Tropical Dermatology

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Second Edition

EDITED BY

Stephen K. Tyring, MD, PhD
Professor of Dermatology
Microbiology/Molecular Genetics and Internal Medicine
University of Texas Health Science Center
Houston, TX, USA

Omar Lupi, MD, MSc, PhD
Professor of Dermatology
Federal University of the State of Rio de Janeiro (UNIRIO),
Professor of Immunology
Federal University of Rio de Janeiro (UFRI),
Chairman and Titular Professor of Dermatology
General Polyclinic of Rio de Janeiro,
Vice President
Ibero Latin American College of Dermatology (CILAD)
Rio de Janeiro, RJ, Brazil

Ulrich R. Hengge, MD, MBA
Professor of Dermatology, Allergology and Venereology
Department of Dermatology
University of Düsseldorf
Düsseldorf, Germany

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Senior Content Strategist: Belinda Kuhn
Senior Content Development Specialist: Nani Clansey
Content Coordinator: Joshua Mearns
Senior Project Manager: Beula Christopher
Senior Design: Miles Hitchen
Illustration Manager: Karen Giacomucci
Marketing Manager: Kristin Koehler

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I would like to dedicate this book to my wonderful wife, Patricia, for her love and patience.

STEPHEN K. TYRING

I would like to dedicate this book to my beloved wife, Andreia and my sons, João Pedro, and Anna Clara for all their patience and love.

OMAR LUPI

To my beloved son Fynn and his mother Silja.

ULRICH R. HENGGE

LIST OF CONTRIBUTORS

The editor(s) would like to acknowledge and offer grateful thanks for the input of all previous editions' contributors, without whom this new edition would not have been possible.

João Pedro Almeida, MD
Department of Dermatology
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Claudia Pires Amaral Maia, MD, MSc
Senior Clinical Research Fellow
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Caroline Fattori Assed Saad, MD
Dermatologist
Central Army Hospital (HCE)
Rio de Janeiro, RJ, Brazil

Francis T. Assimwe, MD
Department of Dermatology
Mbarara University Hospital
Mbara, Uganda

Ross Barnetson, MD, FRCP, FRACP, FACD, FAAD
Professor Emeritus
Department of Medicine (Dermatology)
University of Sydney
Sydney, NSW, Australia

Col. Paul M. Benson, MD
Department of Dermatology
Walter Reed Army Medical Center
Washington, DC, USA

Priscila Tortelli Bitencourt, MD
Dermatologist
Federal University of the State of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Manuela Boleira, MD, MSc
Senior Clinical Research Fellow
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Francisco G. Bravo, MD, PhD
Associate Professor Pathology
Peruvian University Cayetano Heredia
Lima, Peru

Anne E. Burdick, MD, MPH
Professor of Dermatology
Leprosy Program Director
Associate Dean for TeleHealth and Clinical Outreach
University of Miami Miller School of Medicine
Miami, FL, USA

Mark Burnett, MD
Chief, Pediatric Infectious Diseases
Pediatrics
Tripler Army Medical Center
Honolulu, Hawaii, USA

Ivan D. Camacho, MD
Voluntary Assistant Professor
Department of Dermatology and Cutaneous Surgery
University of Miami Miller School of Medicine
Miami, FL, USA

Andréa Ramos Correa, MD, MSc
Board Certificate
Brazilian Dermatology Society
Belo Horizonte, MG, Brazil

Laura M. Corsini, MD
Dermatology Resident, PGY-3
Division of Dermatology and Cutaneous Surgery
University of Texas Health Science Center San Antonio
San Antonio, TX, USA

Paula Periquito Cosenza, MD, MSc
Senior Clinical Research Fellow
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Paulo Rowilson Cunha, MD, PhD
Chairman
Dermatologia
Faculty of Medicine of Jundiai
Jundiai, SP, Brazil

Bart J. Currie, MD
Professor of Medicine and Head
Tropical and Emerging Infectious Diseases Division
Menzies School of Health Research
Charles Darwin University and Northern Territory Clinical School
Flinders University
Royal Darwin Hospital
Casuarina, NT, Australia

Omar da Rosa Santos, MD, PhD
Emeritus Professor of Nephrology
Federal University of the State of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Guilherme Almeida Rosa da Silva, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Marilda Aparecida Milanez Morgado de Abreu, MD, PhD
Department of Dermatology
Regional Hospital of Presidente Prudente
University of Oeste Paulista
Presidente Prudente, SP, Brazil

Fernanda Costa de Aguiar, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Fernado Raphael de Almeida Ferry, MD, PhD
Professor of Internal Medicine
General Medicine Department
Federal University of the Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Mauricio Mota de Avelar Alchorne, MD
Chairman
Dermatology
Faculty of Medicine of the University Ninth of July
Bauru, SP, Brazil

Luisa Kelmer Côrtes de Barros, MD
Dermatologist
UNESA
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Christiane Maria de Castro Dani, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Ana Maria Mosca de Cerqueira, MD, MSc
Head of Pediatric Dermatology Sector
Hospital Jesus,
Professor of Dermatology
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Renata de Queiroz Varella, MD
Sexually Transmitted Diseases Sector
Fluminense Federal University
Rio de Janeiro, RJ, Brazil

Carolina Barbosa de Sousa Padilha, MD
Dermatologist
Department of Dermatology
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Felipe de Souza Cardoso, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Roberto de Souza Salles, MD, PhD
Full Professor
Discipline of Virology
Department of Microbiology and Parasitology,
Faculty of Medicine
Former Dean
Federal Fluminense University
Rio de Janeiro, RJ, Brazil

Leninha Valerio do Nascimento, MD, PhD
Professor of Dermatology
Central Army Hospital
Rio de Janeiro, RJ, Brazil

Antonio Carlos Francesconi do Valle, MD, PhD
Senior Researcher
Evandro Chagas Hospital
Oswaldo Cruz Foundation (FIOCRUZ)
Rio de Janeiro, RJ, Brazil

Jose Eleutério Jr., MD, PhD
Professor
Department of Maternal and Child Health,
Faculty of Medicine
Federal University of Ceará, Board member
Brazilian Society of Sexually Transmitted Diseases (SBDST), Member
International Academy of Cytology
Rio de Janeiro, RJ, Brazil

Lynne Elson, PhD, MPH
Consultant and Founder
WAJIMIDA Jigger Campaign
Watamu, Kenya

Dirk M. Elston, MD
Professor and Chairman
Department of Dermatology and Dermatologic Surgery
Medical University of South Carolina
Charleston, SC, USA

Charles D. Ericsson, MD
Professor of Medicine
Dr. and Mrs. Carl V. Vartian Professor of Infectious Diseases
University of Texas Medical School at Houston
Houston, TX, USA

Hermann Feldmeier, MD, PhD
Professor of Tropical Medicine
Charite University Medicine
Berlin, Germany

Gunter Hans Filho, MD, PhD
Assistant Professor of Dermatology
University of Mato Grosso
Campo Grande, MS, Brazil

Ulrika Fillinger, MSc, PhD
Public Health Entolomogist
International Centre of Insect Physiology and Ecology
Mbita, Kenya;
London School of Hygiene and Tropical Medicine
London, UK

Valeska A. Francesconi, MD
Dermatologist
Tropical Medicine Foundation Dr. Heitor Vieira Dourado,
Professor of Dermatology
Amazonas State University
Manaus, AM, Brazil

Fabio Francesconi, MD
Dermatology Researcher
Department of Dermatology
Amazon Tropical Medicine Foundation,
Assistant Professor
Department of Dermatology
Amazon Federal University
Manaus, AM, Brazil

Glaucia Francesconi, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Eduardo Gotuzzo, MD
Professor of Medicine
Alberto Hurtado Faculty of Medicine,
Director
Alexander von Humboldt Institute of Tropical Medicine
Peruvian University Cayetano Heredia
Lima, Peru

Maria G. Guzman, MD, PhD
Professor
Head Virology Department
"Pedro Kouri" Tropical Medicine Institute (IPK)
Havana, Cuba

Vidal Haddad Jr., MD, PhD
Associate Professor
Botucatu Medical School
University Estadual Paulista
São Paulo, SP, Brazil

Ulrich R. Hengge, MD, MBA
Professor of Dermatology, Allergology and Venereology
Department of Dermatology
University of Düsseldorf
Düsseldorf, Germany

Adriana Hozannah, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

David B. Huang, MD, PhD
Assistant Professor
Internal Medicine, Division of Infectious Diseases
Rutgers New Jersey Medical School
Newark, NJ, USA

Alex Panizza Jalkh, MD
Federal University of Amazonas
Manaus, AM, Brazil

Marcio Lobo Jardim, MD, PhD (†)
Titural Professor of Dermatology
Federal University of Pernambuco (UFPE)
Recife, PE, Brazil

Sam Kalungi, MBChB, MMED, PhD
Consultant
Department of Pathology
Mulago Hospital
Kampala, Uganda

Ratnakar Kamath, MD
Department of Dermatology
Venereology and AIDS Medicine
G.T. Hospital, Grant Medical College
Mumbai, MH, India

Laila Klotz, MD
Dermatologist
General Polyclinic of Rio de Janeiro Dermatology Service
Rio de Janeiro, RJ, Brazil

Christine Ko, MD
Associate Professor of Dermatology and Pathology
Yale University
New Haven, CT, USA

Ramya Kollipara, MD
Dermatology Resident
Department of Dermatology
Texas Tech University Health Sciences Center
Lubbock, TX, USA

Gustavo Kouri, MD, PhD, DRSc
Head Professor and Head Researcher
Department of Virology
"Pedro Kouri" Tropical Medicine Institute (IPK)
Havana, Cuba

Luiza Laborne, MD
Dermatologist
Holy House of Belo Horizonte
Belo Horizonte, MG, Brazil

Mauro Romero Leal Passos, MD, MSc, PhD
Full Professor
Department of Microbiology and Parasitology
Chief, Sector of Sexually Transmitted Diseases
Faculty of Medicine
Federal Fluminense University,
President
Brazilian Society of Sexually Transmitted Diseases (SBDST)
Rio de Janeiro, RJ, Brazil

Peter Leutscher, MD
Danish Bilharziasis Laboratory
Jaegersborg, Charlottenlund, Denmark

Nelson Eddi Liou, MD
Assistant Professor
Otolaryngology Head and Neck Surgery
Baylor College of Medicine
Houston, TX, USA

Omar Lupi, MD, MSc, PhD
Professor of Dermatology
Federal University of the State of Rio de Janeiro (UNIRIO),
Professor of Immunology
Federal University of Rio de Janeiro (UFRI),
Chairman and Titular Professor of Dermatology
General Polyclinic of Rio de Janeiro
Vice President,
Ibero Latin American College of Dermatology (CILAD)
Rio de Janeiro, RJ, Brazil

Jackson Machado-Pinto, MD, PhD
Chairman
Dermatology
Holy House of Belo Horizonte
Belo Horizonte, MG, Brazil

Pascal Magnussen, MD
Senior Researcher
Danish Bilharziasis Laboratory
Jaegersborg, Charlottenlund, Denmark

Janak K. Maniar, MD
Professor
Dermatology and STD
K J Somaiya Medical College
Consultant
HIV Medicine
Jaslok Hospital and Research Centre
Mumbai, MH, India

Priscila Coelho Mariano, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Silvio Alencar Marques, MD, PhD
Professor
Department of Dermatology and Radiotherapy
Botucatu School of Medicine
São Paulo State University (Unesp)
São Paulo, SP, Brazil

Michael R. McGinnis, PhD
Director
Medical Mycology Research Center
Professor of Pathology, Dermatology, Microbiology and Immunology
Department of Pathology
University of Texas Medical Branch
Galveston, TX, USA

Jeffrey A. Meixner, PhD
Associate Professor
Clinical Laboratory Science
Winston Salem State University
Winston Salem, NC, USA

Rojelio Mejia, MD
Assistant Professor of Infectious Diseases and Pediatrics
Laboratory of Clinical Parasitology and Diagnostics
National School of Tropical Medicine
Baylor College of Medicine
Houston, TX, USA

Luciana Mendes, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Vineet Mishra, MD
Director of Mohs Surgery and Procedural Dermatology
Division of Dermatology and Cutaneous Surgery
University of Texas Health Science Center San Antonio
San Antonio, TX, USA

Livia Montelo, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

William J. Moss, MD, MPH
Associate Professor
Epidemiology Department
Johns Hopkins Bloomberg, School of Public Health
Baltimore, MD, USA

Rogerio Neves Motta, MD, MSc
Assistant Professor of Internal Medicine and Infectious Diseases
Federal University of State of Rio de Janeiro (UNIRIO)
Rio de Janeiro, RJ, Brazil

Frank Mwesigye, MD
Senior Consultant Ophthalmologist
Department of Ophthalmology
Mulago National Referral Hospital
Kampala, Uganda

Edilbert Pellegrini Nahn Jr., MD
Professor of Internal Medicine
Faculty of Medicine
Federal University of Rio de Janeiro, Campus Macaé,
Professor of Dermatology
Faculty of Medicine of Campos, RJ,
Board Member
Brazilian Society of Sexually Transmitted Diseases (SBDST)
Rio de Janeiro, RJ, Brazil

Josephine Nguyen, MD
Department of Dermatology
Stanford University
Stanford, CA, USA

Joao Paulo Niemeyer-Corbellini, MD
Dermatologist
Federal University of Rio de Janeiro (UFRJ)
Rio de Janeiro, RJ, Brazil

Timothy O'Brien, MB, BS, FACD
Visiting Consultant
Dermatology
Geelong Hospital
Geelong, VIC, Australia

Mina Pastagia, MD, MS
Laboratory of Bacterial Pathogenesis and Immunology
The Rockefeller University
New York, NY, USA

Seema Patel, MD
Visiting Scientist
Department of Pathology
University of Texas Medical Branch
Galveston, TX, USA

Wingfield Rehmus, MD, MPH
Clinical Instructor, Co-Director of Clinical Trials Unit
Department of Dermatology
Stanford University
Stanford, CA, USA

Joachim Richter, MD, DTM&PH
Adjunct Professor
University Hospital
Tropical Medicine Unit
Gastroenterology, Hepatology and Infectious Diseases
Heinrich-Heine-University
Düsseldorf, Germany

Mario Cesar Salinas-Carmona, PhD
Professor of Immunology
Head of the Department of Immunology
University Hospital, UANL
Monterrey, Nuevo Leon, Mexico

David M. Scollard, MD, PhD
Director (retired)
National Hansen's Disease Programs
Baton Rouge, LA, USA

Ivan Semenovitch, MD, MSc, PhD
Professor of Dermatology
Department of Dermatology
General Polyclinic of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

Michael B. Smith, MD
Director
Division of Clinical Microbiology
Department of Pathology
University of Texas Medical Branch
Galveston, TX, USA

Sinesio Talhari, PhD
Professor
Department of Dermatology
Federal University of Amazonas
Manaus, AM, Brazil

Carolina Talhari, MD, PhD
Director of Studies and Research at the Alfredo da Matta Foundation
University of the State of Amazonas
Nilton Lins University
Manaus, AM, Brazil

Lynnette Tumwine, MBChB, MMED
Honorary Lecturer
Department of Pathology
Faculty of Medicine
Makerere University
Kampala, Uganda

Stephen K. Tyring, MD, PhD
Professor of Dermatology
Microbiology/Molecular Genetics and Internal Medicine
University of Texas Health Science Center
Houston, TX, USA

Resham Vasani, MD, DNB, FCPS, DDV
Assistant Professor
Department of Dermatology, Venereology and Leprosy
K J Somaiya Medical College and Research Centre
Mumbai, MH, India

John Verrinder Veasey, MD
Physician/Dermatologist
Clinic of Dermatology
Holy House of São Paulo Hospital
São Paulo, SP, Brazil

Virgínia Vilasboas, MD
Board Certificate
Brazilian Dermatology Society
Rio de Janeiro, RJ, Brazil

Oliverio Welsh, MD
Emeritus Professor Active
Dermatology Department
University Hospital, UANL
Monterrey, Nuevo Leon, Mexico

Anthony White, MBBS, FACD
Clinical Senior Lecturer
University of Sydney
Bondi Junction
Sydney, NWS, Australia

Mauricio Younes-Ibrahim, MD, PhD
Associate Professor
Internal Medicine
University of the State of Rio de Janeiro
Rio de Janeiro, RJ, Brazil

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PREFACE

During the decade since the publication of the first edition of *Tropical Dermatology*, we have seen outbreaks of tropical infectious diseases in temperate parts of the world that local physicians and other health care workers expected to encounter only in textbooks – for example, diseases caused by the Ebola virus in the United States of America and Europe, as well as Chikungunya and Zika viruses throughout the Western Hemisphere. These arboviruses have followed a path similar to that taken by the West Nile virus in the late 1990s. During the past year, however, we have also learned that insect vectors (e.g. mosquitoes) are no longer the only source of arbovirus infections (i.e. sexual transmission of the Zika virus). Furthermore, tropical diseases such as dengue have spread further into temperate locations. In this edition we have expanded the sections of this book dealing with these emerging infectious diseases and have updated sections on other infectious diseases as well as non-infectious cutaneous problems in the tropical world.

Patients with tropical diseases, however, are presenting to physicians in temperate areas with increasing frequency due to other reasons, such as increased travel to tropical countries for work or pleasure. In addition, wars as well as social and economic difficulties are resulting in more refugees and immigrants fleeing their homelands to seek refuge in temperate counties – as the ongoing Syrian war so sadly illustrates and has resulted in a marked increase of leishmaniasis cases in Europe. Likewise, adoptees are frequently born in tropical lands and may be asymptomatic carriers of infectious diseases.

Some tropical diseases were common in temperate lands until the 21st century, but became much less common owing to vaccination (e.g. measles, rubella, mumps and chickenpox). Measles, which is associated with high rates of morbidity and mortality in the tropics, where malnutrition is common but vaccination is rare, is becoming less prevalent as a result of improved conditions. Paradoxically, however, the prevalence of measles has increased in the past 2 years in the United States of America owing to non-compliance with recommended vaccinations. Most cases of measles in North America and Europe are imported, often resulting from unvaccinated citizens of these areas returning from the tropics and spreading this highly infectious virus to others.

Although infectious diseases receive the most media attention, non-infectious diseases are more often the cause of cutaneous problems in the returned traveler. Examples of these non-infectious sources of skin problems include excessive sun exposure and mucocutaneous reactions to medications taken for prophylaxis or therapy, including phototoxic reactions. Exposure to tropical plants may cause allergic reactions or make the patient photosensitive (e.g. photophytodermatitis). Contacts with invertebrates and other animals as well as marine and freshwater organisms are also frequent causes of cutaneous complaints.

It is important to note, however, that most physician visits by the returned traveler for mucocutaneous problems are unrelated to the patient's travel or national origin, but rather are the same conditions seen daily in patients who have never left their local communities. Therefore, the goal of this second edition of *Tropical Dermatology* is to provide a guide for health care workers to the mucocutaneous manifestations of tropical diseases. In order to formulate a differential diagnosis, the morphology and distribution pattern of the skin lesions must be considered in view of the patient's symptoms, physical examination, general medical condition and exposure history as well as the vaccination record and current medications. Laboratory and histology results can often be used to reach a diagnosis and help determine the appropriate management.

Stephen K. Tyring, MD, PhD
Houston
Omar Lupi, MD, MSc, PhD
Rio de Janeiro
Ulrich R. Hengge, MD, MBA
Düsseldorf

1 Syndromal Tropical Dermatology

STEPHEN K. TYRING

CHAPTER OUTLINE

Introduction

With increasing numbers of persons from industrialized, temperate countries traveling and/or working in tropical lands, there is a marked need for physicians to be able to diagnose accurately and treat tropical diseases with mucocutaneous manifestations. While some studies demonstrate that approximately one-third to two-thirds of travelers returning from tropical countries experience some health problem, diarrhea is the most prevalent complaint. Mucocutaneous problems, however, are among the top five health complaints of the returned traveler, and comprise 10–15% of health concerns of persons returning from the tropics.[1]

During international conflicts, soldiers from North America, Europe, and Australia are often required to serve in tropical lands and sometimes develop diseases not familiar to physicians of their home countries. This was the case for French soldiers serving in Vietnam in the 1950s and American soldiers serving there in the 1960s and 1970s. Recently hundreds of American and allied troops serving in Iraq and Afghanistan have developed "Baghdad boils" (i.e., leishmaniasis), transmitted by sand fly bites (Fig. 1-1).

Likewise, millions of persons from tropical countries now live and work in temperate lands and may present with medical problems with which the physician is not familiar. Whereas the cutaneous problems in the returned traveler are frequently the result of infectious diseases, skin diseases of non-infectious etiologies usually predominate. Such non-infectious sources of skin problems include excessive sun exposure, cutaneous reactions to medications taken for prophylaxis (including phototoxic reactions) or exposures to marine, freshwater, or other irritants. Furthermore, whether it is the traveler or the immigrant presenting to the physician, many cutaneous complaints are unrelated to the person's travel or national origin, but are the same conditions seen daily in every physician's office. Therefore, the physician should not ignore the common sources of dermatologic problems while searching for an exotic etiology.

Another, somewhat recent, source of patients with tropical skin diseases is adoptees who frequently originate in Central America or Southeast Asia. These children could be infected with organisms having a long incubation period that may not have been detected by physical examinations and are not preventable by available vaccines.

Tropical infections in temperate lands, however, are not totally unique to travelers. For example, the outbreak of monkeypox in Wisconsin, USA, in 2003 was a result of prairie dogs acquiring the virus from Gambian rats housed in adjacent cages in pet stores. The prairie dogs then transmitted the infection to humans who had never been near the usual range of monkeypox (i.e., central Africa).

Occasionally, the patient with a tropical disease is neither the traveler nor someone exposed to an animal carrying an infectious agent. The carrier may be a friend or relative who is a returned traveler who has acquired a tropical infection and who has not yet developed signs or symptoms. This possibility has recently been given much attention due to the potential spread of severe acute respiratory syndrome (SARS), which originated in China in 2002, Middle East respiratory syndrome (MERS),

Figure 1-1 Female *Phlebotomus* spp. sand fly, a vector of leishmaniasis. *(Courtesy of World Health Organization.)*

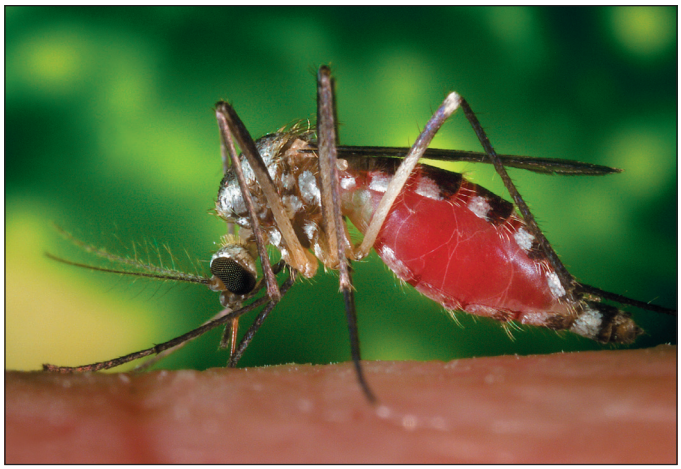

Figure 1-2 *Ochlerotatus (Aedes) triseriatus* mosquito feeding on a human hand. *(Courtesy of Centers for Disease Control and Prevention.)*

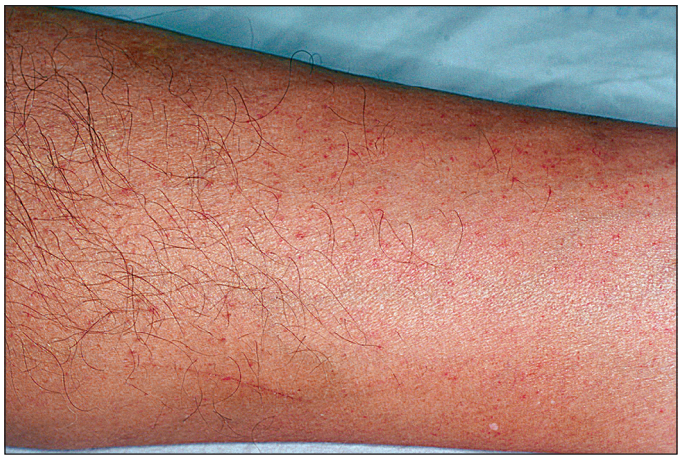

Figure 1-3 Erythematous macules associated with West Nile virus infection. *(Courtesy of Dr David Huang.)*

first reported in Saudi Arabia in 2012, or avian influenza virus. On the other hand, contaminated food may have originated in a tropical or subtropical area, such as when oysters from the Gulf of Mexico are shipped to the Midwest USA and are consumed raw. The resulting *Vibrio vulnificus* or hepatitis A infection thus produces gastrointestinal and cutaneous manifestations in individuals who may not have visited the source of the shellfish. Therefore, it is always important to ask about new pets, changes in diet, or any other change in persons with a suspected tropical disease. On the other hand, travelers may have purchased non-consumable items that are the source of their dermatoses. For example, animal skins used for rugs or blankets may be the source of anthrax. A non-infectious cause may include nickel-containing jewelry to which the patient has developed contact dermatitis.

Whereas travelers naturally fear large carnivores while on camera safari, or sharks and a variety of other aquatic animals while swimming or diving, it must be remembered that the animal (indirectly) responsible for most morbidity and mortality is the mosquito (i.e., malaria, dengue, etc.) (Fig. 1-2). An example of a mosquito-borne disease that was considered primarily "tropical" in the recent past but is now relatively common in much of North America is infection with the West Nile virus (Fig. 1-3).

Sometimes the skin findings on physical examination are not the reason for the visit to a physician or even the patient's complaint. Such skin findings may be cultural, such as tattoos or scarification, or the result of the use of kava or of chewing betel nuts. Some cultural practices, however, would be considered abuse in industrialized countries, but are widely accepted religious/cultural practices in certain lands. An example of such practice is female circumcision, which is practiced in many countries in sub-Saharan Africa. On the other hand, the skin changes may be much more benign, transient, and may even be the result of previous therapies, such as cupping and coining, widely practiced by immigrants from Southeast Asia.

Considerations for deciding the differential diagnosis of cutaneous manifestations of tropical diseases and/or of diseases acquired while traveling must be based not only on the type of lesions and systemic symptoms but also on the patient's history of travel. Because the incubation period of various infectious diseases differs widely, it is important to know when the person traveled. For frequent travelers, the history may become complex if patients report having visited many destinations within the past few months. Because vectors differ with the climate, the season of travel is also noteworthy. Even in a tropical country where the temperature is always hot or warm, there may be a dry season and a rainy season. Because seasons are reversed north and south of the Equator, it is important to know the season at the destination. The duration of the stay is significant, not only because a longer stay increases the chance of acquiring an infectious disease, but also because it tells the physician whether the person was in the tropics during the incubation period of the suspected disease. Whether the visitor was only in an urban environment or also in a rural area is relevant. Whereas a sexually transmitted disease (STD) could be acquired in either location, an arbovirus or a zoonosis might be more likely in a rural situation. The altitude of the destination could provide a clue to the etiology of the skin condition, as could the type of sleeping condition. For example, a sexually transmitted disease could easily be acquired in a five-star hotel, but an infection transmitted by a flea, louse, or mite would be more likely in someone who had slept on the ground and/or in a tent.

The type and preparation of food and drink consumed by the traveler would not only help explain gastrointestinal symptoms, but could also be a clue to cutaneous signs (i.e., unsafe drinking water or milk or raw or undercooked meat, fish, or shellfish).

A list of the patient's current and recent medications can be very useful and should include prescription drugs, illicit drugs, and herbal remedies, because the source of the cutaneous problem may not be directly related to the travel destination, but rather may be due to medications taken to prevent travel-related illnesses. For example, many antimalarials, such as chloroquine, mefloquine, proguanil, quinine, and halofantrine, can cause cutaneous reactions, and chloroquine, doxycycline, and quinine can cause photosensitivity. Interestingly, chloroquine can worsen psoriasis. A number of agents taken to treat or prevent diarrhea can also cause cutaneous reactions, such as quinolones (ciprofloxacin, ofloxacin, sparfloxacin, levofloxacin), furazolidone, metronidazole, trimethoprim-sulfamethoxazole and bismuth sulfate; quinolones are particularly likely to produce photosensitivity. Anthelmintic medications, such as

ivermectin, albendazole, and diethylcarbamazine, can also produce pruritus and rash. Even diethyltoluamide (DEET), used to prevent arthropod bites, can cause an irritant dermatitis when used in high concentrations.

Because many medications in tropical countries are sold over the counter and/or have different trade names to those in industrialized lands, patients are not always certain what they have received if treated during their travel. Likewise, an injection or transfusion given in a tropical country might also carry an increased risk of contamination. A similar risk might be taken by having acupuncture, tattoos, or body piercing in tropical lands, but these procedures can be hazardous even in industrialized countries because the first intervention is occasionally done by non-medical personnel and the other two are almost never done by medically trained persons.

A history of pretravel vaccinations and/or immunoglobulins would be useful for possible exclusion of certain suspected etiologies. For example, if the yellow fever vaccine and the hepatitis A and/or B vaccine series were administered in sufficient time before the travel, it is less likely that these viruses were the source of the medical complaint.

The traveler's occupational or recreational exposure to dirt, water, or animals can be an important component of the history. An animal bite or scratch should be easy to remember, but the bite of many arthropods may not even be noticed until after a cutaneous reaction has appeared and the fly, mite, or flea that is responsible has moved on to the next victim. Exposure to some animals may be more indirect. For example, the spelunker (cave explorer) may inhale aerosolized bat guano and develop rabies without ever touching a bat. A history of swimming, boating, or surfing can be a clue to an aquatic/marine etiology. Such fresh- or brackish-water activities may increase the risk of infection with schistosomiasis or with free-living ameba, whereas marine activities may be associated with jellyfish stings, contact with the venomous spines of certain fish, or irritant dermatitis from fire coral. A preexisting skin abrasion or laceration, or a puncture wound from a sea urchin or sting ray, may result in a secondary bacterial infection.

Thus, a complete medical and travel history and physical examination are imperative in helping to narrow the differential diagnoses in the returned traveler, the immigrant, or the adoptee with a tropical origin. The qualitative and quantitative nature of the skin lesions is very important and is discussed in detail later in this chapter. Specific attention must be given to the age of the patient as well as to the person who is immunocompromised due to human immunodeficiency virus (HIV), internal malignancy, organ transplantation, or another iatrogenic source of immunocompromise. Blood tests (e.g., liver/kidney function tests, complete blood counts [CBC] with differentials, urinalysis, skin scraping, biopsy, and/or culture) are often necessary to confirm the diagnosis. A recent example of the importance of knowing both the patient's national origin and their immune status was seen when an HIV-seropositive man from Myanmar presented with the first case of *Penicillium marneffei*, recently renamed *Talaromyces marneffei*,[2] reported from Houston, TX (Fig. 1-4).

Many viral diseases that were not considered "tropical" 50 years ago are now much more frequently seen in immigrants from tropical countries, or in travelers who did not receive their recommended childhood vaccines. Three common examples are measles, rubella, and hepatitis B. Until the 1960s, measles and rubella were very common sources of infection in

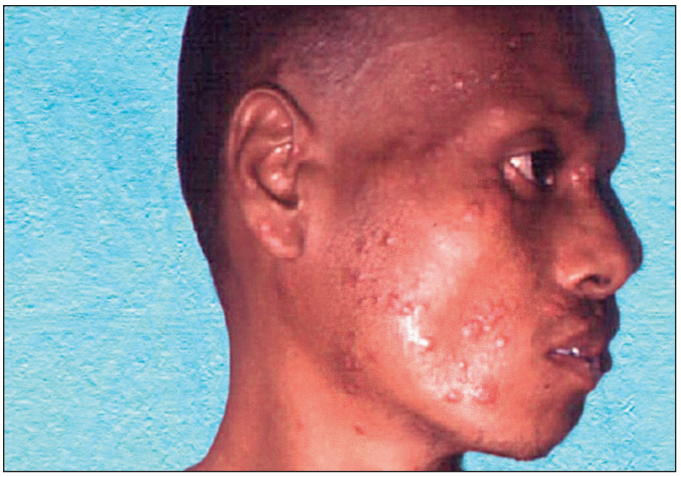

Figure 1-4 Umbilicated papules of the face secondary to *Penicillium marneffei* in a human immunodeficiency virus (HIV)-seropositive patient from Myanmar who presented to a clinic in Houston, TX. *(Courtesy of Dr Khanh Nguyen.)*

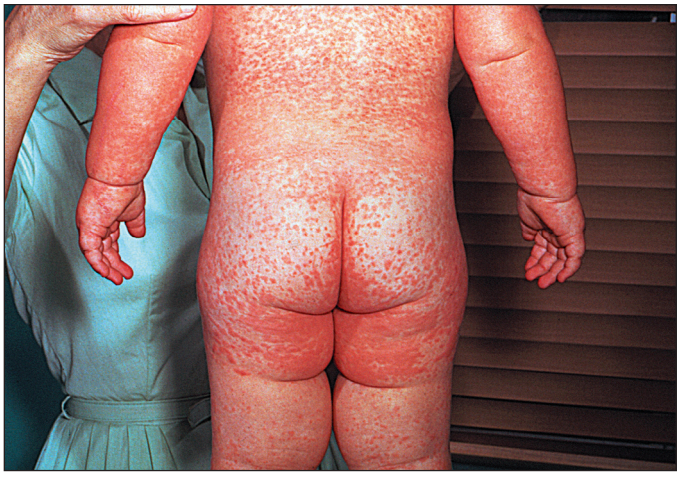

Figure 1-5 Erythematous macules of measles on day 3 of the rash. *(Courtesy of Centers for Disease Control and Prevention.)*

temperate countries, but in the 21st century they have become rare in industrialized countries, except for imported cases. Due to non-compliance with recommended vaccinations, however, 644 measles cases were reported in the US in 2014, the highest number in the 21st century.[3] A single outbreak in early 2015, resulting from an infected person visiting Disneyland, California, resulted in 125 cases.[4] Worldwide, however, almost one million children die of measles annually (Fig. 1-5) and rubella still causes many congenital abnormalities. Measles is still the number one vaccine-preventable killer of children in the world. Morbidity and mortality are often the result of secondary bacterial infections developing in malnourished infants with measles (Fig. 1-6). In east Asia, sub-Saharan Africa, and many other parts of the tropical world, hepatitis B is very common and a major source of morbidity and mortality. Although measles, rubella, and hepatitis B should not be a problem in the immunized traveler, many travelers have not received the proper immunizations because they or their parents had unfounded concerns about the safety of the vaccines. This problem continues to grow as more people reach child-bearing age without

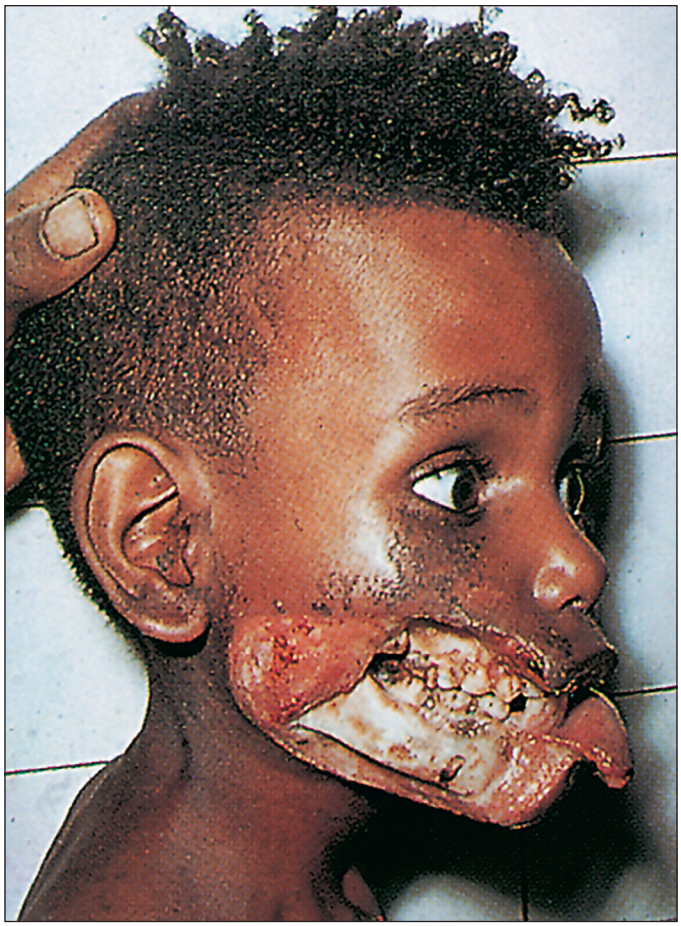

Figure 1-6 Cancrum oris (Noma) of the facial region is associated with malnutrition and poor oral hygiene in the presence of *Treponema vincentii* plus Gram-negative bacteria following a systemic disease such as measles. *(Reproduced from Peters W. and Pasvol G. (eds).* Tropical Medicine and Parasitology, *5th edition, Mosby, London 2002, image 870.)*

ever knowing anyone who has suffered from the childhood diseases common in the first half of the 20th century. Therefore, they do not understand that the approved vaccines are a million-fold safer than the diseases they are designed to prevent.

Sexually Transmitted Diseases

STDs should be considered at the top of the differential diagnoses when a patient presents with genital lesions and/or urogenital discharge.[5–7] Although many of the same considerations would be true whether or not the patient was a recent traveler, certain factors should be given attention in travelers:

- Was the person traveling without his/her spouse/family and therefore outside his/her usual social structure?
- Did the person travel to countries where sex workers are readily available? Although sex workers are available in most parts of the world, legally or illegally, the traveler might be less likely to acquire an STD in Mecca during a haj than in Amsterdam, Bangkok, or Nairobi, where sex workers are very prevalent.
- Did the person attend parties where large amounts of alcohol and/or drugs were consumed (e.g., "spring break" in the USA)?
- If the traveler is strongly suspected of having an STD, did he/she visit a destination where chancroid, granuloma inguinale (GI), or lymphogranuloma venereum (LGV) (L serovars of *Chlamydia trachomatis*) is prevalent? If so, the diagnostic tests and therapy might need to be expanded beyond those under consideration for STDs acquired in temperate lands.

When one STD is confirmed, there is an increased possibility of acquisition of additional STDs. Not only is this the case because the source partner(s) may have had multiple STDs, but also because having certain STDs makes a person more susceptible to other STDs. The best example of this phenomenon is the two- to fivefold greater risk of acquiring HIV if the person with a genital ulcer disease (GUD) has sex with an HIV-positive individual. The reasons for this increased risk include the reduced epithelial barrier in all GUDs, as well as the infiltrate of CD4+ cells in certain GUDs such as genital herpes. These CD4+ cells are the targets for HIV infection. Genital herpes is the most prevalent GUD in industrialized countries. In fact, the Centers for Disease Control and Prevention (CDC) estimate that there are 45 million herpes simplex virus type 2 (HSV-2)-seropositive persons in the USA. In the tropics, chancroid has been the most frequently diagnosed GUD, followed by syphilis and genital herpes, but the last two diseases are becoming more prevalent in certain tropical countries. Depending on the travel destination, LGV and GI must also be considered. The dates and duration of travel are important components of the history because the primary clinical presentation of all these GUDs ranges between 2 and 3 days (genital herpes and chancroid) and 4 weeks (syphilis and GI).

Currently, the World Health Organization (WHO) estimates that there are 46 million HIV-seropositive persons in the world. Many of these people have GUD, which may be changed both qualitatively and quantitatively by HIV. Therefore the traveler may have a "non-classical" presentation of GUD. In addition, it should be remembered that the signs and symptoms of GUD can also appear on the perianal area/buttock or in or around the mouth. Other locations are possible, but less likely.

In general, however, multiple painful, usually bilateral, vesicles that progress to ulcers on skin or start as ulcers on mucous membranes, then heal over after 3–4 weeks without therapy or within 2–3 weeks with antiviral therapy, are consistent with genital herpes. Because most true primary cases of genital herpes recur, a history of multiple recurrences of the vesicles or ulcers is highly consistent with genital herpes. This diagnosis can be confirmed by viral culture or serology. In the absence of these tools, a useful test is the Tzanck smear, which usually demonstrates multinucleated giant cells in herpetic lesions, but is of low sensitivity and specificity. Genital herpes, however, can present many diagnostic dilemmas because the first recognized clinical occurrence is often not the result of a recent infection but rather represents a first-episode, non-primary outbreak. Whereas a true primary outbreak of genital herpes is usually consistent with acquisition of the virus 2 days to 2 weeks previously, a first-episode, non-primary outbreak may be consistent with an infection at any time in the past. In this case, the patient's recent travel history may be of less importance than his/her sexual encounters of the more-distant past.

Although syphilis is much more common in many developing countries than in the USA, western Europe, or Australia, a lack of travel certainly does not exclude syphilis. This diagnosis should be suspected when the patient presents with a single,

non-tender, genital, perianal, or lip ulcer associated with non-tender lymphadenopathy. Whereas chancroid is uncommonly reported in industrialized countries, it is very common in the tropics. It is usually characterized by one or more painful genital ulcers and painful lymphadenopathy. In LGV the primary lesion is usually very transient and is often not seen. The clinical presentation is usually that of tender inguinal lymphadenopathy, sometimes with a suppurating bubo. The diagnosis of GI is very rarely made outside the tropics. The presentation is usually that of one or more non-tender genital ulcers with inguinal swelling. If any of these bacterial GUDs is suspected, the appropriate diagnostic tests must be initiated (i.e., serology for syphilis and LGV, culture for chancroid and LGV, or tissue examination for GI) and the appropriate antibiotic started.

Whereas a history of multiple recurrences of genital vesicles or ulcers would be consistent with genital herpes, a more difficult scenario is represented by the patient who reports a single outbreak of non-specific genital signs and symptoms that are resolved by the clinic visit. A western blot or type-specific serologic test for HSV-2 would determine whether the person was infected with this virus, but it would not be definitive proof that that HSV-2 was responsible for the resolved outbreak. For example, a HSV-2 serologically positive person may acquire syphilis, but the genital ulcer may resolve without therapy, or with inadequate treatment, before the clinic visit at home. Thus, a careful history may reveal the need for serology for HSV-2 as well as for syphilis. Because HIV can be acquired concomitantly with or subsequently to these GUDs, but not produce genital manifestations, HIV testing should be conducted as well. Although many patients may be hesitant to admit sexual activity that puts them at risk for STDs, others will worry about these activities following travel (or any time) and ask to be tested for "everything." If the sexual encounter with a new partner has been very recent, the serologic test may be false negative because serology for syphilis, HIV, or HSV-2 may require weeks to become positive in the majority of persons after initial infection.

Patients who ignore their primary genital lesions because of denial or difficulty finding medical care during their travels may believe that the problem is gone because the lesion has resolved. If syphilis is the cause of the GUD, it may reappear weeks or months later as non-genital cutaneous manifestations in the form of secondary (or tertiary) syphilis (Fig. 1-7). A careful history regarding the primary lesion may lead to the appropriate diagnostic tests and therapy. Some STDs may not produce any genital signs or symptoms and the disease may be diagnosed long after the travel (or the non-travel acquisition), making it more difficult to find the source of the infection. Although over 90% of HIV-seropositive persons eventually develop indirect mucocutaneous manifestations of infection, the primary rash of seroconversion (if present) is not noticed by most patients. Therefore, the diagnosis is usually made when the patient develops systemic signs and symptoms (e.g., fever, chills, diarrhea, weight loss, lymphadenopathy) and/or develops one or more of the opportunistic infections, neoplasms, or inflammatory skin problems frequently seen in HIV patients. Similar to HIV, primary infection with hepatitis B rarely produces genital lesions. Diagnosis is usually made long after infection due to systemic symptoms or non-specific skin changes such as jaundice. Hepatitis B was the first STD for which a prophylactic vaccine was available. Therefore, a history of successful hepatitis B vaccination makes this diagnosis less likely.

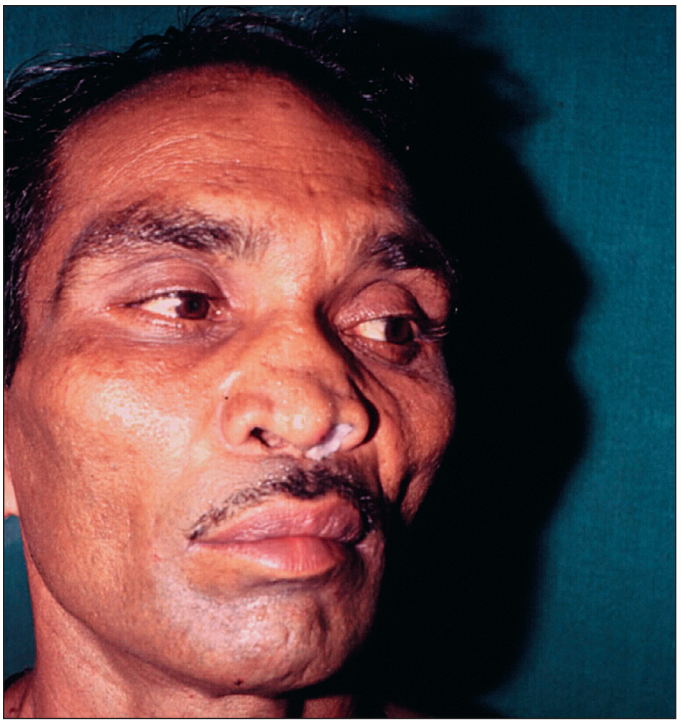

Figure 1-7 Saddle-nose deformity due to tertiary syphilis in a human immunodeficiency virus (HIV)-seropositive man in India. *(Courtesy of Dr J. K. Maniar.)*

Fortunately, human papillomavirus (HPV) vaccines are now widely available, which can prevent up to nine of these sexually transmitted viruses.

Although the pustules of disseminated gonococcemia are distinctive, the consequences of untreated *Neisseria gonorrhoeae* (gonococcus) are usually pelvic inflammatory disease, epididymitis, proctitis, pharyngitis, or conjunctivitis. Pelvic inflammatory disease can also be caused by *Chlamydia trachomatis* (non-L serovars), *Mycoplasma hominis*, or various anaerobic bacteria. The non-L serovars of *C. trachomatis* can also cause epididymitis, proctitis, and conjunctivitis. Pharyngitis can also be due to HSV-2 or *Entamoeba histolytica*. The initial presentation of GC, *C. trachomatis* (non-L serovars), *Ureaplasma urealyticum*, *Mycoplasma genitalium*, *Trichomonas vaginalis*, or even HSV-2 may be urethritis. Vaginal discharge can be caused by any of these organisms as well as by *Candida albicans*, *Gardnerella vaginalis*, peptostreptococci, *Bacteroides* spp. or *Mobiluncus* spp. These organisms can usually be diagnosed by smear, wet-mount, DNA detection, serology, or culture. Antimicrobial therapy is usually initiated based on the physical examination and smear or wet-mount and modified, as needed, when other laboratory studies are completed.

Infection with HPV is one of the most common STDs in the world, but the clinical implications of the infection vary widely. There are over 20 HPV types that can cause genital lesions, but most infections do not result in any visible lesions. Because the incubation period of HPVs can be months, or even years, if and when genital lesions do develop, it is often very difficult for the patient to determine the source partner. Therefore, it is usually a challenge for the physician to relate HPV lesions to travel, especially recent travel. Non-oncogenic genital HPV, such as types 6 and 11, result in condyloma acuminatum, which can be treated with cytodestructive therapy, surgery, or with the

immune response modifier imiquimod. Oncogenic genital HPV, such as types 16 and 18, can result in anogenital cancer, the most prevalent of which is cervical cancer. Cervical cancer is the second most prevalent cancer killer of women in the world and over 99% of all cervical cancer is caused by HPV. Most cervical cancer deaths are in tropical countries, making HPV one of the world's deadliest tropical diseases (although rarely listed with the other major tropical diseases). There are many reasons why more cervical cancer deaths occur in tropical countries. First, in industrialized countries most women receive regular Pap smears, which result in early detection and subsequent therapy of cervical abnormalities, thus reducing progression to cervical cancer. If cancer is detected, surgery, radiation therapy, or chemotherapy is available. In addition HPV vaccines are now widely available in most industrialized countries. In most tropical countries, regular Pap smears are not the standard of care. Therefore, cervical cancer is often detected too late for successful intervention, even if this is available. Second, there appears to be a genetic susceptibility that allows oncogenic HPV to progress to malignancy. This genetic susceptibility appears to be more prevalent in certain tropical countries. The rarity of male circumcision in many tropical countries appears to be a risk factor for the development of cervical cancer in these males' partners. Third, most of the world's estimated 46 million HIV-seropositive individuals live in tropical countries where no antiretroviral therapy is available. Not only is cervical cancer an acquired immunodeficiency syndrome (AIDS)-defining illness in HIV-seropositive women, but the same HPV can also cause anal cancer, which is a major problem in homosexual men with HIV.

Molluscum contagiosum (MC) is a poxvirus that can be sexually transmitted, resulting in wart-like lesions on the genitalia. In contrast to HPV, however, MC does not progress to malignancy. Like condyloma acuminatum, however, MC can be treated with cytodestructive therapy, surgery, or imiquimod.

Ectoparasites such as scabies, *Sarcoptes scabiei*, and pubic lice, *Phthirus pubis*, can be sexually transmitted. In contrast to many STDs, however, these ectoparasites can be easily treated with topical medications such as lindane or permethrin. Like all STDs, if the sexual partner is not treated concomitantly then reinfection is common.

Fever and Rash

The most common cause of fever after tropical travel is malaria, which usually does not have specific cutaneous manifestations. Dengue fever is the second most common cause of fever in the traveler and does have somewhat specific cutaneous manifestations, making dengue fever the leading cause of fever with rash in the traveler returning from a tropical destination (Fig. 1-8). Other common causes of fever and rash include hepatitis viruses, rickettsia, and some enteric fevers. It should always be kept in mind, however, that fever in the returned traveler may not be due to exposure during travel. For example, the fatigue of travel (i.e., jet lag) may make one more susceptible to influenza or other common infections in temperate lands.

When both fever and rash are seen, the time between travel and onset of signs and symptoms becomes increasingly important. If travel preceded fever and rash by less than 1–2 weeks, considerations should include anthrax, dengue fever, diphtheria, ehrlichiosis, hemorrhagic fever viruses, leptospirosis, Lyme disease, measles, meningococcal infections, plague, rickettsia,

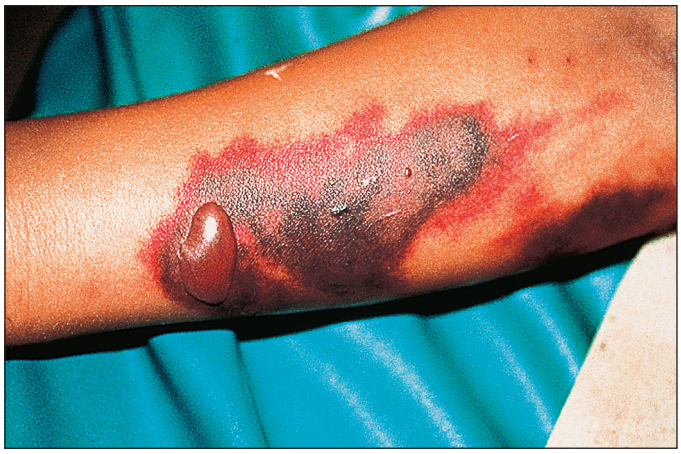

Figure 1-8 Hemorrhagic bullae in dengue virus infection. *(Reproduced with permission from WHO.)*

toxoplasmosis, trichinosis, tularemia, typhoid fever, and yellow fever. If the period between travel and fever/rash is up to a month, the list should be expanded to include hepatitis viruses (A, C, and E), HIV, rubella, schistosomiasis, and trypanosomiasis. If at least 3 months separate travel from fever/rash, the following infections should be considered: bartonellosis, filariasis, gnathostomiasis, hepatitis viruses (B and C), histoplasmosis, HIV, leishmaniasis, Lyme disease, melioidosis, penicilliosis, syphilis, trypanosomiasis, and tuberculosis. In each case, however, the nature of the fever, the type of rash, the destination of the travel, and any other symptoms must be considered.

Because many infections producing fever with rash can be rapidly fatal and/or easily spread, it is imperative to initiate immediately diagnostic tests and antimicrobial therapy for the presumed cause of the infection. Such infections include anthrax, bartonellosis, *Candida* (macronodules), diphtheria, disseminated gonorrhoeae (papules and pustules over joints), hepatitis viruses, leptospirosis, meningitis (asymmetrical, scattered, petechiae, and purpura), plague, *Pseudomonas* (ecthyma gangrenosum), relapsing fevers, rickettsia (scattered petechiae and purpura), *Staphylococcus* (Osler's nodes, diffuse toxic erythema), *Streptococcus* (Janeway lesions, diffuse toxic erythema), *Strongyloides* (migratory petechiae and purpura), syphilis, tuberculosis, typhoid fever (rose spots) (Fig. 1-9), various Gram-negative bacteria (i.e., peripheral gangrene), *Vibrio* (especially *V. vulnificus*), and viral hemorrhagic fevers (petechiae, purpura, hemorrhage).

Rash and Eosinophilia

Eosinophilia may be due to diverse processes, such as allergic, neoplastic, and infectious diseases.[8] Although an allergic reaction could easily result from an exposure during travel, eosinophilia in the returned traveler may have nothing directly to do with the travel. On the other hand, it may be due to an infectious process or to a drug taken for prophylaxis or therapy during travel. If an infection is the cause of the eosinophilia, it is usually a parasitic disease, especially that due to a helminth. Only a few viral, bacterial, or fungal diseases are associated with both rash and eosinophilia, for example, streptococcal fever (i.e., scarlet fever), tuberculosis, HIV, and coccidioidomycosis. Protozoa only rarely provoke eosinophilia.

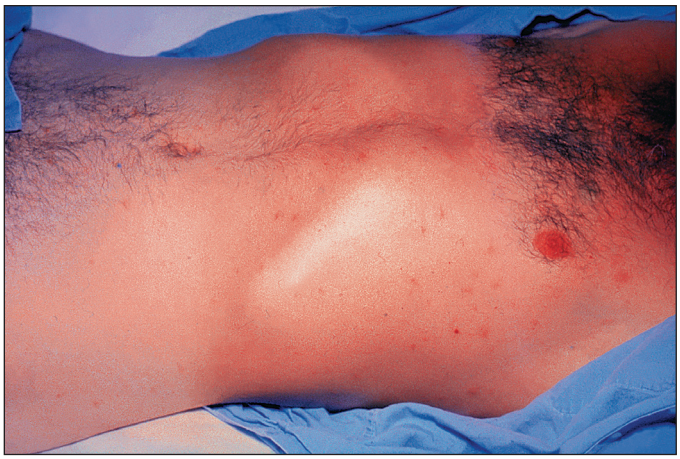

Figure 1-9 Rose spots in a patient with typhoid fever due to *Salmonella typhi*. *(Courtesy of Centers for Disease Control and Prevention/Armed Forces Institute of Pathology, Charles N. Farmer.)*

The principal helminth that causes eosinophilia is *Strongyloides*. When *Strongyloides* is disseminated, such as in the hyperinfection syndrome, skin lesions such as urticaria, papules, vesicles, petechiae, and migratory serpiginous lesions become common, especially if the patient is given systemic corticosteroids (because *Strongyloides* was not considered).

Pruritic, erythematous papules can be seen as a result of schistosomal cercariae, as in swimmer's itch. Eosinophils may be seen in the skin biopsy as well as in the blood.

Pruritic lesions of the skin and subcutaneous tissues are commonly associated with eosinophilia in onchocerciasis. Lymphangitis, orchitis, and epididymitis are also commonly observed.

In loiasis, fever and eosinophilia are typically seen. Migratory lesions, especially angioedema, are usually erythematous and pruritic.

Likewise, gnathostomiasis produces recurrent edema after ingestion of raw fish. The skin lesions are usually erythematous, pruritic, and/or painful.

Drug hypersensitivity is a relatively common cause of eosinophilia and may be associated with non-specific skin changes, such as urticaria and/or phototoxic reactions. Although most drugs that cause eosinophilia may not be taken for purposes related to traveling, increased sun exposure during travel may make the problem clinically apparent. Because antibiotics may be taken for prophylaxis or therapy more frequently during traveling, they should be given careful consideration when eosinophilia is detected. Such antibiotics include penicillins, cephalosporins, quinolones, isoniazid, rifampin, and trimethoprim-sulfamethoxazole.

Ulcers and Other Specific Skin Lesions

PRURITUS AND URTICARIA

Non-specific cutaneous manifestations of tropical diseases may include pruritus and urticaria. Frequently, more specific signs may accompany pruritus and urticaria, which are useful in narrowing the differential diagnoses. If eosinophilia is found with the pruritus and urticaria, helminthic infections should be considered. Therefore, consideration should be given to trichinellosis, strongyloidiasis, schistosomiasis, onchocerciasis, loiasis, hookworms, gnathostomiasis, dracunculiasis, and cutaneous larva migrans. Pinworms, as well as protozoan infections such as amebiasis, giardiasis, and trypanosomiasis, are less likely to produce eosinophilia. Pruritus and urticaria are possible with spirochetes such as *Borrelia* (e.g., relapsing fevers), *Spirillum* (e.g., rat-bite fever) and *Treponema* (i.e., syphilis and pinta). *Yersinia* (e.g., plague) is another bacteria that produces pruritus and urticaria, which can be present before buboes form. The hepatitis viruses (e.g., A, B, and C) can produce pruritus and urticaria, as can a number of ectoparasites and biting arthropods (e.g., ticks, scabies, bedbugs, lice, fleas, mites, and flies).[9–13]

JAUNDICE

Although hepatitis viruses can produce pruritus and urticaria, jaundice is a more specific indication that the problem has a hepatitic etiology. Not only can all the hepatitis viruses (A–E) produce jaundice, other tropical viruses also do so commonly, e.g., yellow fever and Rift Valley fever. Less frequently, dengue and Epstein–Barr viruses can cause jaundice, as can bacteria such as *Leptospira* (i.e., leptospirosis), *Coxiella* (i.e., Q fever) and *Treponema* (i.e., syphilis). Protozoa, such as malaria, and drug reactions can also be responsible.

VESICLES AND BULLAE

Although vesicles and bullae can appear as a result of contact dermatitis or drug eruption, including photodermatitis and photo-exacerbated drug eruptions as well as toxic epidermal necrolysis, many cases represent the early stages of a viral or bacterial infection. The most common viral etiology in the traveler or non-traveler includes the herpesviruses, especially herpes simplex virus 1 and 2, as well as varicella-zoster virus, both primary varicella and herpes zoster. Measles and many enteroviruses (e.g., hand, foot, and mouth disease) can present with vesicles, as can certain alphaviruses. A number of poxviruses, such as vaccinia, variola, orf, tanapox, and monkeypox, can produce vesicles. Less commonly, vesicles comprise an early stage of certain bacterial diseases such as those caused by *Vibrio vulnificus*, *Bacillus anthracis*, *Brucella* spp., *Mycobacteria tuberculosis*, *Mycoplasma* spp., *Rickettsia akaru*, and *Staphylococcus* (bullous impetigo). Other organisms such as fungi that cause tinea pedis, protozoa (e.g., *Leishmania brasiliensis*), and helminths (e.g., *Necator americanus*) can occasionally cause vesicles.

MACULES AND PAPULES

A wide variety of infectious and non-infectious etiologies are related to both macules and papules. Almost any of the vesicular diseases listed above may initiate first as a macule, then as a papule, before becoming a vesicle. A number of drugs, arthropod bites (e.g., mosquito or flea) and infestations (e.g., scabies and other mites) commonly cause macules and/or papules. A variety of terrestrial, freshwater, and marine contactants can elicit these cutaneous reactions, as can a spectrum of drugs. Viral etiologies include HIV, as in the HIV seroconversion syndrome, Epstein–Barr virus (infectious mononucleosis), human herpesvirus 6 (roseola), parvovirus B-19 (fifth disease), measles,

rubella, and various hemorrhagic fever viruses. Many bacteria can be responsible, such as *Rickettsia*, *Bacillus anthracis*, spirochetes (*Spirillum*, *Leptospira*, *Borrelia*, *Treponema*), *Coxiella burnetii*, *Yersinia pestis*, *Salmonella typhi*, *Bartonella bacilliformis*, and *Brucella*. Histoplasmosis and coccidioidomycosis are fungal diseases commonly associated with macules and/or papules. Certain protozoa such as *Toxoplasma gondii* and *Leishmania* can also induce these types of lesions. Among helminth diseases, hookworm disease, strongyloidiasis, and onchocerciasis can be associated with macules and/or papules.

NODULES

Although otherwise similar, papules are usually less than 0.5–1.0 cm in diameter, whereas nodules are larger than 0.5–1.0 cm. Except for certain poxviruses that cause orf and milker's nodules, as well as warts and malignancies induced by HPV, viruses rarely form nodules. On the other hand, all subcutaneous and systemic mycoses can induce nodules. Bacterial causes of nodules include *Bartonella* (verruga peruana and cat-scratch disease), *Buckholderia mallei* (glanders), *Calymmatobacterium granulomatis* (GI), *Chlamydia trachomatis* (LGV), *Klebsiella rhinoscleromatis* (rhinoscleroma), *Leptospira autumnalis* (leptospirosis), *Mycobacteria* spp. (atypical mycobacteria, cutaneous tuberculosis, leprosy, etc.), *Nocardia brasiliensis* (and other bacterial causes of mycetoma), and *Treponema pallidum* (bejel, yaws). Protozoan causes of nodules include amebiasis, leishmaniasis, and trypanosomiasis. Almost all helminthic infections that have mucocutaneous manifestations can induce nodules (e.g., coenurosis, cysticercosis, dirofilariasis, dracunculiasis, echinococcosis, filariasis, gnathostomiasis, loiasis, onchocerciasis, paragonimiasis, schistosomiasis, sparganosis, and visceral larval migrans). If the helminthic nodule contains sufficient fluid, it will produce a cyst. Cysts can be seen in helminthic infections such as coenurosis, echinococcosis, filariasis, gnathostomiasis, loiasis, and onchocerciasis. There are also arthropod causes of nodules such as myiasis, scabies, tick granulomas, and tungiasis.

ULCERS

Although ulcers can form as a result of breakdown of previously normal skin, they frequently develop from nodules after inflammation destroys the epidermis and papillary layer of the dermis. Herpes simplex virus is a very common cause of ulcers in both tropical and temperate regions of the world. Other causes of GUD are bacterial (e.g., chancroid, GI, LGV, and primary syphilis). Other bacterial diseases that commonly cause ulcers include anthrax, bacterial mycetomas, diphtheria, glanders, melioidosis, mycobacterial diseases (e.g., Buruli ulcer, leprosy, tuberculosis), plague, rickettsia, tropical ulcers, tularemia, and yaws. A number of fungi can form nodules that break down into ulcers, or they can induce ulcers from systemic spread (e.g., blastomycosis, chromomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, lobomycosis, mycetomas, paracoccidioidomycosis, penicilliosis, and sporotrichosis). The most common helminthic cause of cutaneous ulcers is dracunculiasis, when the worm erupts from the skin. Two protozoan diseases cause ulcers – amebiasis and leishmaniasis. Arthropod causes of ulcers include myiasis and tungiasis. Many bites (e.g., those of brown recluse spiders and various snakes), stings (e.g., insect, jellyfish, and scorpion), or venomous spines of various fish can also induce ulcers.

ESCHARS

An eschar can be seen in both temperate and tropical lands due to *Pseudomonas aeruginosa* (i.e., ecthyma gangrenosum), but the most common infectious causes of eschars are *Rickettsia*. Eschars due to anthrax can be seen in persons who work with animal skins, but anthrax has received much attention recently owing to its potential use in bioterrorism. The best-recognized etiology of a non-infectious eschar is a bite from a brown recluse spider.

PETECHIAE AND PURPURA

Petechiae and purpura can result from adverse reactions to a number of drugs. The most important infectious cause of petechiae and/or ecchymoses with fever is meningococcemia, which has a high rate of morbidity and mortality, is widespread throughout the tropical world, and is found sporadically in industrialized countries. Other bacterial causes include *Borrelia*, *Burkholderia*, *Enterococcus*, *Haemophilus*, *Leptospira*, *Pseudomonas*, *Rickettsia*, *Streptobacillis*, *Treponema*, *Vibrio*, and *Yersinia*. A number of hemorrhagic fever viruses can cause petechial or purpuric lesions, but the most prevalent viral causes are enteroviruses, cytomegalovirus, dengue, and yellow fever. Protozoal diseases (e.g., malaria and toxoplasmosis) and helminths (e.g., trichinellosis) can also induce this clinical presentation.

HYPOPIGMENTATION AND HYPERPIGMENTATION

Changes in pigmentation can be seen after a variety of medications, many of which are taken for prophylaxis or therapy related to travel. These agents include a spectrum of drugs such as antibiotics, antidiarrheals, anthelmintics, and antimalarials, many of which can also elicit photosensitization. A number of infectious agents can also alter pigmentation. Leishmaniasis, pinta, and tinea versicolor may be associated with hypopigmentation or hyperpigmentation. Leprosy, onchocerciasis, syphilis, and yaws are more often associated with hypopigmentation. Erythrasma, HIV, chikungunya and loiasis are more frequently causes of hyperpigmentation.

MIGRATORY SKIN LESIONS

With the exception of the movements of scabies and the larvae of myiasis, mucocutaneous migratory lesions are usually due to infections with helminths. The best-recognized example is cutaneous larval migrans, but migratory lesions can also be due to dracunculiasis, fascioliasis, gnathostomiasis (Fig. 1-10), hookworms, loiasis, paragonamiasis, sparganosis, or strongyloidiasis.

Recent Changes in the Epidemiology of Tropical Dermatology

Since the first publication of *Tropical Dermatology* in 2006, many tropical diseases previously unknown in temperate countries have been reported to have been transmitted outside the tropics (e.g., Ebola, Chikungunya, and Zika viruses), or have markedly increased their endemic areas (e.g., Chagas disease). In addition, certain non-infectious diseases such as podoconiosis have become more widely recognized.

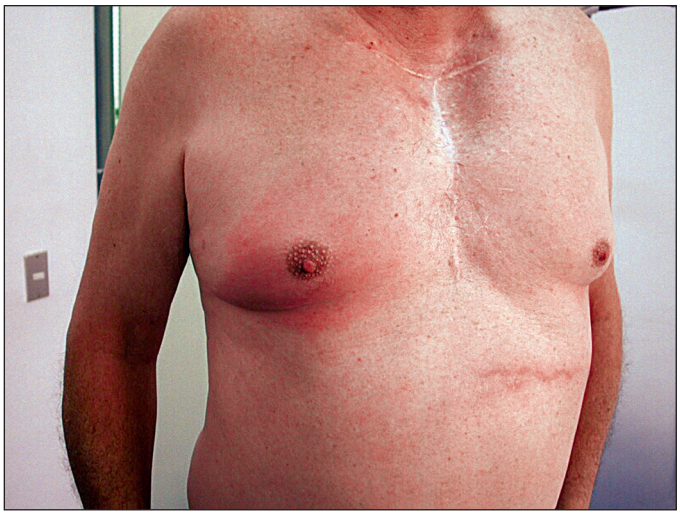

Figure 1-10 Migratory erythema secondary to gnathostomiasis in a patient in Peru. *(Courtesy of Dr Francisco Bravo.)*

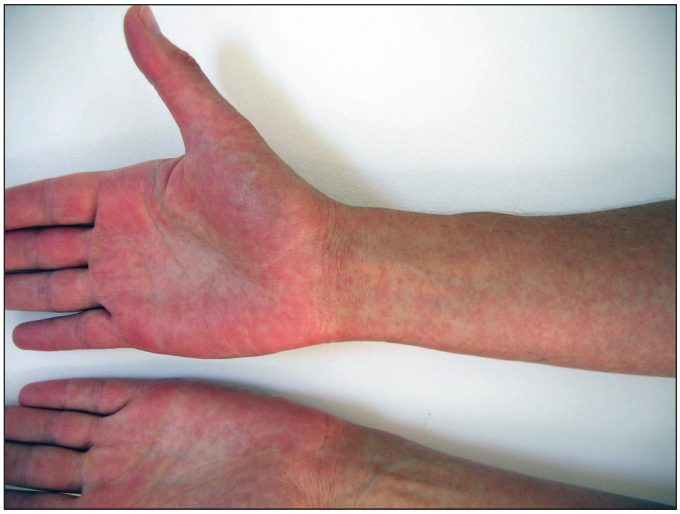

Figure 1-11 Chikungunya macular eruption.

Ebola is a hemorrhagic fever disease caused by Ebola virus, a member of the Filoviridae family. Ebola was first discovered in 1976 near the Ebola River in Congo. Since then, outbreaks have appeared sporadically in Central Africa. The largest epidemic in history occurred in 2014, affecting multiple countries in West Africa.[14] Five different Ebola viruses are known, with Zaire Ebola virus being the most virulent and causative agent in the most recent epidemic.[15] With a fatality rate of up to 90%, the World Health Organization (WHO) declared Ebola a 'Public Health Emergency of International Concern'.[16] In the United States (USA) two imported cases, including one death, and two locally acquired cases in health-care workers were reported. Ebola can be transmitted via direct contact with body fluids. Dermatologists should be cautious of the high risk of contamination through skin biopsies and dermatologic examination.

Chikungunya is an acute febrile illness caused by the Chikungunya virus, of the Togaviridae family, and transmitted by *Aedes* mosquitoes (Fig. 1-11). The spread of Chikungunya worldwide has been attributed to a multitude of factors including mutation of the virus, absence of herd immunity, lack of efficient vector

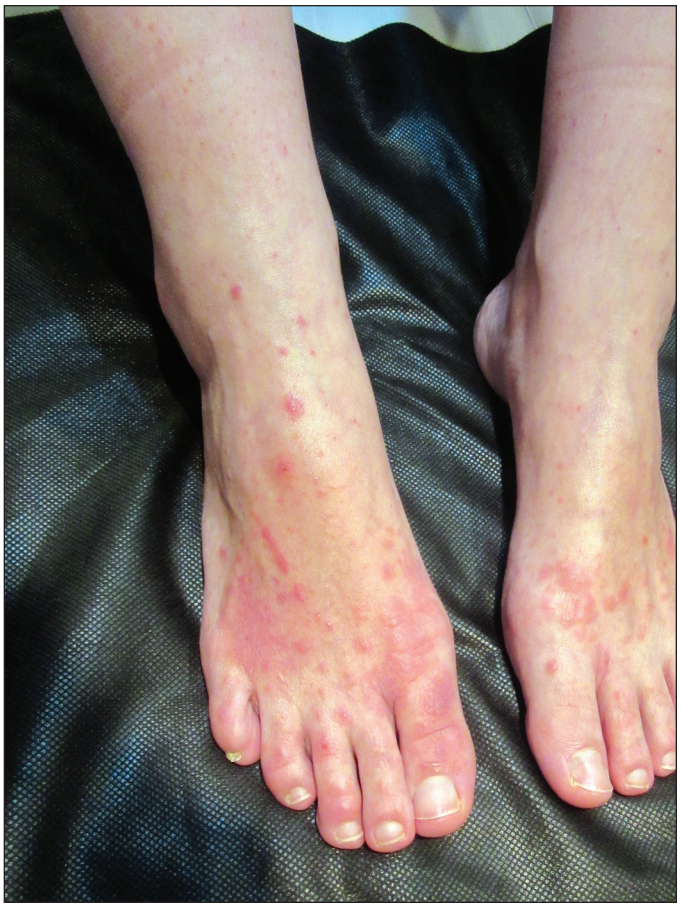

Figure 1-12 Zika virus infection: macules and papules.

control, globalization, and emergence of another vector, *A. albopictus*, in addition to the main vector, *A. aegypti*.[17] Travel-associated cases have been reported in the USA since 2006, with a significant increase in 2014 following the first case in the western hemisphere in December 2013 and the start of domestic transmission in 2014.[18]

Zika virus is a member of the family Flaviviridae related to West Nile, dengue, and yellow fever viruses (Fig. 1-12).[19] From 1951 through 1981, serologic evidence of human infection was reported from African countries and in parts of Asia.[20] Zika virus is transmitted to humans primarily through *Aedes* mosquitoes.[21] In 2007, an outbreak of 185 cases was reported in Yap Island, Micronesia.[20] Since then, outbreaks have been reported in French Polynesia,[22] and most recently in Brazil and other countries in tropical South America.[23] Zika virus transmission has not yet been documented in the USA, but cases have been reported in returning travelers. These imported cases, and the fact that the vector is the same as for dengue and Chikungunya, may result in local spread of the virus in some areas of the USA.[21,24–26]

American trypanosomiais, also known as Chagas disease (CD), is caused by *Trypanosoma cruzi*. The disease is transmitted to humans by triatomine insects (blood-sucking bugs of the Reduviidae family). These insects deposit their feces, which are laden with *T. cruzi*, at the time of biting. However, CD can also be transmitted via mother-to-child transmission,[27] food-borne transmission, and blood transfusion. For this reason, screening of the US blood supply for CD began in early 2007. CD infects

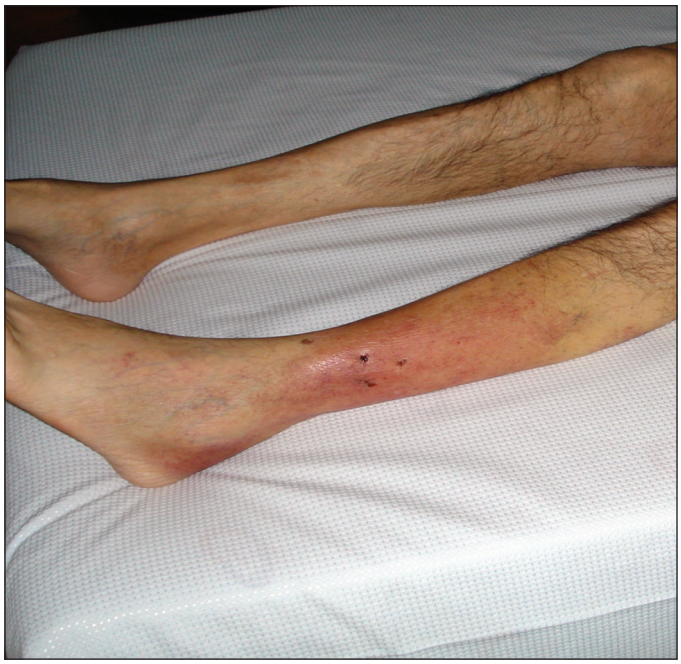

Figure 1-13 Chagastic panniculitis. *(Courtesy of Ricardo Romiti, MD, PhD University of São Paulo, Brasil)*

approximately 12 million people and kills about 60 000 yearly.[28] In some preliminary estimates, Mexico ranks number three, and the USA number seven, in terms of the number of infected individuals with CD in the world.[27–28] In the USA, approximately 300 000 cases are believed to be present,[29] although one alternative estimate reports more than 250 000 cases in Texas alone,[29–30] with up to one million or more cases nationwide. Furthermore, CD is a leading cause of heart disease among people living in extreme poverty in the western hemisphere, especially in Latin America (Fig. 1-13).

Podoconiosis, a non-communicable, non-infectious, tropical disease, is a common cause of lower-leg lymphedema in tropical volcanic highland areas above 1000 meters with high annual rainfall.[31] Clinical characteristics include below-the-knee bilateral lower-limb elephantiasis. It is found in barefoot subsistence farmers in fields with red soils formed from alkaline volcanic rock (see Fig. 3-6). Although it was only recently designated a "neglected tropical disease" by WHO, it is responsible for a significant public health burden in Ethiopia and nine other countries in the horn of Africa, Northern India, and Latin America. The finding of an association of certain HLA class II loci with susceptibility to podoconiosis suggests that it is a genetically predisposed, T-cell-mediated inflammatory disease.[32]

Conclusion

In conclusion, the differential diagnoses of mucocutaneous lesions in the returned traveler, immigrant, or adoptee should be based on the morphology of the lesions, but the patient's symptoms, general medical, and exposure history must all be considered.[33–47] The physical examination and laboratory results must be integrated with the patient's vaccination and medication record. The travel destination(s), travel duration, living, work / recreation conditions, food and drink ingestion, and activities while traveling must all be taken into consideration. It must not be forgotten, however, that many mucocutaneous problems in the returned traveler or the immigrant / adoptee are not related to the travel or the country of origin, but can be the same disorders seen daily in patients who have never left their local communities.

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2 Issues for Travelers

DAVID B. HUANG | MINA PASTAGIA | CHARLES D. ERICSSON

CHAPTER OUTLINE

KEY POINTS

Among travelers to developing countries, both tropical and non-tropical diseases are commonly reported problems and most of these are self-limited illnesses such as diarrhea, respiratory infections, and skin disorders.

Of the non-tropical diseases, dermatosis including cutaneous larva migrans, insect bites, and bacterial infections are the most frequent skin problems in ill travelers who seek medical care.

Physicians with patients who travel should be familiar with potential travel-related dermatoses, infectious diseases, and environmental hazards specific to the area of patient travel, and physicians should also discuss general preventive measures against dermatoses, infectious diseases, and environmental hazards, including vaccinations.

Travelers should be educated and prepared for travel-health-related issues including: blood clot risks; the effects of high-altitude destinations; jet lag; acclimatization; potential contaminated water, food and beverages; prolonged exposure to the sun, insect or animal bites; transmission of sexually transmitted diseases; malaria prophylaxis; and traveler's diarrhea.

Evaluation of travelers with skin lesions or fevers (>38°C) must include an extensive travel history with discussion of epidemiologic exposures along with a complete physical examination, and differential diagnosis will depend on travel location, length of stay, exposures, physical exam, skin lesions based on morphology (e.g., macule, papule, vesicle, and nodule), clinical presentation, and microbiological, serologic, and laboratory studies.

Introduction

Both tropical and non-tropical diseases are commonly reported problems among travelers to a developing country.[1,2] More than 522 million people from developed countries travel overseas and an estimated 50–100 million people travel to developing countries.[3] Approximately 8% of travelers to the developing world require medical care during or after travel. Most of the medical problems are self-limiting, such as diarrhea, respiratory infections, and skin disorders. Gastrointestinal symptoms, fever, and dermatologic complaints are among the most common reasons for returning travelers to visit doctors.[4]

The GeoSentinel Global Surveillance System is the largest repository of provider-based data on travel-related illness from specialized travel or tropical-medicine clinics on six continents.[5] From 2000 to 2010 the most common destinations from which travelers returned ill were sub-Saharan Africa (26%), Southeast Asia (17%), South–Central Asia (15%), and South America (10%).[6] Among travelers evaluated in US GeoSentinel sites after returning ill from international travel, gastrointestinal diagnoses were the most frequent patient complaint (the incidence rate is 20–90% depending on the country visited).[7] For all regions except Southeast Asia, parasite-induced diarrhea was more common than bacterial diarrhea among ill returned travelers; patients with bacterial diarrhea presented most commonly after travel to Southeast Asia.[4] The most common febrile / systemic diagnosis was *Plasmodium falciparum* malaria, which constitutes an important risk in some frequently visited areas such as tropical Africa (where up to 95% of infections are due to *P. falciparum*), Asia, and Latin America.[8] Travelers with dengue presented more frequently than those with malaria for every region except sub-Saharan Africa and Central America.[4] In the developing world, tuberculosis infection rates exceed those in the developed world, with prevalence reaching 35% in sub-Saharan Africa; contact with locals and greater length of stay increase infection risk.[9] The finding that fewer than half of all patients reported having made a pretravel visit with a health-care provider indicates that a substantial portion of US travelers might not be following the Centers for Disease Control and Prevention (CDC) travelers' health recommendations for international travel.[5]

Of the non-tropical diseases, dermatosis has been reported to be one of the three most common reasons (12–18%) that a traveler sought consultation from a physician.[2,10,11] The largest case series of dermatologic problems in returned travelers from the GeoSentinel Surveillance Network between 1997 and 2006 showed that cutaneous larva migrans, insect bites, abscesses, and bacterial infections were the most frequent skin problems in ill travelers who sought medical care, making up over 30% of the 4742 diagnoses (Table 2-1).[11] Cutaneous larva migrans is

the most common dermatologic disorder among patients presenting after travel to the Caribbean, whereas bacterial skin infections are more commonly found among patients returning from sub-Saharan Africa, South–Central Asia, or Southeast Asia[4] (Table 2-2). A retrospective analysis in travelers who acquired leishmaniasis within Europe diagnosed between 2000 and 2012 found 40 cases, the majority of which were acquired in Spain (n = 20, 50%), Malta and Italy (each n = 7, 18%).[12] In one prospective study of 269 consecutive patients (out of 7886) who presented to a French tropical disease unit during or after return from short-term travel over a 2-year period,[2] 61% presented during travel and 39% after travel, and cutaneous larva migrans, pyodermas, and arthropod bites were among the top diagnoses. Physicians with patients who travel should be familiar with potential travel-related dermatoses, infectious diseases, and environmental hazards (Table 2-3) specific to the area of travel. The physician should also discuss general preventive measures against dermatoses, infectious diseases, and environmental hazards, including vaccinations that are recommended to the traveler (Tables 2-4 and 2-5). With an increasing number of children traveling internationally, dermatologic problems are among the leading health concerns affecting children during and after return from international travel.[13] Most are mild and self-limited; children may be especially at risk for infections related to environmental exposures, arthropod-related problems, and animal bites.[14]

TABLE 2-1 Skin Lesions in Returned Travelers, by Cause, from the Geosentinel Surveillance Network, 1997–2006

Skin Lesion	Percentage of all Dermatological Diagnoses (n = 4742)
Cutaneous larva migrans	9.8
Insect bite	8.2
Skin abscess	7.7
Superinfected insect bite	6.8
Allergic rash	5.5
Rash, unknown origin	5.5
Dog bite	4.3
Superficial fungal infection	4.0
Dengue	3.4
Leishmaniasis	3.3
Myiasis	2.7
Spotted-fever group rickettsiae	1.5
Scabies	1.5
Cellulitis	1.5

TABLE 2-3 Potential Environmental Hazards Associated with Travel

Environment	Factors and Potential Hazards to Consider
Terrain concerns	Traversing safely and maintaining orientation Ability to find camping/safe shelter Exposure to air, wind, and solar radiation Exposure to animals or insects that may cause bites, injury, or infection
Extreme temperatures/weather	Appropriate clothing for extreme temperatures (i.e., risk for hypothermia and heat stroke) and prevention of solar radiation exposure Carry plenty of water to prevent dehydration
Air	Existing pulmonary disease and airway hyperreactivity Outdoor pollutants Indoor pollutants from fossil fuels/inadequate ventilation High altitudes and mountain sickness
Water	Exposure, including ingestion of and direct contact with contaminated water with water-borne infectious diseases (e.g., schistosomiasis, leptospirosis), industrial waste dumping, chemical toxins Exposure to aquatic life that may cause bites, injury, or infection

TABLE 2-2 Top Dermatological Disorders from Geosentinel Sites According to Travel Region (1996–2004)*

Dermatological disorder (n=2947)	All Regions	Caribbean	Central America	South America	Sub-Saharan Africa	South–Central Asia	Southeast Asia	Other or Multiple Regions
Insect bite with or without superinfection	187	192	235	156	194	201	179	166
Cutaneous larva migrans	129	299	134	122	86	64	171	68
Allergic rash or reaction	113	148	128	97	105	112	93	132
Skin abscess	97	34	47	50	136	144	122	105
Animal bite requiring rabies prophylaxis	47	3	13	25	9	90	124	4
Leishmaniasis	38	0	64	143	14	19	0	36
Myiasis	35	0	101	100	40	0	0	14

*Data is number of cases per 1000 patients with syndrome.

TABLE 2-4 Routine and Recommended Commercially Available Vaccines for International Travel

Vaccine	Antigenic form	Schedule/indications	Adverse effects
REQUIRED BY LAW			
Yellow fever	Live-attenuated	One dose, 10 days before travel, with a booster every 10 years for those travelling to endemic areas	Fever (2–5%), headache, myalgia
ROUTINE			
Diptheria–tetanus–pertussis	Inactivated	Three doses at 2, 4, and 6 months of age	Local reactions[a], occasional risk of systemic reactions[b]
H. influenzae b	Capsular polysaccharide	Four doses at 2, 4, 6, and 12–15 months of age	Local reactions, occasional risk of systemic reactions
Influenza	Inactivated	One dose annually to travelers at increased risk of complications from influenza	Local reactions, occasional risk of systemic reaction
MMR	Live-attenuated	Two doses given to all persons born after 1956	Fever (5–15%), rash (5%) joint pains (up to 40% in postpubertal females), local reactions (4–55%)
Poliomyelitis	Inactivated	Three doses: the first two are given at 4–8-week intervals; the third is given 6–12 months after the second, for non-vaccinated persons > 18 years and immunocompromised hosts at increased risk of exposure to poliovirus; a single booster dose is given prior to departure to certain countries	Local reactions
Tetanus–diphtheria	Adsorbed toxoids	Previously unvaccinated adults, 1 dose of Tdap followed by Td every 10 years for all adults	Local reactions, occasional systemic symptoms
Varicella	Live-attenuated	Two doses 4–8 weeks apart for persons without a history of varicella	Local reactions (25–30%), fever (10%), rash (8%)
Meningococcal (A, C, Y, W-135)	Polysaccharide	One dose, with a booster every 5 years for those traveling to Saudi Arabia or sub-Saharan meningococcal belt, Haj pilgrims, and those who have had a splenectomy	Local reactions, fever (2%)
RECOMMENDED			
Encephalitis, Japanese (Ixiaro)	Inactivated	Two doses, 28 days apart, for those traveling to endemic areas (Asia and Southeast Asia)	Local reactions at injection site, systemic reactions (≥10%)
Hepatitis A	Inactivated	Two doses, 6–12 months apart for those traveling to all developing countries	Local reactions, systemic reactions (10%)
Hepatitis B	Recombinant-derived hepatitis B surface antigen	Three doses: two doses 1 month apart; third dose 5 months after dose 2 for health-care workers and persons in contact with blood, body fluids, or potentially contaminated medical instruments, and persons (i.e., expatriates) residing in areas of high endemicity for hepatitis B surface antigen Accelerated regimen: 0, 7, 21–30 days and 1 month 12 booster dose	Local reactions (10–20%), systemic reactions (rare)
Combined hepatitis A/B	Inactivated hepatitis A/recombinant B surface antigen	Three doses: two doses 1 month apart; third dose 5 months after dose 2 as listed above Accelerated regimen: 0, 7, 21–30 days and 1 month 12 booster dose	Local reactions, systemic reactions (rare)
Pneumococcal	Capsular polysaccharide 13-valent pneumococcal conjugate vaccine (Prevnar 13)	One dose for immunocompromised hosts, splenectomy, and the elderly One dose for immunocompromised hosts, functional or anatomic asplenia, cerebrospinal fluid leak, cochlear implant, or immunocompetent adults aged ≥ 65 years with none of the above conditions	Local reactions, fever, rash, arthritis, serum sickness Local reactions, fever, rash arthritis, immune complex reactions
Rabies	Inactivated	Three doses at days 0, 7, and 21 or 28 for travelers to areas for > 1 month where rabies risk is considerable: a booster may be given 1 year later	Local reactions (30%), systemic reactions, immune complex reactions (6%)
Typhoid	Live-attenuated (oral) Vi capsular polysaccharide	Four doses at days 0, 2, 4, 6 for travelers to endemic areas boost every 5 years One dose and a booster every 2–3 years for travelers to endemic areas	Gastrointestinal symptoms[c], systemic reactions Local reactions, systemic symptoms (rare)

[a]Local reactions include pain, swelling, and induration at site of injection.
[b]Systemic symptoms include fever, headaches, and malaise.
[c]Gastrointestinal symptoms include nausea, vomiting, and diarrhea.