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Dermatological Drug Dosage in the Elderly*

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ABSTRACT

The elderly population is increasing and drug dosing requires special considerations for efficacy and decreasing toxicity. This overview provides algorithms for adjusting drug and dosage based on current evidence-based knowledge with emphasis on drugs prescribed in dermatological practice.

Key Words: *elderly, drug dosing, dermatological drugs*

The proportion of elderly people in the general population continues to grow rapidly[1] and dermatological diseases are common in this group,[2] making drug dosage and administration particularly important. Furthermore, the elderly are vulnerable to adverse drug reactions (ADRs).[3] Some dermatological drugs, such as methotrexate (MTX), may result in serious toxic effects in the elderly if the dosage is not reduced.[4] Evaluating the factors that could influence drug pharmacokinetics and pharmacodynamics is worthwhile in order to improve drug treatment in this population.

Adverse Drug Reactions in the Elderly

Anti-Infective Agents

Infections are a common problem among the elderly, and anti-infective agents are frequently prescribed to them.[5] In elderly patients, ADRs, as well as drug interactions, should be considered when selecting an anti-infective regimen. Common drug interactions with anti-infective agents involve macrolide antibacterials and fluoroquinolones.[6]

Erythromycin and troleandomycin are strong inhibitors of the cytochrome P450 enzyme CYP3A4, and may therefore be responsible for toxicity of coadministered drugs by decreasing their clearance (Table I).[6] Example substrates of CYP3A4 include benzodiazepines, calcium channel antagonists, immunosuppressive agents (e.g., cyclosporin, tacrolimus [Protopic®, Astellas]), and anticoagulants.[7] Elderly patients receiving macrolides should be monitored for adverse events resulting from drug interactions.

Fluoroquinolones are antibacterials that are frequently used in infections affecting the elderly.[8] One of the most important drug interactions of fluoroquinolones is the ability of ciprofloxacin (Cipro®, Bayer) and enoxacin to inhibit the metabolism of theophylline by CYP1A2, resulting in theophylline accumulation and toxicity.[6] Seizures may occur at therapeutic theophylline levels as a result of its additive effects on the central nervous system (CNS).[6]

Corticosteroids

Corticosteroids have adverse effects on many organ systems,[9] ranging from those that are not necessarily serious (e.g., Cushingoid appearance), to those that are life-threatening (e.g., serious infections). Some of these adverse effects may be aggravated in the elderly. Patients receiving prednisolone 5–40mg/day for at least 1 year had a partial loss of explicit memory, and elderly patients may be more susceptible to memory impairment with less protracted treatment (Table 1).[10] The risk of developing diabetes mellitus more than doubles in elderly patients who are newly initiated on oral corticosteroid therapy.[11]

A higher risk for peptic ulcer disease was reported in corticosteroid users who were receiving nonsteroidal anti-inflammatory drugs (NSAIDs) concurrently (Table 1).[12] Those receiving NSAIDs and corticosteroids showed a risk for peptic ulcer disease 15 times greater than that of nonusers of either drug.[12]

Antihistamines

Elderly persons treated with first-generation histamine H1 receptor antagonists (antihistamines) may be at greater risk of adverse effects involving the CNS, such as sedation or impaired cognitive function.[13]

Diphenhydramine administration in hospitalized patients ≥70 years of age was associated with a higher risk of cognitive decline compared with nonexposed patients (Table 1).[14] These findings strongly suggest caution when prescribing this drug to the elderly. Reports by Mann, et al. of sedation with second-generation antihistamines loratadine, cetirizine (Zyrtek®, Pfizer), fexofenadine (Allegra®, sanofi-aventis) and acrivastine (Sempra®, GlaxoSmithKline) were infrequent, but this study did not focus on the elderly. Affrime et al.[15] studied pharmacokinetics and adverse events of desloratadine (Aerius®, Schering) in different age groups and suggested that no dosage adjustment of desloratadine is required in the elderly.

Immunobiological Agents

Three immunobiological agents have been approved by the US FDA for the treatment of moderate-to-severe psoriasis: alefacept (Amevive®, Astellas), efalizumab (Raptiva®, Genentech), and etanercept (Enbrel®, Amgen Wyeth).[16] A recent study found alefacept to be well tolerated and effective in elderly, obese, and diabetic patients with moderate-to-severe plaque psoriasis.[17] Accidental injury, headache, and pharyngitis were among the most common adverse events. Infections were primarily colds, with no opportunistic infections being reported. In psoriatic patients ≥65 years of age treated with efalizumab, the overall rates of adverse events were comparable to those seen in patients <65 years of age, although a higher rate of serious adverse events was observed in the older group.[18]

Drug	Key Point	References
Erythromycin	Strong inhibitor of CYP3A4; may lead to increase in toxicity of coadministered drugs such as benzodiazepines, calcium channel blockers, cyclosporin, tacrolimus, and warfarin.	6,7
Ciprofloxacin	Inhibits the metabolism of theophylline by CYP1A2; may result in theophylline accumulation and toxicity; may increase risk of developing seizures.	6
Oral corticosteroids	Elderly may be more susceptible to memory impairment; higher risk of developing diabetes mellitus; higher risk for peptic ulcer disease in patients who are receiving NSAIDs concurrently.	10,11,12
Diphenhydramine	Increased risk of cognitive impairment.	14
Hydroxyzine	Prolonged half-life and possible increase in receptor sensitivity.	24
Cetirizine	Total body clearance reduced in patients with decreased renal function; in these patients dose should be reduced by 50%.	13,38
Methotrexate	Serious potential for adverse effects with decreased renal function; contraindicated in severe renal impairment (GFR <9mL/min); in mild renal impairment, dose should be reduced to 50% of normal.	4,33,54
Itraconazole	Should be used with caution in patients with history of liver impairment.	56
Acitretin	Dosage should be reduced in patients with liver disease.	58

Table 1: Specific points on the effects of dermatological drugs prescribed for the elderly

A recent study evaluated the safety profile of etanercept in patients with chronic, moderate-to-severe plaque psoriasis.[19] Pooled safety results from the first 12 weeks of treatment suggest that short-term etanercept treatment is generally safe and well tolerated. No overall differences in safety were observed between older and younger patients.

Changes in Pharmacokinetics

Absorption

There appear to be no major alterations in intestinal drug absorption in the elderly.[20] However, percutaneous absorption of hydrocortisone, benzoic acid, acetylsalicylic acid, and caffeine was significantly lower in the elderly when compared with younger subjects, whereas absorption of testosterone and estradiol was not.[21] These results suggest that aging can affect percutaneous drug absorption and that relatively hydrophilic compounds are particularly sensitive.

Physiological age-related changes in the skin may impair percutaneous drug absorption (see Table 2).[21] The diminished lipid content of aged skin implies a diminished dissolution for percutaneous administered drugs, and the reduced water content may make aged skin less attractive to more hydrophilic compounds. Furthermore, comprised microcirculation may lead to poorer absorption capability.

Organ	Age-related changes	References
Kidney	↓ GFR ↓ Renal blood flow ↓ Tubular function	40,41
Liver	↓ Liver size ↓ Liver blood flow	46,47
Skin	↓ Hydration of stratum corneum ↓ Skin surface lipids ↓ Skin microcirculation	21
Body composition	↓ Lean body mass ↓ Total body water ↑ Body fat	22,23

Table 2: Changes in body composition and body function with aging; GFR=glomerular filtration rate

Distribution

Changes in body composition in the elderly may lead to altered drug distribution. Lean body mass and total body water decrease with age, whereas fat as a percentage of body weight increases with age.[22,23] As a result, the volume of distribution is lower for hydrophilic drugs leading to potentially higher plasma concentrations. In contrast, the volume of distribution is higher for lipophilic drugs, often resulting in retention and prolonged half-life, as shown for hydroxyzine.[24] When considering volume of distribution, elderly patients may have significantly reduced body weight,[25] which is a major risk factor for overmedication.[26]

Drugs may be bound to plasma proteins with only the free fraction being pharmacologically active. The two plasma proteins to which drugs can bind are albumin and α-1-acid glycoprotein, and these may change with age.[27] Albumin levels tend to decrease with advancing age, whereas α-1-acid glycoprotein may increase.[28,29] Thus, the ratio of bound to free drug may be altered. However, the extent to which these changes in plasma protein binding are clinically relevant is controversial. Changes of >50% in the free fraction were documented for only a few drugs, such as naproxen, salicylates, and valproic acid,[30] and greater drug elimination may counterbalance the increase in free drug concentration.[31]

Elimination

Decreased renal function can result in prolongation of the half-life of many drugs, which can accumulate to toxic levels if the dosage is not reduced.[32] Thus, to avoid excessive drug dosing, renal function assessment is essential in elderly patients, especially when prescribing drugs with a low therapeutic index, such as MTX,[33] which is mainly eliminated by the kidney.[34] Studies have described a significant increase in its half-life in patients with impaired renal function, as defined by creatinine clearance (CLcr).[35,36] Patients with renal impairment have a higher overall rate of toxicity and are at higher risk of severe and respiratory toxicities than those with normal CLcr.[4]

Like MTX, the second generation antihistamine cetirizine is predominantly eliminated unchanged in the urine.[37] In elderly subjects with impaired renal function, the elimination half-life of cetirizine was significantly prolonged (i.e., an increase of 159% in patients with a mean CLcr of approximately 44mL/min) and apparent total body clearance was significantly reduced by 64%.[38] Therefore, Kaliner suggested that cetirizine dosage be reduced by 50% in patients with renal disease.[13] Prescribing the second generation antihistamine fexofenadine may be considered in this setting, as the pharmacokinetics of fexofenadine are not affected by decreased renal function.[39]

Renal function generally declines with age. Specifically, renal blood flow is reduced and tubular function is impaired, thus reducing the kidney's ability to maintain homeostasis under stressful conditions.[40] The glomerular filtration rate (GFR), measured by creatinine clearance (CLcr), declines by approximately 30% between 30–80 years of age in about two thirds of the population.[41,42] It is important to remember, however, that CLcr provides only a rough estimate of the GFR because creatinine is also secreted in small amounts by the kidney.[43]

CLcr can be estimated utilizing the Cockcroft and Gault equation[44] by correcting the serum creatinine for age, sex, and weight:

$$\text{Estimated creatinine clearance (mL/min)} = \frac{1.2 \times (140 - \text{age[year]}) \times \text{weight (kg)}}{\text{Serum creatinine (µmol/L)}}$$

(× 0.85 for women)

Using this equation is probably the easiest way to estimate a patient's renal function. However, CLcr estimated using this method can significantly differ from true CLcr, particularly in elderly patients.[45] Moreover, their serum creatinine might be lower because of lower muscle mass, and as a result, it might not rise significantly even when renal function is significantly impaired.[41] This could lead to an overestimation of CLcr as has been shown by Goldberg and Finkelstein [45].

If a more precise measure is needed, a standard 24-hour CLcr measurement should be performed; however, even with this test, unreliable results are possible. Urine collection by patients might be incomplete, perhaps because of a forgotten urine specimen,[45] and CLcr might exceed the true GFR. An EDTA clearance or insulin clearance test should be performed, if available, because it provides a more accurate assessment of renal function.[33]

Degrees of renal impairment can be classified as mild (GFR 20–50mL/min), moderate (GFR 10–19mL/min), or severe (GFR <9mL/min) and therapeutic drug levels may be maintained either by reducing the dose, by increasing the interval between doses, or by doing both.[33]

Metabolism

The hepatic clearance of many drugs is lower in the elderly, mainly because of a reduction in liver size of approximately 20%–40% [46] and a reduction in liver blood flow.[47] Drug metabolism proceeds via Phase I and Phase II reactions. While there may be changes in Phase I reactions with aging,[48] Phase II reactions seem to be less affected.[49]

Hepatic drug metabolism in the elderly is a controversial matter. Sotaniemi, et al.[48] showed a reduction of CYP-P450-linked drug metabolism by approximately 30% after 70 years of age in an investigation of CYP-P450 content and microsomal enzyme activity in the human liver. Conversely, other studies found no significant age-related differences in the activities and contents of human liver microsomal enzymes.[50,51]

Drug-induced liver disease seems to occur more frequently in the elderly.[52] For example, isoniazid-induced hepatitis, which is uncommon in younger age groups, occurred in approximately 2% of persons ≥50 years of age.[53] No studies have been published that evaluate whether elderly patients are more susceptible to potentially hepatotoxic drugs used in dermatological practice. However, caution may be indicated for this group.

Several commonly prescribed dermatological drugs, such as MTX, can potentially cause liver damage,[54] and the age at onset of therapy has been shown to be one risk factor.[55] Close attention should be paid to the recommendations for monitoring elderly patients taking MTX.

Itraconazole (Sporanox®, Janssen Pharmaceutica) should be used with caution in patients with history of liver impairment.[56] Itraconazole users are at a higher risk of liver damage, which is associated with a cholestatic pattern of injury.[57,58] Although serious liver problems, including liver failure and death, are rare with the use of this drug,[58] liver function tests should be conducted in patients who have pre-existing hepatic dysfunction.[56]

Severe hepatic injury with the use of acitretin (Soriatane®, Connetics) has been reported,[57] but appears to be a rare side-effect of treatment with this drug. However, in patients with liver disease, the dose of acitretin should be reduced and liver function tests monitored closely.[58] Other potentially hepatotoxic drugs used in dermatology include agents such as tetracyclines, erythromycin, flucloxacillin, ketoconazole, azathioprine, synthetic androgens, and dapsone.[58]

Changes in Pharmacodynamics

Pharmacodynamic considerations include receptor number and affinity, signal transduction mechanisms, cellular responses, and homeostatic regulation.[59] Sensitivity to certain drugs may be either increased or decreased in the elderly, e.g., sensitivity to benzodiazepines is greater in older patients,[60] as is the response to some opioids and anticoagulants.

Conversely, the elderly seem to be less responsive to certain β-adrenoceptor agonists and antagonists.[27] Simons, et al. studied H1-receptor sensitivity to hydroxyzine by measuring changes in suppression of histamine-induced wheal and flare and suggested an enhanced suppression of H1-receptor activity in the elderly.[24]

Prescribing in the Elderly: General Considerations

How a drug is handled by the body may change in the elderly. Alterations in drug metabolism and elimination, and a higher prevalence of multidrug regimens make this population more susceptible to ADRs. What makes prescribing to the elderly even more challenging is the fact that they are known to tolerate a number of drugs less well, but they handle other drugs as well as younger individuals. In addition, drug response in the elderly shows a large inter-individual variability.[31] There are no simple rules for prescribing that can apply to the elderly population in general; the right dosage must be determined for every elderly person individually.[31] A general approach when prescribing drugs to this population would be to:

1. Start, when possible, with a small initial dose and titrate this dose to a clearly defined therapeutic response (dosage guidelines may help you find out about initial dosage reduction).
2. Reduce the number of drugs administered simultaneously as much as possible.
3. Take a careful drug history.
4. Check for possible ADRs or drug interactions.[27,31,32]

Noncompliance with drug therapy regimens is a common reason for hospital admission for elderly patients.[61] Risk factors include the patients' inability to recall their medication regimen, medication costs, using several physicians, polypharmacy, and complicated drug regimens.[61] Cognitive impairment and physical dependency are additional risk factors for poor medication management in this group.[62] To enhance drug management in the elderly, it is crucial to simplify the drug regimen as much as possible, e.g., try to use drugs that can be taken at the same time of day.[32]

Conclusions

Some commonly prescribed dermatological drugs such as MTX and cetirizine are likely to be eliminated more slowly in the elderly. Dosage reduction is recommended not only with these agents, but with any drug that is predominantly eliminated by the kidney. Potentially hepatotoxic drugs such as MTX, itraconazole, and acitretin should be used with caution in the elderly, and liver function tests should be performed when these drugs are given in order to lower the risk of hepatotoxicity. Absorption of percutaneously administered drugs may be lowered in the elderly and altered distribution may lead to prolonged half-life, as shown for hydroxyzine, or to a higher plasma concentration of hydrophilic drugs. Further research is needed in order to determine how specific dermatological drugs are handled by the elderly so that pharmacotherapy in this part of the population can be improved.

*Modified with permission from: *Drugs Aging* 23(3):203-15 (2006).

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Pigmentary Disorders in Asian Skin: Treatment With Laser and Intense Pulsed Light Sources

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ABSTRACT

The development of selective photothermolysis has enabled removal of targets such as melanin. Both lasers and intense pulsed light (IPL) sources have been used in the treatment of pigmented lesions, however careful selection is important to ensure success. This is especially true in darker skinned individuals where the risk of postinflammatory hyperpigmentation (PIH) is high. The advent of the Q-switched laser, IPL, and now fractional photothermolysis (Fraxel®, Reliant Technologies) offers a variety of ways to treat epidermal and dermal pigmentary disorders.

Key Words: *laser, intense pulsed light, Q-switched laser, fractional photothermolysis, pigmentary disorder, postinflammatory hyperpigmentation*

In darker skinned individuals photodamage more commonly presents as pigmentary changes rather than wrinkling. This difference is partially due to the higher epidermal melanin content, which can predispose these patients to a higher risk for hyperpigmentation from light source treatment. Although several of these pigmented lesions are common among all skin types, we will focus on the parameters associated with Asian skin.

Epidermal Lesions

Lentigines

Lentigines are common in individuals from sun-exposed sites, and histologically demonstrate melanocyte proliferation without nest formation along the basement membrane. Q-switched (QS) lasers deliver short bursts of wavelength-specific energy that can be absorbed by melanocytes, i.e., QS Nd:YAG lasers (532nm or 1064nm), the QS alexandrite laser (755nm), and the QS ruby laser (694nm). The risk of postinflammatory hyperpigmentation (PIH) in the Asian population is estimated to be about 10%–25% with QS lasers, which have the advantage of achieving significant clearing even after one treatment session and are particularly effective for lightly pigmented lentigines. We routinely test spot, to minimize the risk of PIH.

Another approach to removing lentigines is to use longer pulsed lasers in the microsecond domain that match the thermal relaxation time of the epidermis, thus confining the thermal injury to the epidermis. Without the photomechanical effect associated with the use of QS laser, the risk of PIH associated with long pulsed laser is lower. For example, we use a long pulse 532nm Nd:YAG laser (2ms pulse duration, 6.5J/cm^2 fluence, 2mm spot size without cooling or 12 J/cm^2 with cooling sapphire window).

Recently, traditional vascular lasers have been employed to remove lentigines. Long pulsed dye laser (LPDL) (595nm) targets both hemoglobin and melanin. Compressing the skin surface during treatment and emptying the blood vessel minimizes damage of the vessels that can lead to bruising and subsequent PIH. A recent study in the treatment of lentigines in Asians, compared the use of LPDL (595nm) (fluence of 10–13J/cm^2, pulse duration of 1.5ms) attached with a compression window vs. a QS ruby laser (694nm) (fluence of 6–7J/cm^2, pulse duration of 30ns). The LPDL with compression window arm demonstrated superior results and fewer adverse effects.[1]

Intense pulsed light (IPL) sources that emit a broad band of visible light (400–1,200nm) from a noncoherent filtered flashlamp, affects pigmentation via photothermal effects. IPL has been studied for the treatment of lentigines and ephelides with cutoff filters ranging from 550–590nm, a fluence of 25–35J/cm^2, and a pulse width of 4.0ms.[2] These studies have been performed on Asian skin with surprisingly no PIH. This lower risk of PIH and the limited postoperative downtime have made IPL a popular choice. The patient should understand,

however, that multiple treatments may be necessary. In our practice, for those who do not wish to have any downtime, or for those who wish to improve not only their pigmentation, but also pore size and skin texture, we offer IPL treatment combined with other laser modalities in the same treatment session to obtain a better outcome.

Café au Lait Macules

Café au lait macules are seen at birth and may increase in size over time. Although multiple lesions are associated with neurofibromatosis, *café au lait* macules are a common finding at birth. They do not signify an increased risk of melanoma and can be removed for cosmetic reasons.

The use of Q-switched lasers in the treatment of *café au lait* patches has yielded variable results with a high risk of recurrence if pigment is left behind. There have also been reported incidences of paradoxical darkening. Comparison of frequency-doubled QS neodymium:YAG laser (532nm; spot size 2.0mm) and the QS ruby laser (694nm; spot size, 5.0mm) at a fluence of 6.0J/cm^2 demonstrated variable responses. Our current approach is to use a long pulsed pigment laser to remove not only the epidermal melanocytes but also the hair follicle melanocytes. Our experience suggests a lower risk of recurrence (~40%) (See Figure 1).

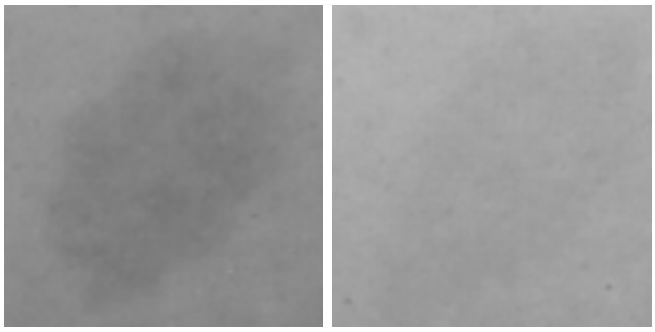


Figure 1: **Left:** *Café au Lait* patch prior to treatment, cross-polarized photo.

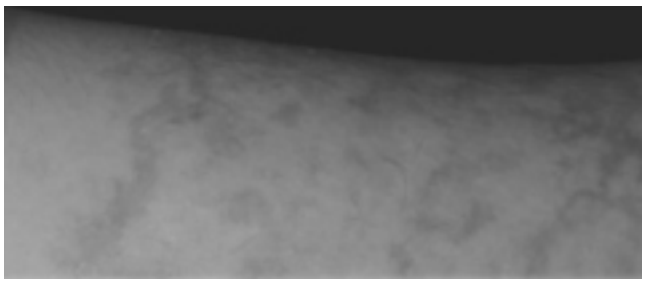
Right: After 9 treatments with long pulsed alexandrite (755nm, 30–50 J/cm^2, 10mm spot size, 3ms pulse width) every 6 weeks, cross-polarized photo.

Becker's Nevus

Becker's nevus, or pigmented hair epidermal nevus, is an uncommon hamartoma that can represent significant cosmetic concern. Histologically, there may be greater pigmentation in the basal region, increased melanophages, and large numbers of irregular, enlarged, smooth muscle fibers in the dermis. In the past, nonspecific treatments such as an argon or CO_2 laser were used with associated scarring or permanent hypopigmentation.

We employ long pulse alexandrite 755nm (30–50J/cm^2, 10mm spot size, 1.5ms) to target the pigment and surrounding hair follicle. We inform the patients of an approximately 50% success rate after four to eight treatment sessions. Scarring and hypopigmentation are possible side-effects. Other cases report superiority of the erbium:YAG laser 2940nm (28J/cm^2, 3mm spot size) as compared to the QS 1064nm Nd:YAG laser (10J/cm^2, 10ns pulse width, 3mm spot size).[3] In a study of 22 patients treated with one pass mode erbium:YAG laser at 2-year follow-up, 54% achieved complete clearance while >50% improvement was noted by 100% of the patients.[3] Slow repigmentation takes place over years but patients should be aware of potential mild permanent hypopigmentation (See Figure 2).

Figure 2: A) Becker's nevus on right forearm prior to treatment with diffuse hyperpigmentation and hypertrichosis.



B) After 8 treatments with long pulsed alexandrite (755nm, 20–30 J/cm^2, 10mm spot size, 3ms, pulse width) Note hypopigmentation and mild scarring with loss of hair. Kenacort and 5-FU injections were supplemented to minimize scarring.

Tips for Laser Treatment of Epidermal Pigmentation:

- Sun avoidance and/or pretreatment with chemical suppressants of melanin production such as 4% hydroquinone is important before and after the treatment.

- Test spots should always be done for QS lasers to reduce the risk of PIH.
- For long pulsed lasers, patients should be warned that several treatments will be necessary to achieve a significant degree of improvement, but there is less downtime and lower risk of PIH.
- Becker's nevi can be removed with pigment removing lasers, but there is a risk of recurrence. It is to be further determined whether combination with ablative lasers will have a lower risk of recurrence.

Dermal or Mixed Lesions

Nevus of Ota/Hori's Nevus

Two forms of primarily dermal pigmentation commonly seen in Asian patients include:

1) Nevus of Ota appears as slate blue pigmentation in a unilateral trigeminal nerve distribution emerging at birth or in young adulthood.

2) Hori's nevus, also known as acquired bilateral nevus of Ota-like macules (ABNOM), or acquired dermal melanocytosis (ADM), presents as bilateral facial bluish-gray macules. Seen in 0.8% of the Asian population, Hori's nevus typically affects the malar region, but the lateral temples, alae nasi, eyelids, and forehead can also be involved. Unlike nevus of Ota, the pigmentation in Hori's nevus is acquired and does not involve the mucosa. Not uncommonly, melasma and Hori's nevus can present concurrently.

The treatments for both types of dermal pigmentation are similar and again include the QS lasers. QS ruby (694nm), QS Alexandrite (755nm), and QS 1064nm Nd:YAG have all been used for the treatment of nevus of Ota with excellent results and similar minimal risk of complications. In our retrospective study of 46 children and 107 adults, >75% achieved a complete response with Q-switched ruby (694nm wavelength, 30ns pulse duration, 4mm spot size, 5–7J/cm^2 fluence at 3–4-month intervals). Treatment is optimal at a younger age, as there is a lower number of mean treatments and lower rate of complications.[4]

Compared to nevus of Ota, Hori's nevus is particularly challenging to treat and there are at least two potential reasons for this: 1) melanocytes are located perivascularly leading to a higher likelihood of PIH after laser therapy, and 2) there is a frequent association with melasma and thus, the associated presence of epidermal pigmentation. As such, combination approaches are frequently used. Recently, the concurrent use of QS 532nm Nd:YAG in combination with the QS 1064nm Nd:YAG laser in a small study was shown to be more effective in reducing the degree of pigmentation of Hori's nevus.[5] Other employed techniques include the use of topical bleaching agents such as 0.1% tretinoin aqueous gel and 5% hydroquinone ointment containing 7% lactic acid to discharge epidermal melanin 4–6 weeks prior to treatment. PIH was documented in 10.5% of these cases as opposed to 50%–73% of patients in prior studies.[6] We also treat our patients with both preoperative and postoperative topical bleaching agents.

The main issue for patients with Hori's nevus is the downtime associated with frequent use of QS lasers. We are currently investigating the use of contact cooling together with a pulsed light source at the red light region (690–1000nm). The aim of this treatment is to achieve removal of these lesions by inducing apoptosis of the melanocytes after repeat treatments, and to reduce downtime.

Melasma

Melasma is a common yet difficult to treat pigmentary disorder, typically found symmetrically on the face of women. Risk factors include sun exposure, increased hormones, genetic predisposition, and phototoxic medications. While topical agents remain the first-line treatment for epidermal and mixed type of melasma, a laser or light source has been used for the more refractory lesions.

IPL theoretically offers an attractive alternative with minimal downtime, but may not be an effective, long-term treatment as a solo agent. IPL, used at 570nm and 590–615nm filters in 4-week intervals for a total of four treatments, was tested on Asian patients. There was a 39.8% improvement of the relative melanin index in the treatment groups compared with 11.6% improvement in the control group at week 16. There was however, repigmentation at the end of the 36-week treatment suggesting that maintenance therapy may be necessary.[7] Patient expectations should include microcrust formation 2–3 days after irradiation with resolution within 1–2 weeks. QS 1064nm Nd:YAG laser (6mm spot size, 1.6J/cm^2) can also be used for the treatment of melasma. Mild erythema can be used as the clinical endpoint and patients will require monthly treatment.

The newest addition to the armamentarium is fractional photothermolysis (FP) (Fraxel®, Reliant Technologies). FP involves the use of an infrared laser (1450nm or 1540nm) to create microcolumns of thermal injury

surrounded by uninjured tissue. The columns of thermal injury surrounded by uninjured tissue are called microscopic treatment zones (MTZs). The density of MTZs can be varied for a given energy level. Reported side-effects are sunburn-like erythema that lasts 1–3 days. The original proof of principle study by Tannous, et al. demonstrated a marked reduction in both epidermal and dermal pigmentation 6 months after two full face FP treatments spaced 3 weeks apart.[8] In a 10 patient study (Fitzpatrick skin types III-V) with 6–12mJ/MTZ and 2,000–3,500MTZ/cm^2 for 4–6 treatments, 60% of the patients had 75%–100% clearing. Only 1/10 patients had PIH.[9]

We recently published an abstract on a study of 16 Asian patients using a lower dose of 125MTZ/cm^2 at energy of 8mJ, every 2–4 weeks. Lower energy and density reduced pain and downtime. High density is not significantly effective and has a risk of hyperpigmentation in this skin-type population. The selective MTZs created by FP have been studied histologically. Microscopic epidermal necrotic debris (MENDs) forms by day 1 and is shed with the epidermis within 7 days. MENDs has been shown to contain melanin pigment and may serve as a "melanin shuttle", which is rapidly eliminated by the keratinocyte migration from the borders of the MTZs. Furthermore, there is decreased melanin content in the basal cell layer after treatment. There was no reported relapse in melanin pigment at 3 months.[10]

Tips for Laser Treatment of Dermal and Mixed Pigmentation:

- A Wood's lamp is helpful in determining the degree of epidermal and dermal components. Cross-polarizing magnification can help distinguish the 2 components during treatment.
- Reducing epidermal pigmentation with topicals or normal pulse laser may allow for deeper penetration of pigment lasers.
- Before and after photography is essential to help the patient appreciate improvement.

Conclusions

- Epidermal pigmentation is effectively targeted with Q-switched lasers. Pretreatment with melanin-inhibitory substances, longer pulse duration, and compression of vessels can help reduce the risk of PIH.
- IPL is an effective method of removing epidermal pigmentation with reduced downtime, but may require multiple treatments.
- Dermal pigmentation may be best treated with a combination of lasers such as Q-switched 532nm Nd:YAG in combination with the 1064nm laser.
- FP is an effective treatment of melasma and reduced density is important in the Asian skin type to reduce the risk of PIH.

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Class	Name/Company	Approval Dates and Comments
Antifungal	**Ketoconazole 2% Gel** *Xolegel™ Cream* Barrier Therapeutics	The US FDA approved this antifungal agent in July 2006 for the topical treatment of seborrheic dermatitis in immunocompetent adults and children ≥12 years of age. Xolegel™ is the first prescription gel formulation of ketoconazole approved in the US.
Antiviral	**Famciclovir Tablets** *Famvir®* Novartis Pharmaceuticals	The US FDA approved this antiviral agent in July 2006 as a single-day treatment for immunocompetent patients with recurrent genital herpes, in the new approved dose of 1,000mg twice daily for one day. It was also approved as a single-dose treatment for recurrent herpes labialis (cold sores) in immunocompetent patients.
Sunscreen	**Ecamsule 2% + Avobenzone 2%/ Octocrylene 10% Cream** *Anthelios SX®* L'Oreal/ LaRoche-Posay	The US FDA approved this over-the-counter sunscreen in July 2006 for the prevention of sunburn and protection from the entire spectrum of UV rays including the type of UV rays that are linked to some cancers. This product has a sun protection factor rating of 15.

Drug News

Insect Bite Guide	Researchers at Johns Hopkins Children's Center in Baltimore MD have developed a new quick tool to sort out insect bites in children, which can often be misdiagnosed. This tool is called SCRATCH, an acronym for: **S**ymmetry – eruptions are usually symmetrical and appear on exposed parts of the body **C**lusters – lesions caused by bedbugs or fleas appear as linear or triangular clusters **R**over not required – i.e. the presence of pets is not necessary because the bite might occur away from home **A**ge specific – most prevalent in children between 2–10 years of age **T**arget/ Time – target shaped lesions are typical of insect-bite hypersensitivity; time indicates the chronic or recurrent nature of eruptions, i.e., many may have delayed reactions) **C**onfusion – parents often express confusion and disbelief at the suggestion that there might be fleas or bedbugs in their homes **H**ousehold –unlike conditions that have similar symptoms (e.g., scabies or eczema), insect-bite rashes often appear in a single member of a family. It is a guide to the symptoms and features that help pediatricians and others to recognize the source of the rash. *Hernandez RG, Cohen BA. *Pediatrics* 118(1):e189-96 (2006 Jul).
Lice Treatment	A unique pediculicide rinse called Resultz™ (Atlanta Pharma) is now available in pharmacies across Canada in time for the new school year. This product contains 50% isopropyl myristate and 50% ST-cyclomethicone, and, in a Canadian-led study, was shown to be 96% effective in treating head lice.* It does not contain pesticides and resistance is unlikely to develop because of its unique mode of action, i.e., dissolving the wax that covers the exoskeleton of the lice causing dehydration and death. **Kaul N, et al. In vivo efficacy and safety of an experimental pediculicide rinse.* Presented at: 63rd Meeting of the American Academy of Dermatology, New Orleans (2005).

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