistent erythematous lesions developed in the test areas within 3 weeks after 8 repeated MED exposures. Cripps and Rankin[3] produced LE-like skin lesions in disseminated discoid LE patients with 8 to 13 MEDs of monochromatic radiation at 250 to 313nm.

Recently, Stern and Docken[8] and Tronnier et al.[9] reported exacerbations of systemic LE in patients who visited tanning parlors. Because these irradiation sources emit mainly UVA, a possible role of UVA in the induction of lesions was stressed. Emerit and Michelson[10] demonstrated the activation of a photosensitizing compound in the lymphocytes and serum of LE patients by radiation at 360 to 400 nm. Lymphocytes from healthy control subjects were unaffected. Holzle et al.[11] have reviewed their experience with phototesting patients with LE. They found that in 90% of patients with subacute cutaneous LE, 40% with discoid LE and 10% with systemic LE, characteristic skin lesions were provoked. All the positive test results were induced with UVB, and half the group also reacted to UVA. Lehmann et al.[4] reported that both UVA and UVB radiation can induce reproduction of LE lesions by a provocative phototest in his patients with discoid LE, subacute LE, and systemic LE. The action spectrum of the induced lesions was within the UVB range in 33%, in the UVA range in 14%, and in both UVB and UVA range in 53% of patients.

One of our patients developed LE lesions by both UVB and UVA radiation. The other patient showed reproduction only by UVA. The development of positive phototest reactions in patients with LE was considerably slower and persisted longer than phototest reactions in other photodermatoses[11, 12]. In our cases of discoid LE, the papules developed slowly over a period of 5 days to 10 days. The lesions lasted 3 weeks after irradiation. Histopathologic findings in the irradiated sites strongly suggested LE: epidermal flattening, liquefaction degeneration of the basal cell layer and lymphohistiocytic dermal infiltration.

Because sunlight contains about 500 times more UVA than UVB, photosensitivity to UVA may be an important factor for patients with LE.

## REFERENCES

1. Epstein JH: *Polymorphous light eruptions: phototest technique studies. Arch Dermatol 85:502-504, 1962.*
2. Freeman RG, Knox JM, Owens DW: *Cutaneous lesions of lupus erythematosus induced by monochromatic light. Arch Dermatol 100;677-682, 1969.*
3. Cripps DJ, Rankin J: *Action spectra of lupus erythematosus and experimental immunofluorescence. Arch Dermatol 107:563-567, 1973.*
4. Lehmann P, Holzle E, Kind P et al.: *Experimental reproduction of skin lesions in lupus erythematosus by UVA and UVB radiation. J Am Acad Dermatol 22:181-187, 1990.*
5. Fuhs E: *Lupus erythematodes subacutus mit ausgesprochener Überempfindlichkeit gegen Quarzlicht. Z Hautkr 30:308-309, 1929. Cited from reference 4.*
6. Bear RL, Harber LC: *Photobiology of lupus erythematosus. Arch Dermatol 92:124-128, 1965.*
7. Everett MA, Olson RL: *Response of cutaneous lupus erythematosus to ultraviolet light. J Invest Dermatol 44:133-139, 1965.*
8. Stern RS, Docken W: *An exacerbation of SLE after visiting a tanning salon. JAMA 255:3120, 1986.*
9. Tronnier H, Petri H, Pierchalla P: *UV-provozierte bullöse Hautveränderungen bei systemischem Lupus erythematodes. Z Hautkr 154:617A, 1988. Cited from reference 4.*
10. Emerit I, Michelson AM: *Mechanism of photosensitivity in systemic lupus erythematosus patients. Proc Natl Acad Sci USA 78:2537-2540, 1980.*
11. Hölzle E, Plewig G, Lehmann P: *Photodermatoses-diagnostic procedures and their interpretation. Photodermatology 4:109-114, 1987.*
12. Lehmann P, Holzle E, v, Kries R et al.: *Lichtdiagnostische Verfahren bei Patienten mit Verdacht auf Photodermatosen. Zentrabl Haut 152:667-682, 1986. Cited from reference 4.*