Impetigo: What is Very New?
Lawrence A. Schachner, MD

Impetigo is the leading bacterial skin infection in children, with the most common etiology being *Staphylococcus aureus.* Seventy percent of cases of impetigo are the non-bullous form, while 30% of patients present with bullae or ruptured bullae with a very characteristic collarette of scale. It is also important to recognize the high incidence of secondary impetiginization of chronic skin disease in children. Fortunately, rates of MRSA have recently decreased in both children and adults.

Despite the high incidence, there has not been a change in therapeutic recommendations for impetigo in over 10 years – until very recently. Traditional first-line treatment for localized disease includes topical mupirocin, retapamulin, and fusidic acid (Europe). Systemic treatment options include flucloxacillin, cloxacillin, dicloxacillin, cephalexin, and erythromycin. Pearls about these oral antibiotics include the "bad taste" of dicloxacillin, the very high rates of resistance to erythromycin, and that cephalexin tends to be the most effective and least expensive oral antibiotic. Notably, while many cases of *S. aureus* show in vitro resistance to cephalexin, this may not equate to in vivo resistance, as many "resistant" cases successfully clear with cephalexin therapy.

Many recent studies have shown increased resistance to mupirocin, retapamulin, and fusidic acid. Fortunately, for the first time in 11 years, a new topical antibiotic has been released: ozenoxacin 1% cream. Ozenoxacin is a non-fluorinated antibiotic that blocks DNA gyrase and topoisomerase IV. After 15 studies – including 2 pivotal phase III studies – the cream has been approved for first-line treatment of impetigo caused by *S. aureus*, *S. pyogenes*, and MRSA in children aged 2 months and older. The topical has demonstrated superior clinical and microbiological success, and has been shown to be well-tolerated, very safe, and is non-ototoxic.

In closing, Dr. Schachner encourages all practitioners to practice good antibiotic stewardship. Regularly spot-check impetiginized skin with Gram stain, culture, and sensitivity in order to become familiar with local antibiotic resistance patterns. Further, Dr. Schachner encourages rotating antibiotic creams on a monthly basis to decrease resistance. While impetigo typically has an excellent prognosis, Dr. Schachner emphasized "If you don't look for it, you won't find it. And this may cause you to choose the wrong treatment."

Diagnosis and Prognosis of Malignant Melanoma
Clay Cockerell, MD

Molecular diagnostics is becoming more prevalent and important in dermatology and dermatopathology. Medicine is becoming truly personalized, aiding us in areas such as infectious disease, genetic disease, cancer testing, and predicting drug responsiveness. This is especially important in cutaneous oncology, where companion diagnostics are able to determine if a patient is a candidate for a drug by sequencing cancers to search for target gene

mutations – similar to culture and sensitivity in infectious disease. This is the future of cancer – less surgery and more targeted medical treatment.

The histology of melanocytic neoplasia is not always straightforward. FISH, CGH, and array-based CGH have aided us in detecting genetic fusions, deletions, and aneuploidy associated with malignancy. The newest diagnostic aids are gene expression profiles that can detect specific genetic features, such as *BRAF* mutations. These profiles have become standard in the diagnosis and prognosis of uveal melanoma and are proving to be important in the characterization of Spitz nevi, blue nevi, and, most importantly, melanoma.

Traditionally, the prognosis of melanoma has been based on the AJCC criteria and results from sentinel lymph node biopsy (SLNB). These new gene expression profiles (GEP) have been shown to stratify risk even better than these other prognostic tools. One study showed that SLNB only detects 30% of patients who will die from melanoma, while the GEP can detect over 80% of high-risk melanomas based on both genetic and cellular features of the tumor. Both prospective and retrospective studies have confirmed this data. While Dr. Cockerell still suggests caution in relying solely on these new and exciting techniques, gene expression profiling is predicted to be the next horizon in characterizing difficult-to-diagnose and prognose cases of melanoma.

SRT Reduces Keloid Recurrences Post- Keloidectomy
Dr. Brian Berman, MD, PhD

The clinical problem addressed in this lecture is the recurrence of keloids after excision. Recurrences happen about 71.2 % of the time. In a retrospective study done by Dr. Berman the recurrence rate was 52.6 %. After post-op TAC injection the recurrences rate one year later was still 50%.

X-ray wavelength breaks the RNA and DNA molecule cross-links and makes high energy water components, leading to single stranded and double stranded breaks in the RNA and DNA. The implication of this is that x-ray radiation causes delays in wound healing by increasing apoptosis and inactivating cell proliferation. This can be used to decrease excessive wound healing in patients with keloids.

A retrospective chart review of keloidectomy + BED 30 SRT of 96 excised keloids + SRT (61 patients) with 1 year follow-up in 4 different US sites was conducted. Patients received BED 30 superficial radiation 70 or 100 kV starting on post-op day 1 at the suture closure line. Followed by three 6 Gy fractions on POD 1, 2 and 3. Results showed that 10/96 (10.4%) of the treated keloids recurred within 12 months and 11/96 by 18 months. Kaplan-Meier Survival Probability Estimate cure rate of 85.6 % from 24 months post- SRT treatment end onward.

In a study done of Surgical Keloid Excision With/Without External Beam Radiation vs Brachytherapy it was observed that EBRT was slightly more successful than brachytherapy in

preventing keloid recurrence. Results showed 19% recurrence rate post-excision + EBRT and 23% recurrence post excision + brachytherapy.

Census Guidelines on the Use of Superficial Radiation Therapy for Treating Nonmelanoma Skin Cancers and Keloids shows that post-surgical treatment of keloid excision suture lines with several fractions of SRT significantly reduces keloid recurrence rates. Furthermore, fractionation of the SRT dose reduces the risk of hyperpigmentation and other adverse events. The optional treatment protocol is a biologically effective dose of 3000 cGy in three fractions of 600 cGy on post-operative days 1, 2 and 3. There is little evidence that exposing keloids or surrounding healthy skin to SRT at a 3000 cGy dosing cases skin cancer.

Treatment of Tumors of the Lower Extremities
William I. Roth, MD

Dr. Roth is highly experienced with treating tumors on the lower extremities. Has had 100s of patient cases with great results. This presentation focuses on several examples of more difficult cases such as a case of SCC on the dorsum of the foot which was treated with 14 Fx x 3 months. Patient tolerated treatment very well. Patients with difficult lesions get treated with as little as one Fx per week. An example of this was a patient with a SCC moderately differentiated on the toe that was treated with 1 fx / wk 14 fx 50kv 385.5 cGy/Fx. Toes and finger can be difficult to treat due to the proximity of the bone to the skin.

In a recent publication of a 100 patients treated for lower extremity tumors, there was a 97.3 % cure rate. Most patients did very well with 90% having erythema, scaling and crusting, and 15 patients having ulcerations requiring further care.

Radiogenic ulceration start about 8 weeks after treatment and are associated with connective tissue changes and effects on blood vessels. It may also be associated with co-factors: sun, trauma, bits, infections, allergic reactions, dermatitis, edema. 90% recover with conventional wound care.

For better results when treating lower extremities, comorbidities such as edema, and dermatitis need to be managed. Furthermore lack of circulation may cause treatment failures. Pulse ox test on finger and toe is done in order to determine patients' success rate. For pain management it is best to take more breaks in treatment.

Overall, SRT allows us to treat patients who would otherwise be extremely difficult.

Neonatal Rashes
Lawrence Eichenfield, MD

In neonatal life there is a transition from liquid to air environment. Premature infants, who are essentially immunosuppressed, are especially subject to developing various dermatologic conditions.

Opportunistic Fungal Infections

Neonates of low gestational age/premature are at risk for developing opportunistic fungal infections including but not limited to cutaneous Aspergillosis, Rhizopus, Mucormycosis, Fusarium etc. The fungal organism enters the skin of an immunosuppressed host via breaks in the skin barrier, resulting in localized infection. Individuals are at risk for systemic infection if therapy is not initiated early on. Opportunistic fungal infections most commonly present as ecchymoses with hemorrhagic crusts and erosions. There should be a low threshold to biopsy suspected lesions to confirm diagnosis. Risk factors to neonates for contracting opportunistic fungal infections include exposure to tape (creates breaks in skin when removed and tape itself can be inoculated with fungal organisms), exposure to construction occurring at the hospital, glues/adhesives applied to skin, systemic corticosteroids, broad spectrum antibiotics, and hematologic disease. Neonates with opportunistic fungal infections should be treated with systemic antifungals and gentle debridement.

In contrast to opportunistic fungal infections like Aspergillosis, neonatal HSV presents as vesicles arranged in a cluster of grapes and erosions on an erythematous base. There should be a low threshold for consideration and diagnosis should be aided by HSV PCR.

Systemic Candidiasis

Premature neonates are often colonized by candida. Systemic candidiasis classically presents as periumbilical crusting with superficial cracking. Debridement of a plaque often accentuates cracking and demonstrates superficial red plaques.

Anetoderma of Prematurity

Neonates can easily lose elastic tissue resulting in anetoderma. Anetoderma of prematurity can be associated with removing cardiac leads or adhesives. Presentation includes brown discolored atrophic plaque(s) with tissue paper skin quality, which can sometimes be oriented in accordance to lead placement.

Langerhans Cell Histiocytosis

LCH can have a myriad of presentations. A common presentation is characterized by hemorrhagic blisters. Other presentations include erythema and crusting (often initial), non-healing ulcerations in the inguinal region, petechiae, hemorrhagic papules, and mastocytosis-appearing lesions with associated hemorrhagic crusting. Morphology of lesions or extent of cutaneous involvement does not correlate with presence of extracutaneous disease. Work-up of these patients should include obtaining a biopsy to confirm diagnosis and referral to hematology/oncology. Tzanck smear can show cells with comma shaped nuclei.

Epidermolysis Bullosa (EB)

Most recently there has been a revolution in therapy for EB. A study was performed on a child with generalized junctional EB with homozygous splice mutation of LAMB3, which encodes laminin 332, who presented with extensive denuded skin. Gene transfer therapy was performed by taking a 4 cm biopsy, culturing keratinocytes and transfecting with virally corrected cells. The corrected keratinocytes were then grown as sheets of tissue and surgically attached to denuded areas of skin of the affected patient. Incredible healing was noted as the corrective skin for the LAMB3 mutation grew at a rapid rate. This transduced stem cell therapy could potentially be utilized for other genodermatoses such as mosaic diseases.

The Importance of Histopathology in Cutaneous Radiotherapy
Clay J. Cockerell, MD

Dr. Cockerell began his presentation by showing examples of clinical photographs and histology stains seemingly suggestive of an obvious diagnosis. In each case, he stressed his take home message that an inadequate biopsy often leads to an incorrect diagnosis and ultimately improper treatment. Specifically, cases involving Metatypical Basal Cell Carcinoma, BCC/SCC variants, combined BCC and SCC lesions, SCC in-situ, Primary Cutaneous Carcinosarcoma, Trichilemmal Verruca, Inverted Follicular Keratosis, and Cellular Dermatofibroma with Follicular Induction were discussed. Dr. Cockerell highlighted the appropriate approach to treatment of these lesions- suggesting when SRT is and is not appropriate.

There can be inadequacy in a pre-SRT diagnosis. Routine biopsies may give a diagnosis but may not be truly representative of the behavior of the lesion. Often other techniques are needed. Use of confocal microscopy can aid in delineation of margin. Ultrasound is becoming a newer modality in dermatology to help evaluate depth and volume of neoplasm. If SRT is determined to be the treatment of choice, radiotherapist can be certain that treatment is effective by ensuring to encompass lateral extent of the lesion and to ensure depth of lesion is addressed. Despite the frequent use of SRT among dermatologist, there are challenges. Reimbursement pressures and “turf” wars are often an unfortunate downside for dermatologist who use SRT.

Frequently, radiation oncologists and occasionally Mohs surgeons disparage dermatologist from its use. There is reported inappropriate use of SRT by some providers likely due to poor training and supervision. Despite these challenges, SRT remains an excellent option for treatment of many different conditions. However an accurate and completed diagnosis is essential. If you performed SRT, established a relationship with a dermatopathology lab that understands SRT and will be able to be involved in treatment planning.