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Therapeutic
Year In
Review

■ Therapeutic advances in rosacea, onychomycosis, psoriasis, other conditions, introduced in 2014

by LOUISE GAGNON,
Correspondent, The Chronicle

Breakthroughs in small studies suggesting possible therapies for alopecia, understanding the connection between diet and acne, reports of success with biologic treatment for severe conditions like toxic epidermal necrolysis (TEN), and progress in the treatment of advanced melanoma represent some of the highlights in dermatology in 2014, according to leading Canadian dermatologists.

“The trend in treating [non-resectable] melanoma is to try to combine therapies,” says Dr. Jennifer Beecker, assistant professor, University of Ottawa, Division of Dermatology, the Ottawa Hospital. “Researchers are focusing on getting a more durable response.”

Nivolumab and pembrolizumab are some of the agents being added to the melanoma armamentarium, says Dr. Beecker, although not approved in Canada yet.

Not only are Janus kinase inhibitors like tofacitinib being used to treat psoriatic arthritis and psoriasis, but the treatment may also represent therapy for patients with alopecia in the future, says Dr. Marlene Tan

Dytoc, a dermatologist in Edmonton and associate clinical professor of medicine in the Division of Dermatology and Cutaneous Sciences of at the University of Alberta in Edmonton.

“Bigger controlled studies need to be done to situate it [tofacitinib] in the therapeutic ladder [to treat alopecia],” says Dr. Dytoc.

A case report of one patient found that patient experienced hair regrowth with tofacitinib, notes Dr. Dytoc (*J Invest Dermatol* 2014 Jun 18).

New approach to alopecia

Still another therapy that is being studied to treat alopecia, particularly androgenetic alopecia, is platelet-rich plasma (PRP) injected in the scalp (*Br J Dermatol* 2013; 169(3):690-694). “It’s another way to stimulate regrowth [of hair],” says Dr. Dytoc.

Results of a small study published this year found a significant decrease in hair loss observed between the first and fourth PRP injections (*J Cutan Aesth Surg* 2014 Apr; 7(2):107-111). A Vancouver-based study is being planned to look at the safety and effectiveness of PRP

in androgenetic alopecia in a double-blind, randomized controlled trial.

Clinicians agree that there is raised awareness about curbing the use of antibiotics, both topical and oral, in medicine. U.S. president Barack Obama issued an executive order in Sept. 2014, aimed at combating antibiotic-resistant bacteria. The strategy called for the creation of a task force for combating antibiotic resistance, amongst other initiatives.

“There is a big shift going on with the use of antibiotics,” says Dr. Sandy Skotnicki, assistant professor, University of Toronto and medical director at Bay Dermatology Centre in Toronto. “It’s not acceptable to prescribe antibiotic monotherapy for an extended period such as six months.”

Dr. Skotnicki notes that methicillin-resistant *Staph aureus* is not prevalent in Europe, and postulated that its decreased prevalence there could be attributed to the use of pantothenol rather than polymyxin B, bacitracin, and lidocaine therapies.

The availability of brimonidine in 2014 for rosacea patients has been of



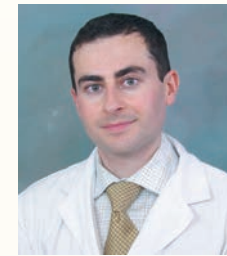
Dr. Jennifer Beecker



Dr. Sandy Skotnicki



Dr. Marlene Tan Dytoc



Dr. Benjamin Barankin

Breakthroughs in therapy in 2014 include brimonidine

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great benefit, notes Toronto dermatologist Dr. Benjamin Barankin, co-founder of the Toronto Dermatology Centre.

"It's a terrific product," says Dr. Barankin. "It is the first-ever, true anti-redness, vasoconstrictive agent. In terms of the effect, it kicks in quickly, and it lasts the whole day. Patients occasionally experience some mild irritation, but it's generally well-tolerated."

New understandings of allergies

Awareness about consumer and industrial products as a source of allergy is on the radar for dermatologists. Benzophenones, ultraviolet light absorbers found in sunscreens, hair sprays, hair dyes, perfumes, shampoos, nail polish, as well as paints and varnishes, were named the 2014 Contact Allergen of the Year.

"They [benzophenones] are found in many products," says Dr. Barankin. "It is important to bring that fact to our attention."

Genital warts can be challenging to manage, and a new topical therapy introduced in 2014, sinecatechins 10% ointment has been a useful addition to clinical treatment choices, notes Dr. Barankin.

"We are lacking in options for genital warts," says Dr. Barankin. "The clearance rate is about 50 per cent, more effective in women than in men, and it's generally well-tolerated."

A practical tip for dermatologists who perform Mohs surgery is that they do not need to use surgical/sterile gloves to avoid the risk of infection, according to Dr. Beecker.

A study published earlier this year found no difference in the prevalence of surgical site infection with the use of sterile and non-sterile gloves for resection and reconstruction during

Mohs surgery (*Derm Surg* 2014 Mar; 40(3):240).

"It's significant because there is a big cost savings to the public health-care system [in using non-surgical gloves], and we are not putting our patients at risk or doing harm," says Dr. Beecker. "The savings could be spent on something else in medicine."

It's a rare adverse event, but when toxic epidermal necrolysis (TEN) occurs, a potentially lethal drug reaction causing the epidermis to detach from the dermis, there are no effective therapies to treat it, and clinicians to date have turned to avenues like intravenous immunoglobulin or supportive care, but a report published this year highlighted that tumour necrosis factor-alpha can be a target, according to Dr. Beecker.

"It's a very severe reaction, and there is no gold standard for treatment," explains Dr. Beecker. "What we are seeing that is novel is that biologics are being used to treat the severe burn-like reaction."

A small, uncontrolled case series of patients with TEN showed that with a single subcutaneous injection of etanercept, patients responded and reached complete re-epithelialization without any side effects, with the median time to healing being 8.5 days (*J Am Acad Dermatol* 2014 Aug; 71(2):278-283).

"It [use of the TNF-alpha inhibitor] has not been proven, but it represents a promising concept,"

notes Dr. Beecker.

The availability of adapalene 0.1%/benzoyl peroxide 2.5% topical gel in a pump dispensing system in 2014 made delivery of the product more convenient for patients with acne. In addition, a modification in the indication of the therapy, so that



it can now be prescribed in children aged nine and older, widens the pool of available patients.

"Many therapies that we use for pediatric patients are off-label, so it's nice to have an option that is on-label," says Dr. Beecker. "We notice that some children are going through puberty earlier, and so they are getting acne earlier."

It's premature to offer a biologic therapy to children with atopic dermatitis, but clinicians are enthused about the prospect of having a biologic therapy in their tool kit for their adult patients in the near future.

"I think dupilumab will be a game changer for atopic dermatitis," says Dr. Dytoc. "There are many biologics for psoriasis, so it will be nice to have one for atopic dermatitis."

Research is also looking at apremilast, an oral phosphodiesterase 4 inhibitor recently approved

in Canada for moderate to severe psoriasis, in the management of atopic dermatitis.

Another advance in 2014 was the availability of a new topical therapy, efinaconazole 10%, for onychomycosis. It can act as an alternative for patients who don't want to take an oral therapy such as itraconazole or terbinafine or for whom oral therapies are contraindicated because of possible drug interactions.

"The mycologic cure rates are better than oral itraconazole but less than oral terbinafine," says Dr. Dytoc, noting the condition can be persistent and recurrent. "It's more effective than ciclopirox lacquer and other topical anti-fungal solutions."

Dr. Skotnicki says patients express a preference for using efinaconazole over ciclopirox lacquer because they can continue to apply and wear nail polish while using efinaconazole because the topical therapy can penetrate through nail polish.

"Women want to be able to cover up their nails, and that was a problem with [ciclopirox lacquer]," says Dr. Skotnicki in an interview. "The percentage of improvement is higher with [efinaconazole] than with [ciclopirox lacquer]. It's an alternative [treatment] for people who don't want to take oral therapies."

Modifications to diet in acne

New pathways are suggesting that for a condition such as acne, modifications to diet can make a difference, notes Dr. Skotnicki.

A study published this year linked a typical Western diet, characterized by a high glycemic load, as possibly playing a role in acne pathogenesis (*J Clin Aesth Dermatol* Jul 2014; 7(7):46-51).

"Acne is more of a Western disease," explains Dr. Skotnicki. "We are really starting to look at the link with diet. The answer is no longer that there is no link between diet and acne."

Dr. Skotnicki says patients can make a choice to follow a low glycemic index to influence the pathogenesis of their acne.

Non-proprietary and brand names of therapies: nivolumab (not available in Canada); pembrolizumab (not available in Canada); tofacitinib (Xeljanz, Pfizer Canada Inc.); brimonidine (Onreltea, Galderma); sincecatchins 15% (Veregen, Paladin Labs); etanercept (Enbrel, Amgen); adapalene 0.1%/benzoyl peroxide 2.5% topical gel (TactuPump, Galderma); dupilumab (not available in Canada); apremilast (Otezla, Celgene Corp.); sincecatchins 10% (Veregen, Paladin Labs); efinaconazole (Jublia, Valeant).