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## **Supportive Oncodermatology Updates: Expert Opinions on Basic Management**

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## Introduction

Advancements in cancer therapy over the last few decades have been nothing short of miraculous and countless patients have added years or even decades to their lives as a result. However, it seems that with every new addition to the armament, new adverse events emerge that range in location, severity, and duration and pose barriers to continuing cancer therapies. The skin, mucosa, hair, and nails are among the most common sites cancer patients experience adverse events and collectively are known as cutaneous adverse events (cAEs). While often underappreciated, the impact cAEs have on cancer patients' quality of life cannot be understated.<sup>1,2,3,4</sup> As a result, dermatologists have become a crucial component of many cancer patients care team, so much so that a subspecialty has arisen, termed supportive oncdermatology.

Supportive oncdermatology would not exist in its current form without the efforts of Dr. Mario Lacouture, Professor of Dermatology at Weill Cornell Medical College and Director of the Oncdermatology Program at Memorial Sloan Kettering Cancer Center. Dr. Lacouture joined Dr. Adam Friedman, Professor and Chair of Dermatology, and Director of the Supportive Oncdermatology Program at the George Washington University School of Medicine and Health Sciences, in a JDD Ask the Investigator podcast titled *Saving Skin, Hair, & Nails with Supportive Oncdermatology: A Call to Action for All Those Involved* available online through the Journal of Drugs in Dermatology. Dr. Lacouture emphasized that 50% of men and 33% of women will experience a cancer diagnosis during their lifetime, and the majority will survive indicating a need to focus on quality of life during and after such diagnoses. Dr. Lacouture also highlighted that 50% of cancer patients receive radiation therapy, which is the topic of the next podcast in the series.<sup>5,6,7,8</sup> In the second podcast, titled *Heal the Burn: Radical Updates for the Management of Radiation Dermatitis*, Dr. Friedman was joined by Dr. Beth McLellan, Associate Professor and Chief of Dermatology at Albert Einstein College of Medicine and Director of Supportive Oncdermatology at Montefiore-Einstein Center for Cancer Care. Drs. Lacouture, McLellan, and Friedman reviewed the fundamentals of supportive oncdermatology and each gave expert insight on this rapidly evolving field. These podcasts were in conjunction with the September 2021 JDD supplement, *US Cutaneous Oncdermatology Management (USCOM): A Practical Algorithm*, of which Drs. Lacouture and McLellan were authors.<sup>1</sup>

## The Algorithm

The USCOM project was initiated by La Roche-Posay to improve cancer patients' and survivors' quality of life by offering tools for prevention and management of cAEs. Dr. Lacouture explained the algorithm was developed following a thorough literature review and extensive discussions among authors to obtain consensus. The eight consensus statements are listed in Table 1. Specifically, the authors sought to define the essential factors that dictate proper skincare at the onset of systemic cancer therapies that should be maintained to prevent potential cAEs. While moisturizing may seem fundamental to dermatologists, many cancer patients, oncologists, radiation oncologists, and oncology nurses are rightly laser focused on treating malignancies and saving lives, so having dermatologists provide basic recommendations can make a significant impact on the cAEs patients and survivors experience.<sup>1</sup>

The algorithm focuses on prevention and treatment of cAEs using simple skincare regimens, including cleansers, moisturizers, and photoprotection to improve patient outcomes and QoL. In addition, the authors sought to determine a consensus approach regarding cAEs for stakeholders in the US.<sup>1</sup> Drs. Lacouture and McLellan both emphasized studies revealing that cAEs were among the most unexpected, yet the most impactful on patients' quality of life during and after treatment. The most common cAEs mentioned were xerosis, pruritus, and skin irritation. Most importantly, dermatologic consultations in cancer patients led to more positive outcomes and reductions in interruption of cancer therapy.<sup>3,6</sup>

Table 1. Consensus Statements from the *USCOM: A Practical Algorithm*<sup>1</sup>

Statement 1	Dermatologic toxicities associated with cancer treatment are common.
Statement 2	Acute and chronic skin reactions can significantly impact quality of life.
Statement 3	Disabling skin reactions are a significant problem for many patients and their treating physicians.
Statement 4	When acute cutaneous reactions develop, effective skincare should be reinforced to reduce further complications and assist in managing toxicities.
Statement 5	Supportive care and appropriate skincare continue to be mainstays of prevention and treatment for acute and chronic dermatologic toxicities.
Statement 6	Early education and skincare use may have benefits for quality of life and prevention of severe skin sequelae for cancer patients and survivors.
Statement 7	Education and proper skincare may help optimize skin health and quality of life in patients undergoing active cancer treatment and cancer survivors.
Statement 8	Skin cleansing, skin hydration, and photoprotection should be considered in cancer patients and survivors to prevent and manage cutaneous side effects before, during, and after cancer therapy.

## Prophylaxis

Drs. Lacouture, McLellan, and Friedman emphasized the importance of prophylactic measures prior to systemic cancer therapies because cAEs like xerosis, pruritus, alopecia, nail toxicities and radiation dermatitis are frequently expected regardless of the more unique eruptions experienced with some targeted therapies. Most importantly, preventable cAEs can lead to dose reductions or even discontinuation of cancer therapies, ultimately affecting clinical outcomes.<sup>3,4,9,10</sup> Dr. Lacouture previously compared responses to proactive and reactive treatment for eruptions secondary to epidermal growth factor inhibitors (EGFRI) with doxycycline 100 mg twice daily, hydrocortisone 1% cream, sunscreen and moisturizer use, and found that both approaches were efficacious, but argued that prevention is the best medicine in supportive oncdermatology for the QoL of patients (Figure 1).<sup>11</sup> Dr. Lacouture also referenced a 2020 study showing that prophylactic therapy for cAEs seen with EGFRI reduces treatment interruptions and may even prolong survival rates although more research is needed.<sup>12</sup>

Figure 1. Papulopustular eruption from EGFRI.



Simple approaches like mild soaps and daily moisturizers are commonly only employed once cAEs are encountered; in fact, Drs. Lacouture and McLellan noted up to 84% of cAEs are never referred to a dermatologist; among patients that consult dermatologists, most are seen after the onset of expected cAEs, rather than prophylactically. Reasons for this include the time delay to see a dermatologist, associated costs, and the lack of knowledge of dermatology as a resource.<sup>13,14</sup> Dr. Lacouture indicated that prior to head and neck radiation or stem cell transplants, patients generally receive a dental evaluation due to the high occurrence of oral adverse events and that such practices are warranted for dermatology as well. The USCOM algorithm importantly suggests measures to take before, during, and after cancer treatments, as well as gradation based assessments for determining the type, severity, and treatment of cAEs.<sup>1</sup>

## Skincare

Sauder et al. (2020) found that an altered skin barrier while on cancer therapies can contribute to xerosis, pruritus, radiation dermatitis, fissures, and hand foot mouth syndrome (Figure 2).<sup>3</sup> Therefore, the algorithm focused on cAEs that can benefit from proper skincare. Drs. Lacouture and McLellan emphasized the necessity of maintaining a proper skin barrier with moisturizers in cancer patients and survivors. Immunosuppression with cytotoxic and targeted therapies combined with defective barrier results in an increased risk of skin infections.<sup>15</sup>

Figure 2. Xerosis secondary to cancer treatments.



Dr. Lacouture noted that cancer patients and survivors commonly have atrophic like skin that also increases the chances of infection, contact dermatitis, and the sensitization to allergens. Moisturizers can benefit these patients by forming a barrier that retains water by preventing transepidermal water loss from the stratum corneum and reduces unwanted pathogens from entering through potential defects.<sup>1</sup>

Dr. Lacouture noted the lack of literature evaluating the tolerability and efficacy of skincare products among cancer patients and survivors. Consequently, the inclusion of studies assessing safety and tolerability of over the counter (OTC) products in this population was integral to the development of the algorithm. Most available studies looked at radiation dermatitis with Rosenthal et al. (2019) finding that formulations of aloe vera, chamomile, ascorbic acid, pantothenol, niacinamide, squalene, glycerin, shea butter, allantoin, dexpanthenol, and trolamine did not show a benefit whereas formulations of hyaluronic acid, epidermal growth factor, granulocyte-macrophage colony stimulating factor, and topical corticosteroids did show some benefit.<sup>16</sup> Similarly, a 2018 study examined 253 breast cancer patients undergoing radiation to evaluate the efficacy and tolerability of a thermal water containing skincare regimen including five commercially available agents: a cleanser, moisturizer, wound healing cream, sunscreen, and thermal water spray. The authors sought to assess effect on cAEs including edema, erythema, xerosis, and desquamation before and after radiation therapy. During a six-week period of radiation, those who used the regimen more frequently, for example on a daily basis, experienced fewer cAEs than those who applied the skincare products less frequently; this effect was particularly evident within 10 days of radiation. Additionally, over 92% of patients reported good to excellent tolerance on the affected radiated skin for each formulation supporting their use in cancer patients and survivors.<sup>17</sup>

The USCOM suggestions include liberally moisturizing the entire body frequently with a vehicle selected based on skin condition, xerosis, and patient preference. Cleansers and moisturizers should have a near physiologic pH of 4.0-6.0 as alkaline skincare products may worsen the skin barrier by impacting stratum corneum formation and desquamation. The algorithm explains that patients can safely use skincare products directly before and after radiation treatments without decreasing efficacy of treatment, which can increase adherence and reduce confusion among patients.<sup>18</sup> Patients undergoing cancer therapy are also at an increased risk of developing photosensitivity, therefore photoprotection is recommended prior to, during, and after treatments, including sun avoidance, protective clothing, and SPF 30+ sunscreens.<sup>1</sup>

Dr. Lacouture suspects many products and therapies are not being used in cancer patients due to the unknown effect on outcomes of cancer therapy, evidenced by Dr. Friedman's study that helped dispel the link of spironolactone use and breast cancer recurrence.<sup>19</sup> Dr. Lacouture found that some OTC skin barrier agents have shown to be beneficial and tolerable in cancer patients in prospective studies.<sup>16,17,20,21</sup> The USCOM algorithm argues that products utilized in this patient population should be devoid of allergens or irritants and have minimal to no fragrance; this is analogous to recommendations for patients with atopic dermatitis, however those patients are generally adept at moisturizing whereas many cancer patients are not and require education and instruction. Soaps, surfactants,

and detergents with an alkaline pH are more likely to impact the formation of stratum corneum lipids and reduce the diversity of the skin microbiome, both of which can be detrimental in cancer patients and survivors.<sup>22,23</sup> When cAEs do occur, effective skincare regimens generally can prevent further exacerbation and/or deterioration aiding in patient comfort and QoL.<sup>3,17,21,24,25</sup>

### Communication and Collaboration

Drs. Lacouture and McLellan stressed the need of communication and collaboration among patients, oncologists, radiation oncologists, oncology nurses and dermatologists during treatment. Dr. McLellan highlighted cancer patients' difficulty accessing dermatologists and argues for keeping appointments available to minimize delays in care as treatment decisions cannot wait weeks in many cases. Cancer patients likely underreport cAEs due to lack of perceived severity, desire not to bother, or risk of interrupting therapy. Patients may assume cAEs are due to an allergy, stress, or diet and may not know who and how to reach in case of questions.<sup>3,22</sup> USCOM provides a glossary of various photos of cAEs and how to manage them for non-dermatologists who are interested in treating these patients.<sup>1</sup> Dr. McLellan also indicated that collaboration between treatment teams will increase reciprocal understanding of each other's treatment style and language. Drs. Lacouture and McLellan noted that oncologists and radiation oncologists commonly want to reduce dosages or discontinue treatments in patients due to perceived severity of cAEs, and a dermatologic consultation can put the oncologic staff at ease and allow patients to resume necessary therapy.

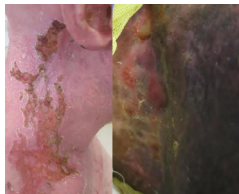
The USCOM offers measures to increase education among cancer patients. These include: proactive contact, frequent communication to build trust, detailed discussions, giving urgent contact information, reinforce prevention and early treatment, explain the rationale behind skincare products, demonstrate application, and provide educational handouts or web sites to access at home.<sup>1</sup> Sauder et al. (2020) underscored the need for frequent communication as well as checking to see if patients have processed and understood the information provided.<sup>3</sup>

Dr. Lacouture works closely with Dr. Anthony Rossi, a procedural dermatologist at Memorial Sloan Kettering Cancer Center, who pioneered the field of restorative oncodermatology, which aims to address sequelae that develop in cancer patients on therapy for more than twelve months as well as cancer survivors. Patients with metastatic disease are now living many years, left with persistent alopecia, scars, dyschromia, and telangiectasias, which are all amenable to topical, oral, or procedural agents. Lasers, scar revisions, hyaluronic acid fillers, and other agents commonly used in cosmetic dermatology are now utilized for cancer patients and survivors.<sup>26</sup> Dr. Lacouture is currently exploring if platelet rich plasma can benefit patients with persistent alopecia, but he emphasized that supportive oncodermatology and restorative oncodermatology should go hand in hand.

### Radiation Dermatitis

Among the cAEs cancer patients encounter, radiation dermatitis is quite common affecting approximately 90% of patients whom receive radiation, most commonly in head and neck, breast, and anogenital cancers.<sup>1,4</sup> Dr. McLellan noted that in spite of and sometimes because of advancements in technology, radiation dermatitis can cause pain, secondary infection, hyperpigmentation, fibrosis, interrupt treatments, and ultimately reduce patients QoL. In fact, new advances such as proton therapy, which precisely targets tumors, can still cause significant skin toxicity.<sup>27</sup> Radiation induces non-specific DNA damage in the treatment area and cutaneous effects vary based on location, dose, and radiation schedule. Acute radiation dermatitis may occur during or shortly after treatments and present with desquamation, erythema, and pruritus or even thin atrophic plaques that easily ulcerate and bleed with minimal trauma and last for days to weeks (Figure 3). Conversely, chronic radiation dermatitis can present with poikilodermatous changes, necrosis, fibrosis, radiation induced morphea and can ultimately

Figure 3. Acute radiation dermatitis.



persist for months to years after treatment. Additionally, following radiation patients have an increased risk of skin cancer, usually basal cell carcinomas, meaning annual skin exams are essential in this population.<sup>16,28</sup>

Radiation dermatitis exhibits significant variability in timing and peak of symptoms, which makes assessing patients difficult due to the issues with access previously discussed. Dr. McLellan noted that many radiation oncologists feel that they caused the radiation dermatitis so they should manage treatment, so much so that she previously found only 15% of radiation dermatitis patients were referred to dermatologists.<sup>13</sup> Dr. McLellan pointed out that radiation dermatitis is commonly perceived to be temporary by patients who may endure tremendous pain among other symptoms that negatively impact their QoL prior to seeking care. Dr. McLellan stressed the need to have a dermatologist on the multidisciplinary team available to accurately diagnosis and treat cAEs allowing for the continuation of cancer therapy that may have otherwise been discontinued.<sup>10,24,29</sup> She also emphasized the importance of performing appropriate bacterial and viral cultures to rule out secondary infections. When active and severe, Dr. McLellan suggests first ruling out infection and contact dermatitis, then treating with topical or systemic agents, pain control, cool compresses, and wound dressings as needed.

Dr. McLellan commonly utilizes topical steroids, topical antibacterial agents, and bland emollients in her radiation dermatitis patients, although she notes limited clinical studies support these or any OTC agents. Ideally, radiation dermatitis would be prevented in every case, but there are limited studies that explore prevention. Some evidence shows mometasone can prevent radiation dermatitis, although due to common institutional based routines, implementing this broadly may be an uphill battle.<sup>30</sup>

Dr. McLellan indicated that dermatologists are not commonly included in initial discussions regarding radiation therapy unless patients or their family reach out. When this does happen, recommendations include maintaining the barrier with moisturizers and remaining vigilant in the search for skin breakage or infection. Dr. Friedman prefers the combination of calcipotriene and a class I topical corticosteroid beginning five to seven days prior to radiation and cycling two weeks on and one week off depending on the formulation. Further research is needed to elucidate which agents are best in the case of both preventing and or treating acute and chronic radiation dermatitis.

## Conclusion

The spectrum of cAEs from cancer treatments has a profound impact on treatment decisions and the overall well-being of cancer patients and survivors. With the continued development of advanced oncologic therapies, the accurate diagnosis and management of associated cAEs is critical to achieving optimal patient outcomes. Drs. Lacouture and McLellan emphasized the need to maintain a proper skin barrier in cancer patients and survivors with OTC skincare products. It is uniformly agreed upon that barriers in communication and collaboration currently prevent optimal care, barriers that need to be rectified to increase dermatologic access to these patients ultimately preventing avoidable treatment interruptions. As oncologists, radiation oncologists, and oncology nurses become more comfortable including dermatologists in the multidisciplinary care team, dermatologists can demonstrate how truly valuable of a resource they can be to reduce treatments pauses and ultimately improve the QoL of cancer patients and survivors.

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