

# The Identification and Treatment of Subclinical Sun Damage With 5-Fluorouracil Cream: A Small, Prospective, Pilot Study

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5-Fluorouracil (5-FU) cream is indicated for the treatment of actinic keratoses (AKs). It generally is applied across a broad area of skin rather than to specific AKs. It has been observed that when 5-FU is applied to the skin, not only do clinically apparent AKs become irritated, erythematous, and/or scaly, but subclinical sun damage also becomes clinically visible. In this small prospective study, 5-FU cream was applied to the faces of 19 participants (12 female, 7 male) between the ages of 35 and 55 years with no medical history of AKs or nonmelanoma skin cancers to determine if subclinical lesions could be identified and treated. The results showed that 100% (19/19) of participants in this study with no clinically apparent AKs had a positive reaction to 5-FU cream, indicating that they had subclinical sun damage that became clinically apparent. Because 5-FU cream is useful for the treatment of clinically apparent actinic lesions, it is believed that subclinical sun damage also is treated.

Clinicians use 5-fluorouracil (5-FU) cream, a fluorinated pyrimidine antimetabolite, for the topical treatment of solar or actinic keratoses (AKs). It has been noted that during treatment of AKs with 5-FU cream, subclinical sun damage often will become clinically apparent.<sup>1,2</sup> Actinically damaged cells grow and divide more rapidly and take up 5-FU at a greater rate than undamaged

healthy skin cells. Once absorbed, it is believed that 5-FU interferes with the synthesis of DNA, and to a lesser extent RNA, which thereby causes cell death that appears clinically as erythema, scaling, and/or ulceration.<sup>3,4</sup>

The purpose of this small, prospective, pilot study was to determine if participants with no clinically apparent AKs had subclinical sun damage that could be identified with the application of 5-FU cream.

## PARTICIPANTS AND METHODS

In this small, prospective, pilot study 5-FU cream was prescribed to 19 adult participants (12 female, 7 male) between the ages of 35 and 55 years. None of the participants had clinical evidence of actinic lesions on the face and had ever been treated for AKs or nonmelanoma skin cancer. Pretreatment photographs of the participants were taken when possible. Participants were asked to

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complete a short questionnaire to help determine their Fitzpatrick skin type and history of sunburns. The participants had Fitzpatrick skin types I through IV and all admitted to a history of either occasional or many sunburns (Figures 1 and 2) The advantages, disadvantages, risks, and benefits of treatment with 5-FU cream were explained to each participant.

The participants were consecutively assigned on an alternating basis to receive either 5-FU cream 0.5% (Carac cream) to be applied once daily for a 2-week period or 5-FU cream 5.0% (Efudex cream) to be applied twice daily for a 2-week period (Figure 3). Although there are various forms of topical 5-FU, for this study 5-FU cream 0.5% and 5-FU cream 5.0% were used. They were selected not as a comparison of the 2 products but because of their observed similar clinical results and hopefully to eliminate any product bias.

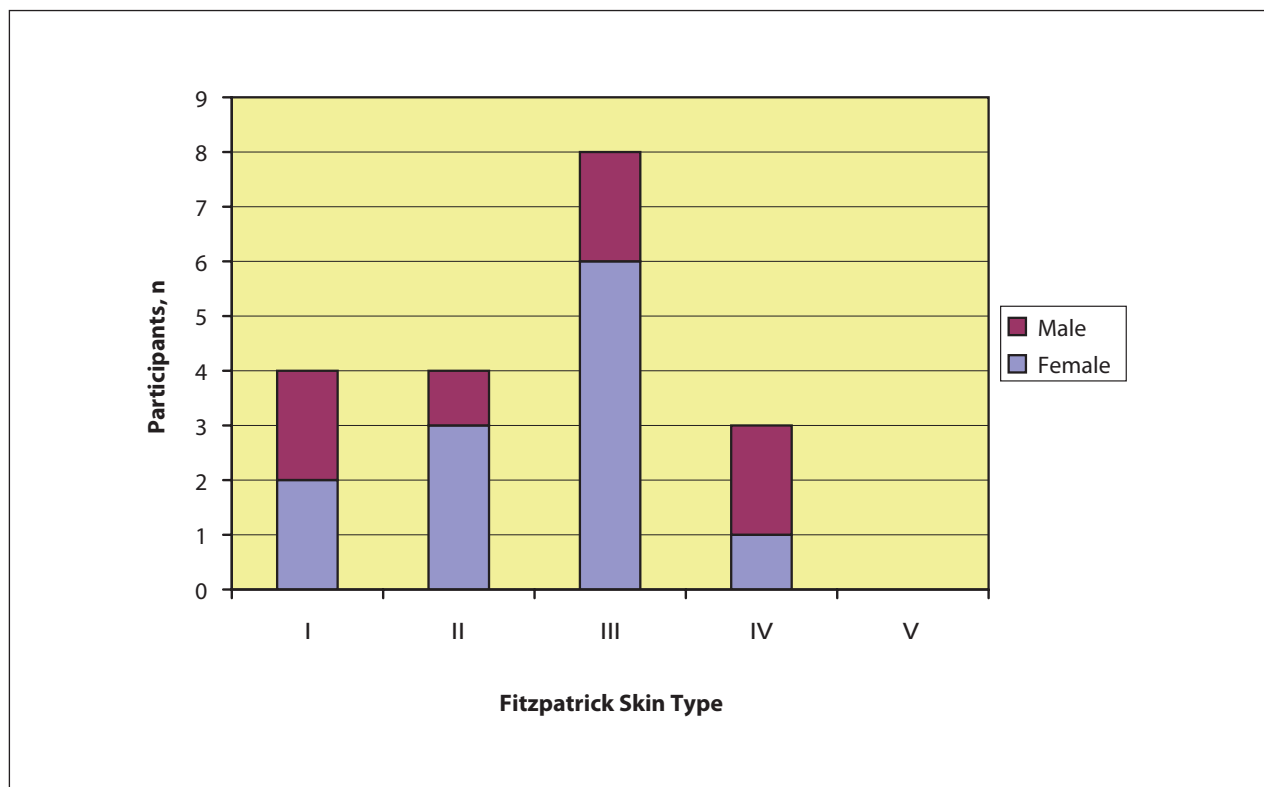
Twelve of the 19 participants (7 female, 5 male) applied the medication for 14 days. The other 7 participants applied the medication with a range of application from 7 to 21 days (Figure 4). At the follow-up visit photographs of the participants were taken and compared with pretreatment photographs when available (Figures 5–9).

## RESULTS

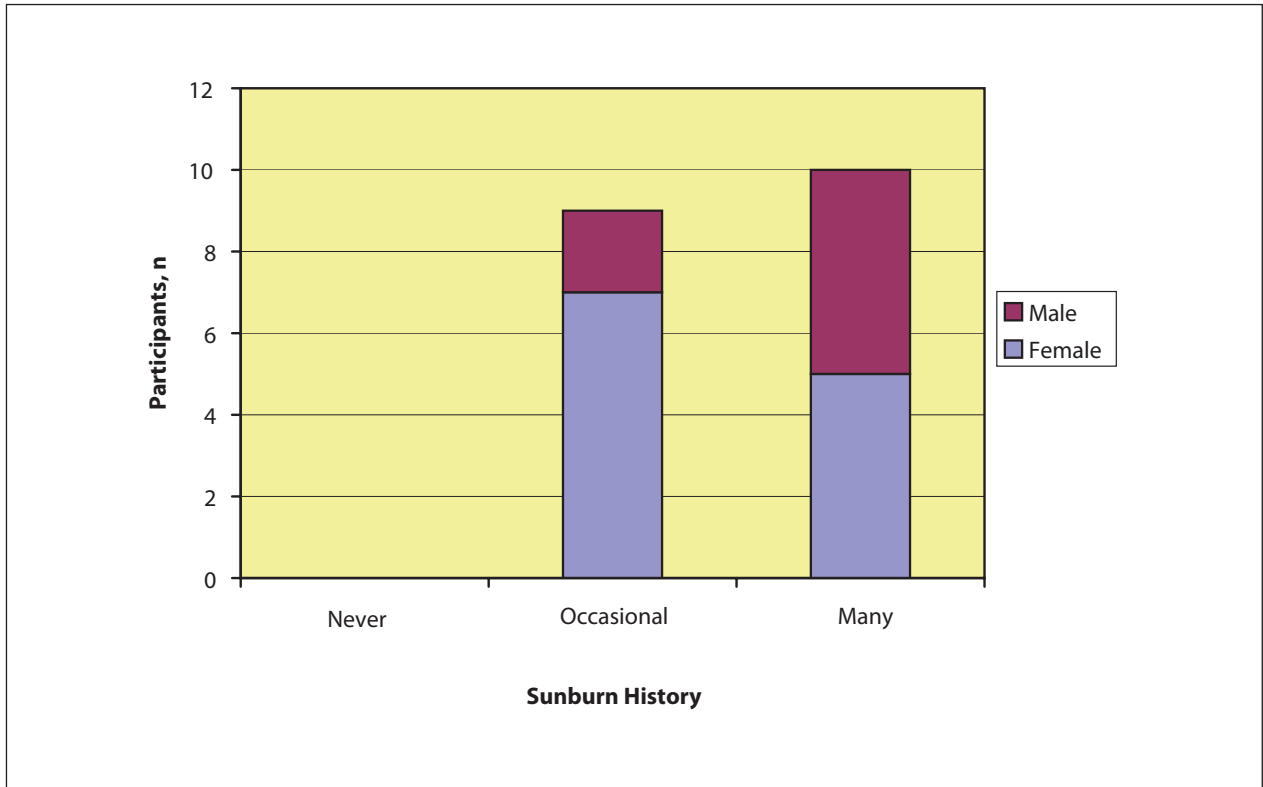
All of the 19 participants in this study that received 5-FU cream developed erythema to some degree with most participants developing erythema with associated scaling and/or crusting. In these participants the erythema and scaling effects of treatment with 5-FU cream resolved within 4 weeks. Anecdotally, it was noted that most participants were very interested and often relieved to have discovered that there was a way to identify and treat their areas of sun-damaged skin and possibly prevent future AKs and nonmelanoma skin cancer.

## COMMENT

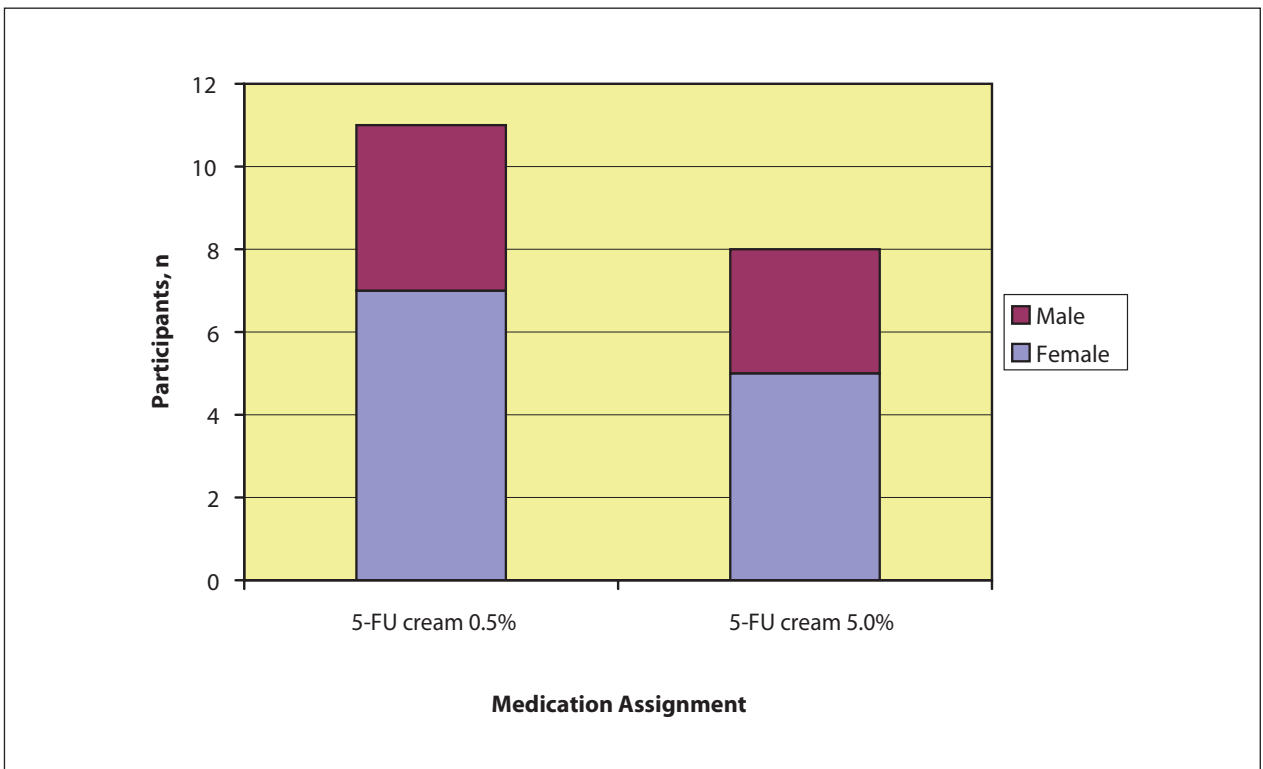
Since the 19th century, there has been an increase in leisure time with much of that time being spent outdoors.<sup>5</sup> As such, many baby boomers and young adults have had moderate to extensive unprotected sun exposure. Generally, the results of cumulative sun exposure are not clinically apparent for many decades after exposure. The first clinical signs of sun damage often are AKs and sometimes nonmelanoma skin cancers. The treatment of AKs and nonmelanoma skin cancers can cause substantial morbidity and scarring as well as costing millions of dollars annually.<sup>6</sup>



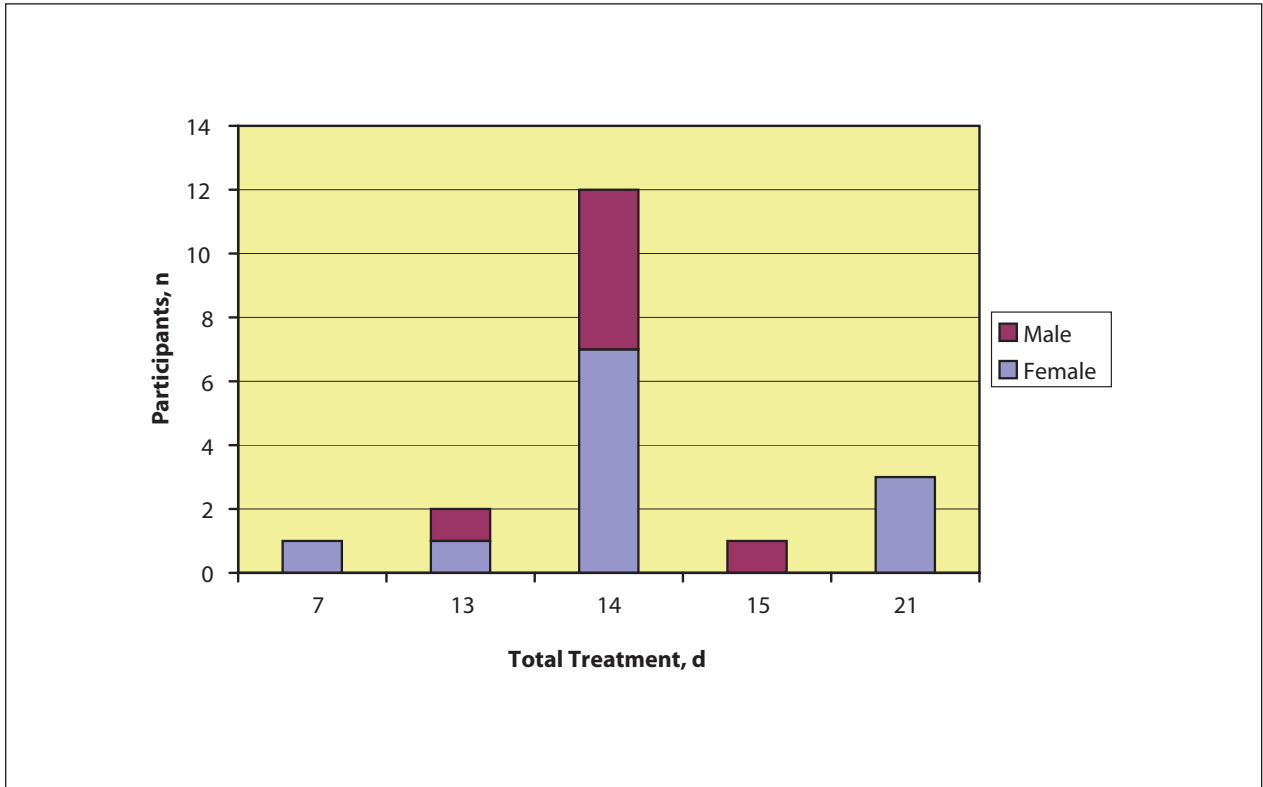
**Figure 1.** Number of male and female study participants by Fitzpatrick skin type.



**Figure 2.** Self-reported history of sunburn frequency in male and female participants.



**Figure 3.** Number of male and female participants selected on an alternating basis to receive either 5-fluorouracil (5-FU) cream 0.5% (Carac cream) or 5-FU cream 5.0% (Efudex cream).



**Figure 4.** Total number of treatment days for male and female participants with 5-fluorouracil cream.



**Figure 5.** A male participant before (A) and after (B) 14 days of treatment with 5-fluorouracil cream 5%.

In this small, prospective, pilot study participants with no history of treatment for AKs or nonmelanoma skin cancer were exposed to 5-FU cream 0.5% or 5.0% to determine whether subclinical sun damage existed and could be identified. The results showed that 100% of

participants who completed the study that were exposed to 5-FU cream had a positive reaction. This reaction suggests that subclinical sun damage was made clinically apparent with the application of 5-FU cream. Similar observations have been noted in other studies.<sup>1,2</sup> Because

## IDENTIFICATION AND TREATMENT OF AKS WITH 5-FU



**Figure 6.** A male participant before (A) and after (B) 14 days of treatment with 5-fluorouracil cream 0.5%.



**Figure 7.** A female participant before (A) and after 7 days of treatment with 5-fluorouracil cream 0.5%.



**Figure 8.** A female participant before (A) and after (B) 14 days of treatment with 5-fluorouracil cream 5.0%.



**Figure 9.** A male participant before (A) and after (B) 14 days of treatment with 5-fluorouracil cream 0.5%.

the application of 5-FU not only identifies AKs but also destroys them, subclinical sun damage also was likely eradicated with topical 5-FU cream.

This prospective pilot study suggests that participants with admitted moderate to extensive sun exposure who have not yet developed clinically apparent AKs could be treated with topical 5-FU cream to prevent the progression of subclinical sun damage into AKs or eventually nonmelanoma skin cancers. Additional studies, including clinical trials, would be of use to confirm these results and the potential improvement in the prevention of AKs and nonmelanoma skin cancers with 5-FU cream.

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