Pearls from México

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

José Darío Martínez, MD, FAAD
“Pearls from México”

DISCLOSURES
I do not have any relevant relationships with industry.
Pearls from México

José Darío Martínez, MD, FAAD
I am going to discuss some FDA approved drugs, and some that are used off-label.
Pearls from México: potpourri

- Cutaneous Leishmaniasis
- Myasis
- Head Lice
- Kerion
- Leprosy
- Lobomycosis
- Ashy dermatosis (EDP)
- Melasma
- Poikiloderma of Civatte
Cutaneous Leishmaniasis: Fast Facts

- Neglected tropical disease
- Occurs worldwide
- CL: 0.7-1.2 million cases/year
- Travelers’ disease
- DX: direct smear/biopsy/PCR
- RX: pentavalent antimonials

Clin Infect Dis 2015;60:1398-1404
Cutaneous leishmaniasis

RX Pearls

- **L. mexicana**: no RX/local or systemic treatment
- **V. braziliensis, L. Panamensis**: systemic treatment only
- **Systemic RX**:
  - Risk of developing ML
  - Failure or prior local RX
  - Size, number and location of lesions
  - Lymphatic spread
  - Toxicity of systemic RX

LeishMan Recommendations for Treatment of Cutaneous and Mucosal Leishmaniasis in Travelers, 2014

Johannes Blum MD, Pierre Buffet MD, Leo Visser MD, Gundel Harms MD, et al. Article first published online: 19 DEC 2013
DOI: 10.1111/jtm.12089 © 2013 International Society of Travel Medicine
Cutaneous Leishmaniasis: Current Treatment Practices in the USA for Returning Travelers

Daniel P. Eiras, MD, MPH*, Laura A. Kirkman, MD, and Henry W. Murray, MD

Opinion statement

Leishmaniasis, a protozoal infection transmitted by sandfly bite, produces a clinical spectrum of disease ranging from asymptomatic infection to ulcerative skin and mucosal lesions to visceral involvement. Leishmaniasis is endemic in regions of Africa, the Middle East, south Asia, southern Europe, northern South America, and Central America. There has been an increase in imported leishmaniasis into developed, non-endemic countries due to increasing global travel. While pentavalent antimonials have been the mainstay of antileishmanial treatment for decades, newer therapeutic options have become available for all forms of infection, including liposomal amphotericin B, miltefosine, fluconazole, and ketoconazole. For the returning traveler with cutaneous leishmaniasis in the USA, treatment approaches are determined based on infecting species, initial presentation, extent and progression of disease, the advantages and drawbacks of available parenteral and oral drugs, and clinician-consultant experience.
CL RX Pearl

Treatment for travelers

- Miltefosine, PO, FDA (2014), 2.5 mg/kg/day/1 month
- Amphotericin B, IV (Liposomal)
- Alternative:
  - Fluconazole, PO (no longer recommended for *V. braziliensis*)
  - Ketoconazole, PO

*Curr Treat Options Infect Dis 2015;7(1):52-62*
Myasis:

Fast Facts

- Infestation of the skin by fly larvae
- *Dermatobia hominis* & *Cordylobia anthropophaga*
- Boil-like lesions, #1-3, furuncular
- Painful, movement inside
- Travelers’ disease
- DX: US, CT scan
- RX: surgery, oral ivermectin

*Seminars in Pediatric Surgery 2012;21:142-150*
Travelers’ maladies

Got the Travel Bug? A Review of Common Infections, Infestations, Bites, and Stings Among Returning Travelers
Matthew P. Vasievich1 • Jose Dario Martinez Villarreal2 • Kenneth J. Tomecki1

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Myiasis RX Pearl

Treatment

- Prevented with repellents (DEET)
- Vaseline, pork fat, mineral oil ➤ top of the furuncle
- Topical 1% ivermectin solution
- Ivermectin PO: 200 µg/kg/once
- Surgical extraction is the best treatment

Head Lice: Fast Facts

- Infestation by *Pediculus humanus capitis*
- Worldwide, 6-12 millions of cases annually
- Most commonly in children 4-13 years old
- Big economic burden in the U.S.
- DX: clinical, nape itch
- RX: topical lotions/physical removal

*J Med Entomology 2017;54(1):167-172*
Lice topical RX: poor efficacy, toxicity and relapses

<table>
<thead>
<tr>
<th>Agent</th>
<th>Group</th>
<th>Mechanism of action</th>
<th>Method of use on day 1 and 8</th>
<th>Risk factors</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Permethrin (1%)</td>
<td>Synthetic pyrethroid</td>
<td>Disrupts the sodium channel current leading to delayed depolarization</td>
<td>Topical application on clean and dry hair for 10 minutes</td>
<td>None</td>
<td>Poor-fair</td>
</tr>
<tr>
<td>Permethrin cream (5%)</td>
<td>Synthetic pyrethroid</td>
<td>Disrupts the sodium channel current leading to delayed depolarization</td>
<td>Topical overnight application to clean dry hair</td>
<td>None</td>
<td>Poor-fair</td>
</tr>
<tr>
<td>Malathion (0.5%)**</td>
<td>Organophosphate</td>
<td>Acetyl cholinesterase inhibitor- respiratory paralysis</td>
<td>Topical application for 8 - 12 hours</td>
<td>Burning, stinging sensation on eroded skin</td>
<td>Excellent</td>
</tr>
<tr>
<td>Carbaryl (0.5%)</td>
<td>Carbamate</td>
<td>Acetyl cholinesterase inhibitor- respiratory paralysis</td>
<td>Topical application for 8 - 12 hours</td>
<td>Cholinesterase inhibitor</td>
<td>Poor-fair</td>
</tr>
<tr>
<td>Lindane (1%)</td>
<td>Organochlorine</td>
<td>CNS toxicity</td>
<td>Topical application for no more than 4 minutes to clean, dry hair, then add water to lather and rinse</td>
<td>Neurological problems, seizure disorders age &lt; 2 years, pregnancy, lactation</td>
<td>Poor</td>
</tr>
<tr>
<td>Topical Ivermectin (1%)</td>
<td>Avermectin</td>
<td>Inhibition of glutamate gated chloride channel</td>
<td>Topical application for 10 minutes</td>
<td>None</td>
<td>Experimental product</td>
</tr>
<tr>
<td>Benzyl Alcohol 5%</td>
<td></td>
<td>kills head lice by asphyxiation</td>
<td>Topically for 10 minutes</td>
<td>Pyoderma and ocular irritation</td>
<td>Not ovicidal</td>
</tr>
</tbody>
</table>

*Approved for individual more than 2 months of age. **Approved for individual more than 6 years of age. *High alcohol content of the product (75% isopropyl alcohol), makes it highly flammable. Patients and their parents, therefore, should be instructed to allow the hair to dry naturally; not to use a hair dryer or flat iron while the hair is wet; and not to smoke near a child receiving treatment.
Lice RX Pearl: Phase 3, ovicidal against eggs (not FDA approved)
In vitro pediculicidal and ovicidal activity of an extract and oil from fruits of *Melia azedarach* L.

María C. Carpinella, PhD, a Mónica Miranda, BSc, b Walter R. Almirón, PhD, c Carlos G. Ferrayoli, PhD, d Francisco Ludueña Almeida, PhD, c and Sara M. Palacios, PhD a
Córdoba, Argentina

**Background:** Head louse infestation is difficult to control because of increasing lice resistance to synthetic pediculicidal drugs.

**Objective:** To test the activity of extract and oil obtained from fruits of *Melia azedarach* L. against the head louse *Pediculus humanus capitis*.

**Methods:** A filter paper diffusion bioassay was carried out in order to determine the pediculicidal and ovicidal activity of extract and oil from *M azedarach* L. fruits.

**Results:** Both vegetable products, tested either individually or in combinations, showed high levels of mortality on adult lice, with values ranging between 62.9% and 96.5%. The highest mortality rate was obtained with a combination of 20% ripe fruit extract with 10% ripe fruit oil. A formulation made with both extract and oil at 10% plus the addition of emulsifier and preserving agents showed 92.3% pediculicidal activity. The products were also successful in delaying or inhibiting nymph emergence, with the formulation being the most effective, with a complete inhibition of emergence.

**Limitations:** Because adult lice are sensitive to starvation and therefore control mortalities are often higher than 20% in tests with field specimens, the results may not reflect the direct effect of the extract.

**Conclusions:** These results demonstrate the possibility of using *Melia* products for controlling head lice, which are difficult to control because of their resistance to the currently used anti-lice agents. (J Am Acad Dermatol 2007;56:250-6.)
Lice Pearl: RX & prevention
Kerion:
Fast Facts

- Is an inflammatory reaction to tinea capitis
- Occurs almost exclusively in children
- Worldwide, antropophilic/zoophilic infection
- *T tonsurans* (multiple) / *M canis* (one)
- One/multiple tender alopecic nodules/areas
- DX: KOH
- RX: griseofulvin, **terbinafine**, itraconazole, fluconazole

*Clinical, Cosmetic and Investigative Dermatology* 2010;3:89-98
A Retrospective Study of the Management of Pediatric Kerion in Trichophyton Tonsurans Infection


Department of Dermatology, King’s College Hospital, London, UK
Kerion RX Pearl

- *T. tonsurans*: terbinafine (4-5 mg/kg/day/4 weeks)
- *M. canis*: fluconazole (5-6 mg/kg/day/4-6 weeks)
- Itraconazole everyday/pulse (5 mg/kg/day/2-6 weeks)
- Oral steroids can be used to reduce scaling/itching/pain

*Pediatric Dermatology* 2011;28(6):655-657
Leprosy: Fast Facts

- *M leprae / M lepromatosis* (DLL in México)
- Chronic and progressive disease (LL)
- Most common: LL (35%), BL (31%), BT (24%)
- Clinical: nodules, plaques, patches (no sensation)
- Zoonosis: armadillos as pets in U.S., México
- DX: ZN stain, biopsy (FF), Lepromin test, PCR
- RX: WHO recommendations

Martínez JD, Cárdenas JA. Curr Treat Options Infect Dis 2017 DOI: 10.1007/s40506-017-0127-7
The Leprosy Agents *Mycobacterium lepromatosis* and *Mycobacterium leprae* in Mexico

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³Instituto de Diagnostico y Referencia Epidemiologicos (InDRE), Mexico DF, Mexico

Summary

Background—*Mycobacterium leprae* was the only known cause of leprosy until 2008, when a new species, named *Mycobacterium lepromatosis*, was found to cause diffuse lepromatous leprosy (DLL), a unique form of leprosy endemic in Mexico.

Methods—We sought to differentiate the leprosy agents among 120 Mexican patients with various clinical forms of leprosy and to compare their relative prevalence and disease features. Archived skin biopsy specimens from these patients were tested for both *M. leprae* and *M. lepromatosis* using polymerase chain reaction-based species-specific assays.

Results—Eighty-seven (72.5%) patients were confirmed for etiologic species, including 55 with *M. lepromatosis*, 18 with *M. leprae*, and 14 with both organisms. The endemic regions of each agent differed but overlapped. Patients with *M. lepromatosis* were younger and from more states, and their clinical diagnoses included 13 DLL, 34 lepromatous leprosy (LL), and eight other forms of leprosy. By contrast, the diagnoses of patients with *M. leprae* included none DLL, 15 LL and three other forms. Thus, *M. lepromatosis* caused DLL specifically (p=0.023). Patients with *M. lepromatosis* also showed more variable skin lesions and the extremities were the commonest biopsy sites. Finally, patients with dual infections manifested all clinical forms and accounted for 16.1% of all species-confirmed cases.

Conclusions—*M. lepromatosis* is another cause of leprosy and is probably more prevalent than *M. leprae* in Mexico. It mainly causes LL and also specifically DLL. Dual infections caused by both species may occur in endemic area.
Leprosy DX Pearl

- Neglected disease
- *M lepromatosis* causes DLL / LL
- In México it´s the leading cause of leprosy
- DLL carries higher mortality than LL
- PCR (16S rRNA) is the best way to make DX

*Int J Dermatol 2012;51(8):952-959*
Lobomycosis: Fast Facts

- *Lacazia loboï* (dimorphic fungus)
- Skin & subcutaneous tissue
- Traumatic inoculation, incubation 1-2 years
- Zoonosis (dolphins)
- DX: biopsy, GG stain
- DDX: keloids
- RX: surgery best treatment

*UpToDate 2016. Lobomycosis. Martínez JD, Francesconi F*
INTRODUCTION
Lobomycosis is a chronic fungal infection of the skin and subcutaneous tissue that primarily occurs in tropical climates of Latin America. The causative organism is *Lacazia lobo* (formerly *Loboa lobo*), a dimorphic fungus found in soil, vegetation, and water. Infection occurs through traumatic implantation of the fungus into the skin. **Lobomycosis affects both humans and dolphins.** The most common presentation in humans consists of slow-growing, keloid-like papules, nodules, or plaques in a localized area on exposed skin. Other manifestations of lobomycosis include ulcerated, infiltrative, verrucous, gumma-like, multifocal, and disseminated lesions. Dx is made by a skin biopsy showing the fungal structures stained with silver stain or PAS. DDX include leprosy, cutaneous leishmaniasis and keloids. Best Rx is surgery for small lesions. For extended lesions itraconazole or posaconazole can be used.
Lobomycosis RX Pearl

Treatment & management

- **Surgical excision in small lesions**
- Cryotherapy
- **No effective systemic treatment:**
  - Itraconazole, clofazimine
  - Posaconazole
  - Combination of treatments

*UpToDate 2016. Lobomycosis. Martínez José Darío, Francesconi Fabio*
Erythema dyschromicum perstans: Fast Facts

- Rare acquired and chronic dermatosis
- Cause unknown
- Asymptomatic and progressive disease
- Ashy-gray macules, confluent
- Upper back & chest, neck, face, limbs
- DX: biopsy
- RX: clofazimine, dapsone

*JAMA Dermatology Letter 2016*
Erythema Dyschromicum Perstans Response to Isotretinoin

Erythema dyschromicum perstans (EDP), also called ashy dermatosis, is a rare acquired and chronic dermatosis, characterized by asymptotically and progressively hyperpigmented macules of various size on the trunk, face, and extremities. Its exact cause is unknown, and its treatment remains controversial. We describe a 48-year-old Chinese man with EDP who was successfully treated with low-dose isotretinoin over a period of 7 years.
Ashy dermatosis RX Pearl

- Traditional RX have minimal success
- **Isotretinoin**: anti-inflammatory and immunomodulatory effects
- Dose: start 20 mg/day → tapered to 10 mg/day
- Long-term RX because recurrence occur when RX is stopped

*JAMA Dermatology Letter 2016*
Melasma: Fast Facts

- Common acquired pigmentary disorder
- Symmetrical hyperpigmented macules (face)
- Race: Asians, Indians, Latinos (IV-VI)
- Pathogenesis unknown, relapses are common
- Factors: UVR, genetic (familial), pregnancy, OC
- DX: clinical
- RX: hydroquinone (gold standard), TCC, kojic acid, azelaic acid, chemical peels, lasers, IPL
Oral tranexamic acid (TA) in the treatment of melasma: A retrospective analysis

Hwee Chyen Lee, MRCP, Tien Guan Steven Thng, MRCP, FRCP, and Chee Leok Goh, MD, MRCP
Singapore

Background: Melasma is a common pigmentary disorder among Asians and treatment is challenging. Oral tranexamic acid (TA) has emerged as a potential treatment for refractory melasma. Large-scale studies on its use, outcomes, and safety are limited.

Objective: We sought to evaluate treatment outcomes and adverse effects of oral TA in melasma in an Asian population.

Methods: We conducted a retrospective analysis of patients who received oral TA for melasma in a tertiary dermatologic center from January 2010 to June 2014.

Results: In all, 561 patients (91.4% female, 8.6% male) were enrolled. Median duration of treatment was 4 months. The majority (503 [89.7%]) improved, 56 (10.0%) had no improvement, and 2 (0.4%) worsened. Patients without family history of melasma had better response rates than those with family history (90.6% vs 60.0%, \( P = .01 \)). Of the 503 who improved, response was seen within 2 months of TA initiation, with a relapse rate of 27.2%. Adverse events occurred in 40 (7.1%). Most were transient, but 1 developed deep vein thrombosis requiring prompt discontinuation. She was later given the diagnosis of familial protein S deficiency.

Limitations: This was a retrospective study.

Conclusion: Oral TA may be an effective adjunct for refractory melasma. Careful screening for personal and familial risk factors for thromboembolism should be done before initiation. (J Am Acad Dermatol 2016;75:385-92.)
Melasma RX Pearl

- **Tranexamic acid**: antifibrinolytic agent
- Inhibits UV-induced plasmin in keratinocytes
- Decreases melanocyte tyrocinase activity
- Decreases vessels size (pigmented-vascular macules)
- Emerged as an adjunct RX for refractory cases
- Oral dose is 250 mg every 12 hours

*J Am Acad Dermatol 2016;75:385-392*
Therapeutic efficacy and safety of oral tranexamic acid and that of tranexamic acid local infiltration with microinjections in patients with melasma: a comparative study.

Sharma R1, Mahajan VK1, Mehta KS1, Chauhan PS1, Rawat R1, Shiny TN1.

Abstract

BACKGROUND:
Tranexamic acid (TXA) has been used orally, intravenously, topically and intradermally (microinjection, microneedling) for treating melasma. However, the comparative efficacy of these different routes of administration remains underevaluated.

AIM:
To ascertain the comparative efficacy of different routes of administration of TXA.

METHODS:
In total, 100 consecutive patients with melasma (8 men, 92 women, age range 18-55 years) were randomly assigned to one of two groups comprising 50 patients each. Group A (3 men, 47 women) received oral TXA 250 mg twice daily, while group B (5 men, 45 women) received intradermal microinjections of TXA 4 mg/mL every 4 weeks. The treatment continued for 12 weeks in both groups. Percentage reduction in baseline Melasma Area and Severity Index (MASI) was assessed at 4-week intervals, and response was scored as very good (> 75% reduction), good (50% to < 75% reduction), moderate (25% to < 50% reduction), mild (< 25% reduction) or no response.

RESULTS:
The study was completed by 39 patients in group A and 41 patients in group B. Very good response was seen in 25 and 32 patients in groups A and B, respectively, while good response was seen in 14 and 9 patients, respectively. Both treatment methods were equally effective, with an average reduction of MASI at 12 weeks of 77.96 ± 9.39 in group A and 79.00 ± 9.64 in group B. The main adverse effects were mild epigastric discomfort, hypomenorrhea, headache and injection site pain, which did not warrant discontinuation of treatment. Two patients in group A had relapses at 24 weeks.

CONCLUSION:
TXA appears to be an effective and safe treatment for melasma, irrespective of its route of administration.

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Poikiloderma of Civatte: Fast Facts

- Common, benign skin condition
- Prevalence: 1.4% (dermatologic patients)
- Pathogenesis unknown, sun exposure (UVR)
- Symmetric lesions: neck, lateral cheeks, upper chest
- Fair skinned middle age men and women
- Vascular and pigmented dyschromia
- RX: no single effective therapy, lasers, IPL

*J of Drugs in Dermatology 2009;8(6):527-534*
Treatment of Poikiloderma of Civatte With Ablative Fractional Laser Resurfacing: Prospective Study and Review of the Literature

Emily P. Tierney MD and C. William Hanke MD MPH
Laser and Skin Surgery Center of Indiana, Carmel, IN

ABSTRACT

**Background:** Previous laser treatments for Poikiloderma of Civatte (PC) (i.e., Pulsed dye, Intense Pulsed Light, KTP and Argon) are limited by side effect profiles and/or efficacy. Given the high degree of safety and efficacy of ablative fractional photothermolysis (AFP) for photoaging, we set out to assess the efficacy of PC with AFP.

**Design:** A prospective pilot study for PC in 10 subjects with a series of 1–3 treatment sessions. Treatment sessions were administered at 6–8 week intervals with blinded physician photographic analysis of improvement at 2 months post-treatment. Evaluation was performed of five clinical indicators, erythema/telangiectasia, dyschromia, skin texture, skin laxity and cosmetic outcome.

**Results:** The number of treatments required for improvement of PC ranged from 1 to 3, with an average of 1.4. For erythema/telangiectasia, the mean score improved 65.0% (95% CI: 60.7%, 69.3%) dyschromia, 66.7% (95% CI: 61.8%, 71.6%), skin texture, 51.7% (95% CI: 48.3%, 55.1%) and skin laxity, 52.5% (95% CI: 49.6%, 55.4%). For cosmetic outcome, the mean score improved 66.7% (95% CI: 62.6%, 70.8%) at 2 months post treatment.

**Conclusion:** In this prospective study, AFP was both safe and effective for the treatment of the vascular, pigmentary and textural components of PC. The degree of improvement observed in wrinkling, creping and laxity after AFP has not been reported with prior laser treatments for PC.
Poikiloderma of Civatte RX Pearl

- **Tranexamic acid**: antifibrinolytic agent
- Inhibits UV-induced plasmin in keratinocytes
- Decreases melanocyte tyrocinase activity
- Decreases vessels size (pigmented-vascular dyschromia)
- Emerged as adjunct RX for refractory cases
- Oral dose is 650 mg/daily
- Personal observation (nothing published)
Pearls from México

Summary

- CL: oral miltefosine
- Myasis: surgery
- Lice: Xeglyze®, Anti-lice Isdin®, Cetaphil shampoo®
- Kerion: oral terbinafine
- Leprosy: *M lepromatosis* new agent
- Lobomycosis: surgery
- Ashy dermatosis: low dose chronic isotretinoin
- Melasma: oral tranexamic acid
- Poikiloderma of Civatte: oral tranexamic acid
Pearls from México…Thank you!
Email: jdariomtz@yahoo.com.mx