

Importance of a Travel History in Evaluation of Respiratory Infections

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Abstract

Purpose of Review International travel has increased at a fast pace and will continue to rapidly rise. Concomitantly, with this increase in travel is the increase in post travel-related diseases, such as respiratory illnesses. Identifying the cause of the posttravel respiratory illness is a complex challenge for many healthcare professionals because similar presentations occur for both infectious and noninfectious causes. Not only is diagnosis important but also transmission prevention. In the last two decades, there have been several severe infectious respiratory syndromes that have spread through international travel causing epidemics in many countries.

Recent Findings A detailed travel history with the chronology of symptoms paired with the patient's medical risk factors and exposures along with some basic knowledge of infectious respiratory illnesses will help facilitate clinical decision making. This framework will help create a broad, but appropriate differential diagnosis to guide clinical workup, prevent delays in diagnosis, and implement the appropriate precautions to prevent transmission if appropriate.

Summary The foundation to diagnosing a travel-related respiratory illness lies within integrating the patient's travel history, comorbid conditions, clinical presentation, exposures, and mode of transmission. A timely and accurate diagnosis benefits not only the patient but also the surrounding community to prevent further individual transmission, epidemics, and pandemics.

Keywords Travel history · Respiratory infections · Travel-related illness

Introduction

International tourist arrivals have grown at a rapid pace from 25 million in 1950 to a record of 1.2 billion in 2015 and are expected to continue to rise [1, 2]. Concordant with this escalation in travel are an increasing number of travel-related illnesses that are associated with certain travel destinations, activities, and exposures. It is estimated that up to 50 % of travelers experience a health problem related to international travel [3]. The most common complaints reported by returning travelers are gastrointestinal infections, febrile illnesses, and dermatologic issues, followed by respiratory illnesses [3]. The diagnosis of the former three categories of illness can usually be determined based on destination history and activities while traveling [4, 5••]. However, identifying the causes of respiratory illnesses is more challenging because of the worldwide distribution and similar presentations of infectious and noninfectious causes of respiratory illness.

Respiratory tract infections have been reported by 11 % of all travelers in a recent GeoSentinel Surveillance survey in returned travelers [5••]. Respiratory tract infections are defined as upper respiratory tract infections involving the

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nose, sinuses, and pharynx or larynx and lower respiratory tract infections, such as pneumonia or bronchitis. These infections were the second most common cause of fever following malaria as highlighted in two published series [2]. As the number of international travelers continues to grow, traveler-associated respiratory infections will continue to rise. The need for understanding risk factors, modes of transmission, clinical presentations, and treatment management plans becomes increasingly important for acute care physicians who will be seeing these patients posttravel. In particular, issues regarding timely diagnosis, the potential need for isolation, and appropriate treatment choice will need to be addressed in order to prevent further transmission of respiratory infections after the traveler returns home.

When considering the diagnosis of respiratory infection, the mechanism of transmission can highlight specific illnesses. The two main routes of transmission are via contact with droplets or the airborne route. Droplet spread involves usually large droplets containing organisms that drop out of the air quickly and require direct contact with the mucus membranes of the subject for transmission (usually within three feet). This occurs in cases of the common cold. Airborne transmission involves the travel of the infectious pathogen attached to dust particles or respiratory droplets that suspend in the air for prolonged periods of time; therefore, close contact is not required. This can lead to widespread transmission particularly in closed environments where recirculation of air leads to increased contact of the infectious particles within the pulmonary bronchioles. A prime example of an airborne disease is tuberculosis.

Precautions for the two main routes of transmission are droplet precautions and airborne precautions, respectively. These precautions should be used in conjunction with standard precautions and/or contact precautions. The main goal of droplet precautions is to prevent transmission of pathogens through respiratory or mucous membrane contact as these pathogens do not remain infectious over a long distance. A single patient room is preferred; however, if there is a shared room, a spatial separation of greater than three feet and drawing the curtain between beds is important to prevent transmission. Healthcare staff should already be wearing a mask prior to entry into the room. The primary goal for airborne precautions is to prevent the transmission of a suspected airborne disease. This requires a single patient room that has specialized ventilation for air handling and filtering which is designed to minimize the transmission of the infectious agent. These rooms are designated as airborne infection isolation rooms also formerly known as negative pressure isolation rooms. Healthcare workers should be fit-tested and wear N95 or

higher level respirators or masks to reduce the likelihood of transmission prior to room entry.

Importance of the Travel History

The patient's history of present illness must be comprehensive, yet focused. The history should detail the patient's respiratory complaints and associated symptoms being mindful of symptomatology in relation to the patient's travel history.

An initial approach to the history of present illness would be to create a chronologic timeline of symptoms in order to assess whether symptoms developed before, during, or after the travel period. Subsequent examination of the patient's reasons for travel, destination choice, duration of travel, and travel-related activities can highlight the patient's potential infectious exposures and risk factors (see Table 1). A functional and efficacious tool for practitioners is to use the Center for Disease Control and Prevention's (CDC) "Traveler's Health" webpage which identifies and reports regional outbreaks of diseases based on destination [6]. It is also important to identify whether the patient traveled in a group and whether anyone else in the party developed similar symptoms as this can suggest certain diagnoses. Focus should be placed on elements of the personal, occupational, and social history that are directly pertinent to the patient's current symptoms. The social history should address active and/or passive smoking as inhaled tobacco exposure has been shown to increase the incidence of respiratory infections [7]. Systematic review of respiratory symptoms, including their character and duration, should be emphasized along with a complete review of symptoms. An up-to-date list of immunizations

Table 1 Important topics to cover in a comprehensive travel history

1. Pretravel counseling/vaccinations
2. Malaria chemoprophylaxis
3. Accommodation type
4. Trekking activities
5. Jungle travel
6. Freshwater exposure
7. Travel sexual history
8. Food and water exposure
9. Insect bites received
10. Sick traveling companions
11. Illness experienced abroad
12. Treatment received in transit or at destination
13. Exposure to natural disaster
14. Duration of travel at each location

can help create a more focused differential diagnosis. In particular, it is important to document recent influenza vaccination as this is one of the most frequently acquired vaccine-preventable illnesses (Table 2).

Medical providers should consider previous historical exposures, such as the patient's country of birth or a history of having household contacts with respiratory illnesses, as well as the childhood medical history. This may identify a patient whose family has a history of tuberculosis, an inherited respiratory disorder such as cystic fibrosis, or those whose families are predisposed to allergic rhinitis or asthma indicating an increased susceptibility for reactive airways disease. A history of childhood asthma or a present history of seasonal respiratory symptoms, such as postnasal

drip, hay fever, asthma, allergies, and sinusitis, is important to consider. These details help build a differential for both domestic and travel-related causes of respiratory illness as a proportion of all illnesses in the posttravel period will be unrelated to travel.

Special consideration must be made to identify the immunocompromised traveler. Certain underlying conditions predispose patients to specific respiratory diseases, such as human immunodeficiency virus, chronic steroid therapy, asplenic patients, chronic renal failure patients, transplant patients on immunosuppressive drugs, and alcoholic cirrhosis patients. The clinical presentations for these patient populations can be atypical and severe. In particular, these patients are at an increased risk of certain

Table 2 Distribution of the most common organisms by region and reservoir

Infectious etiology	Geographical origin	Reservoir/source	Main type of transmission
Viruses			
MERS-CoV	Middle East	Dromedary camels	Droplet contact
SARS-CoV	South China	Chinese horseshoe bats	Droplet contact, airborne
H7N9		Poultry, wild birds	Droplet
Influenza virus	Eastern China, Hong Kong, Taiwan		Droplet
Bacteria			
<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Chlamydomphila pneumoniae</i>	Worldwide	Human	Close contact with infected respiratory secretions; Droplet
<i>Mycoplasma pneumoniae</i> <i>Legionella pneumophila</i>	Worldwide	Contaminated water source	Inhalation of contaminated aerosol
<i>Burkholderia pseudomallei</i>	Southeast Asia, Northern Australia	Soil/contaminated water	Inhalation, ingestion, or direct contact with contaminated soil or water
XDR-TB and MDR-TB	Eastern Europe, Russia, Southern Africa	Human	Airborne
Fungi			
<i>Histoplasma capsulatum</i>	Worldwide	Bats, birds, contaminated soil	Inhalation of contaminated aerosol
<i>Coccidioides immitis</i>	Unites States (California, Arizona, New Mexico, Texas); Central America and South America	Contaminated soil	Inhalation of contaminated aerosol
<i>Paracoccidioides brasiliensis</i>	Central and South America	Contaminated soil, armadillo	Inhalation of contaminated aerosol
<i>Blastomyces dermatitidis</i>	United States (Wisconsin, Illinois, Tennessee, Arkansas), India, South America, Africa	Contaminated soil, beaver, dog, rodent	Inhalation of contaminated aerosol
Parasites			
<i>Strongyloides Stercoralis</i>	Tropics and subtropics	Dogs and primates	Skin penetration by filariform larvae; autoinfection

MERS-CoV Middle East respiratory syndrome coronavirus, *SARS-CoV* severe acute respiratory syndrome coronavirus, *XDR-TB* extensively drug-resistant tuberculosis, *MDR-TB* multidrug-resistant tuberculosis

Adapted from Ref. [84]

diseases such as pneumococcal pneumonia and *Haemophilus influenzae*; therefore, these diseases should be considered in the differential diagnosis of respiratory illnesses in these specific patient populations [8].

Risk Factors for Developing Specific Respiratory Infections

The GeoSentinel Surveillance Network is composed of specialized travel or tropical medicine clinics that contribute clinician-based surveillance data on all patients seen during clinical care for travel-related illnesses. In particular, demographic data based on GeoSentinel research suggest that increasing age, the male sex, timing of travel, trip duration, and type of travel increase the risk of contracting a respiratory infection [9]. Of note, travelers of an older age and male sex were found to have a greater risk of lower respiratory tract infections, particularly pneumonia and bronchitis. Published studies have noted that travelers who visit the Northern Hemisphere in December through February are at greatest risk of contracting influenza [9]. Travelers who had greater than 30 days of travel were more likely to get influenza due to closer contact with the local population. The diagnosis of pneumonia and lower respiratory tract infection correlate with higher admission rates to hospitals compared with other respiratory illnesses [7].

Specific Travel-Related Respiratory Illnesses

Considering the increasing frequency of flights worldwide, there have been relatively few outbreaks of respiratory illnesses associated with travel. However, the epidemics that have been identified, such as Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS), influenza, and tuberculosis, have caused significant morbidity and mortality, therefore raising awareness about the importance of public health initiatives and respiratory illnesses. It is difficult to measure the actual rate of transmission of travel-related respiratory illnesses as accurate epidemiological studies would require collecting data from millions of passengers worldwide. Additionally, the low infectious rate and long incubation periods of certain illnesses also further reduce the reliability of study results and the ability to attribute the transmission of a disease to a specific destination and exposure. Thus, it is important to consider a broad differential diagnosis and have a high index of suspicion for travel-related respiratory illnesses in order to decrease morbidity and mortality for the patient and from a public health perspective.

Viral Respiratory Illnesses

Influenza-Like Illnesses

Influenza viruses cause an acute, febrile illness characterized by cough, sore throat, and myalgias. Outbreaks typically occur with varying severity almost every winter in temperate climates and year-round in tropical climates. Influenza viruses are transmitted by the respiratory route and can cause large epidemics, partly due to the ability of new influenza A virus subtypes (most commonly found in animals) to sporadically emerge as a human disease. Influenza A, B, or H1N1 were diagnosed in 8 % of travelers with a respiratory illness in a GeoSentinel survey of returning travelers from 2007 to 2011 [5••]. In the recent global outbreak of H1N1 in 2009, aircrafts themselves functioned as vehicles for patients infected with influenza to transmit the disease to nonendemic areas [10, 11], and to other passengers during international flights [12, 13]. Of note, there are many illnesses that cause influenza-like symptoms and should be considered in the differential, including self-limited illnesses, such as gastroenteritis and rhinoviral disease, as well as severe diseases, such as meningitis and sepsis. Careful history-taking, thorough physical examination, and review of laboratory studies can improve early diagnostic accuracy.

The majority of cases of influenza are diagnosed based on consistent clinical symptoms and epidemiology. Several studies have demonstrated that during an influenza outbreak the accuracy of forming a diagnosis in young adults based on clinical grounds alone ranges approximately from 80 to 90 % with the best predictors of influenza infections being cough and fever with positive predictive values ranging from 79 to 86 % [14••, 15, 16]. This emphasizes the need for physicians to be aware of the number of influenza cases in their area, as informed by the local infectious disease agency or the CDC, as well as the importance of a detailed clinical history [17]. The diagnosis of influenza can be confirmed by either rapid diagnostic laboratory tests, nucleic acid tests such as the PCR assay, or isolation of virus in cell culture, which is an increasingly less common methodology as it takes 3 days for 90 % of positive cultures to be detected with the remainder identified within 5–7 days [18]. Most cases of influenza, occurring in otherwise healthy individuals with typical symptoms with appropriate seasonal epidemiology, do not need specific viral confirmation. However, outpatients with high risk for complications, namely the elderly, infants, pregnant women, or immunocompromised and all hospitalized patients, should have viral diagnostic confirmation [19]. High clinical suspicion remains one of the most important factors in guiding antiviral treatment for influenza as the treatment is most effective within 48 hours

after onset of illness. However, antiviral treatment might be effective in reducing morbidity and mortality in certain populations after this time period, such as immunocompromised individuals or hospitalized patients. It is recommended to discuss individual cases with the institution's infectious disease consultant. Prevention of transmission includes standard precautions and droplet precautions. In general, it is recommended droplet precautions be implemented for 7 days from the onset of symptoms or until 24 h after the resolution of fever and respiratory symptoms whichever is longer [20]. The exception is in young children and immunocompromised patients who can shed the virus over a prolonged period. In regards to transmission prevention for H1N1, updated guidelines should be accessed via the CDC website, an infectious disease consultant, or the hospital infection control department.

In summary, influenza viruses classically present as an acute, febrile illness characterized by cough, sore throat, and myalgias. Outbreaks occur almost every winter in temperate climates and year-round in tropical climates. Clinical diagnosis is made based on consistent clinical symptoms and epidemiology. Standard and droplet precautions should be implemented and patients triaged quickly so that they may benefit from antiviral therapy.

Severe Acute Respiratory Syndrome

The inherent link between SARS and travel stems from the beginning of the 2002–2003 epidemic. SARS was first identified in Guangdong Province of the People's Republic of China in November 2002 and spread to Hong Kong and then throughout the world to 29 countries resulting in 8098 cases with a mortality rate of 9.6 % by the end of the epidemic [21, 22]. The nephrologist who traveled from China to Hong Kong on 21 February 2003 was the index case contributing to the Hong Kong outbreak that subsequently led to the spread of the virus locally and to many other countries [23]. The transmission of the SARS virus has been reported to occur through contact with respiratory droplets from an index case or by direct contact with contaminated hands or fomites. Although there have been documented cases suggesting that transmission is weakly airborne [24–27], other studies found no relationship between air travel and transmission of SARS [28, 29]. The WHO initiated screening procedures at airports to detect individuals with fever prior to boarding during the SARS outbreak as well as initiation of patient isolation in flight for suspected cases and adherence to infection control measures to decrease travel-related transmission [30].

SARS commonly presents with fevers, dry cough, dyspnea, chills, headache, myalgias, and malaise [23, 31, 32]. The estimated incubation period of SARS is 4.6 days [31]. SARS cases were mainly seen in younger, healthy

individuals although associated comorbidities were noted including diabetes, renal disease, and heart disease [32]. The clinician should ask if the patient has had recent travel within 10 days to mainland China, Hong Kong and Taiwan or close contact with travelers who went to these areas or are employed in a high-risk occupation, such as a health-care worker [33]. Patients with SARS typically presented with lymphopenia, thrombocytopenia, and elevated creatine phosphokinase levels [23, 34]. Radiographic findings in SARS cases commonly included involvement of the lung periphery and the lower lung fields in addition to hilar lymphadenopathy or pleural effusions and the absence of pulmonary cavitations [23]. In a case series, 20 % of cases developed acute respiratory distress syndrome over a period of 3 weeks [35]. Reverse transcriptase PCR (RT-PCR) for upper and lower respiratory tract, blood, stool, and urine specimens were initially used to detect the virus, though specimens were found to be positive in only one third of cases early in the illness [35]. Antibody tests using either indirect immunofluorescence or enzyme-linked immunosorbent techniques have also been developed. During the 2002–2003 epidemic, clinicians empirically treated patients with probable SARS with antibacterial agents, methylprednisolone, and intravenous or oral ribavirin [36]. However, studies later demonstrated that ribavirin has little in vitro activity against SARS, and there was no evidence that the therapies improved outcomes [37, 38]. Clinicians need to have a high index of suspicion in order to identify an unusual pattern and diagnose a potentially new viral respiratory illness. Early identification initiates a downstream effect for rigorous application of hospital and community-based infection control procedures, which includes standard, contact, droplet, and airborne precautions as well as eye protection [27, 39]. Each individual institution should directly contact the infection control department or an infectious disease specialist as early and rigorous implementation has shown to have a major beneficial effect on decreasing disease transmission particularly in SARS [40].

In summary, SARS presents as fevers, dry cough, dyspnea, chills, headache, myalgias, and malaise with radiographic evidence consistent with pneumonia without an alternative diagnosis. Transmission prevention includes standard, contact, and airborne precautions as well as eye protection. Mainstay for treatment for SARS is meticulous supportive care.

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

MERS-CoV was initially reported in 2012 when a new betacoronavirus was isolated from the sputum of a 60-year-old man who died of overwhelming pneumonia and renal

failure in Saudi Arabia [41]. This account was followed by multiple other reports to the WHO identifying a total of 1728 laboratory-confirmed cases of human infection with MERS since September 2012, including at least 624 related deaths (as of April 26, 2016) [42]. Most of the cases have been identified in countries in the Middle East predominantly in the Kingdom of Saudi Arabia, but cases have also been documented in Europe, Africa, and North America in a total of 26 countries with all of the individuals having a direct or indirect link to the Middle East [42]. Transmission occurs through human-to-human contact, especially in hospital settings [43, 44]. Bats have been proposed as the animal reservoir given evidence that demonstrates they can be infected with the same or similar coronaviruses [45], and camels may serve as intermediary hosts [46].

The clinical presentation of MERS varies from asymptomatic to severe pneumonia with acute respiratory distress syndrome (ARDS), septic shock, and multiorgan failure. Common presenting symptoms of MERS include fever, cough, chills, sore throat, myalgias, and arthralgias followed in some cases by dyspnea and progression to pneumonia, often requiring ventilator support [43, 47, 48]. In a review of published MERS cases, the age distribution of patients with MERS-CoV ranged from 14 months to 94 years, but patients tended to be older and male with at least one comorbid illness; fatal cases tended to have at least one underlying comorbid condition, in particular diabetes, renal failure, chronic lung disease, and immunocompromised states [49]. Index or sporadic cases were more often older patients, required hospitalization, and were reported as ‘severe disease’ in comparison with secondary cases [47]. Common laboratory findings of MERS include leukopenia, particularly lymphopenia, with radiological findings consistent with viral pneumonitis and ARDS, with unilateral or bilateral patchy infiltrates, segmented or lobar opacities, ground glass opacities, unilateral or bilateral hilar lymphadenopathy, and small pleural effusions [41, 49]. Diagnosis relies on testing with reverse transcription polymerase chain reaction (RT-PCR) assays. There is no specific treatment for MERS infection, and care is supportive. Some patients have been treated with systemic corticosteroids with unsuccessful outcomes [47]. Since MERS presents early with nonspecific symptoms and a similar clinical syndrome as other respiratory viruses, healthcare workers should apply droplet precautions with all patients with symptoms of acute respiratory infection; additionally, contact precautions and eye protection should be added in cases of suspected or confirmed cases of MERS-CoV infection and airborne precautions when performing aerosol generating procedures [42].

In summary, the clinical presentation of MERS-CoV is a spectrum from being asymptomatic to severe pneumonia with ARDS, septic shock, and multiorgan failure. Initial

clinical presentation can include fever, cough, chills, sore throat, myalgias, and arthralgias. Transmission prevention includes standard, contact, and airborne precautions with protective eyewear. The mainstay for treatment is supportive management of the complications from MERS.

Bacterial Respiratory Illnesses

The common respiratory complaints in returning travelers with bacterial infection include, in order of decreasing prevalence, upper respiratory tract infection, bronchitis, pneumonia, pharyngitis, tonsillitis or laryngitis, sinusitis, and otitis [50, 9]. In one GeoSentinel review of returning travelers published in 2013, the most common bacterial respiratory illnesses were Streptococcal pharyngitis, Pertussis, and Legionella [50]. There was one case report of an adopted infant from Russia with pertussis exposing the child’s family and fellow passengers on a flight back to the United States [50]. Legionella has been reported in multiple returning travelers from around the world in Europe through the European surveillance network for travel-associated Legionnaires’ disease (ELDSNet) most often in men with the largest infectious clusters associated with cruise ship outbreaks [51]. Other common bacterial causes of travel-related respiratory infection are the same organisms considered in local community-acquired infections: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Legionella pneumophila*. Some infections can cause symptoms years after a stay in a foreign destination, such as melioidosis. *Burkholderia pseudomallei*, the causative bacterium of melioidosis, is often reported from Southeast Asia and Northern Australia, but it is also increasingly being recognized in other tropical and subtropical locations and in returning travelers from these destinations who present with sepsis, pneumonia, or abscess formation [52].

Transmission prevention for most bacterial respiratory illnesses is standard precautions and the treatment is antibiotics specific for that infectious agent. In addition to standard precautions, certain organisms such as Legionella can be prevented by properly maintaining water systems. Specific preventative guidelines for transmission of different bacterial organisms can be found at the CDC website.

Fungal Respiratory Infections

An increasing number of fungal infections with pulmonary manifestations have been reported in returning travelers such as histoplasmosis, coccidioidomycosis, paracoccidioidomycosis, and blastomycosis; however, the rare nature

of fungal infections can contribute to their underestimation and misdiagnosis [5•, 53–56]. Certain fungal diseases are endemic to specific regions, but these locations evolve over time with new clusters of both human and animal cases as well as environmental samples improving our understanding of disease transmission [57]. Immunocompromised patients such as those with human immunodeficiency syndrome with a CD4 count <100 cells/ μ L, organ transplantation, recipients of long-term steroids or biological immunomodulators, and those with cellular immune deficiencies, have a high risk of developing fungal infection after travel, specifically those with defects of the interleukin 12/interferon gamma (IFN- γ) axis and/or tumor necrosis factor alpha (TNF- α) [58]. Travel-acquired fungal infections may present acutely or even years after return. Infection through the inhalation route can cause a pneumonia that may lead to dissemination (such as with cutaneous manifestations), particularly in immunocompromised hosts. Infected individuals lack laboratory-confirmed evidence of bacteria and may have cytopenias [59].

Most fungal infections with respiratory symptoms associated with travel are only found in tropical or subtropical regions, and clinicians should be aware of their distribution. Cases of histoplasmosis have been documented in the Americas, Europe, Africa, and Southeast Asia [59]. *H. capsulatum*, a soil-based fungus, has a strong association for bird and bat guano, and it is most often found where the guano has been mixed with soil and decay rather than in fresh specimens [60]. *Coccidioides* spp. are typically found in the soils of only certain regions, usually arid climates, with low rainfall and hot summers. The endemic regions in the United States include the Southwest (Arizona, New Mexico, parts of California, Nevada, and Texas) though nonendemic cases have been documented in Washington. Endemic and nonendemic cases have been documented in Mexico, Central America (Guatemala, Honduras, Nicaragua), and in South America (Argentina, Paraguay, Venezuela, Colombia, Brazil) [61]. Paracoccidioidomycosis, caused by *Paracoccidioides brasiliensis* and a newer species, *Paracoccidioides lutzii*, presents as an acute or subacute disease. It is associated with the involvement of multiple organs including inflammation of lymph nodes, liver, and spleen along with skin manifestations. Chronic progressive disease is more commonly diagnosed in older patients with significant lung involvement and lesions spread throughout other sites in the body. The fungi are limited to Latin American countries with the largest endemic region found in Brazil. Agricultural exposure has been associated with an increased risk of paracoccidioidomycosis [62]. Blastomycosis caused by the dimorphic mold *Blastomyces dermatitidis* most often involves

the lungs though the presentation may be subclinical, and it has an incubation period of 2–6 weeks [63]. Less commonly, it presents with fulminant pulmonary infection with ARDS. Blastomycosis is most frequently documented in the United States in the Mississippi and Ohio River valleys and Mid-western states; however, occasional cases have been documented from Israel, India, Africa, and Central and South America [64–66].

When trying to determine if patients are at risk for travel-acquired fungal infections, clinicians should be suspicious in the case of unexplained fever associated with or without focal symptoms—often respiratory, neurologic, or dermatologic in nature. Clinicians should determine if the patient has been exposed to disruptions of the soil by natural disasters, construction, recreational activity such as spelunking in bat-infested caves, or outdoor trauma with vegetal inoculation, as these factors are associated with high risk of transmission of histoplasmosis and coccidioidomycosis. More common travel-acquired infections such as malaria, dengue, and enteric fever should be excluded. In the case of pulmonary involvement, chest radiography may show normal results at early stages of disease. Immunocompromised hosts may present with severe pneumonia and disseminated disease [58], and differentiating fungal infections from other forms of disease should be done microbiologically. The clinical laboratory should be warned of the concern for dimorphic fungi as the microbiological samples should be managed in biosafety level 3 conditions and potentially incubated for multiple weeks. Indirect diagnostic tools may need to be utilized, such as *Histoplasma* urine antigen assay, *Aspergillus* galactomannan assay, and (1,3)-Beta-D-Glucan assay. In the case of severe or disseminated disease, antifungal therapy may need to be initiated empirically while diagnostic workup is pending. In conclusion, physicians should be aware of the potential role travel-acquired fungal infections may play in the returning traveler with respiratory symptoms as well as the major risk factors and epidemiology. Transmission prevention of fungal respiratory infections includes avoiding activities that are associated with exposure to fungi which means minimizing exposure to places and activities that are associated with disruptions of soil such as construction, spelunking, or natural disasters.

In summary, patients at high risk of fungal infections with pulmonary manifestations are immunocompromised patients and those travelers who have exposure to disrupted soil during travel or bat guano in caves. Clinical presentation includes unexplained fever associated with or without respiratory, neurologic, or dermatologic features. Treatment is based on early targeted therapy depending on the isolated organism.

Mycobacterial Respiratory Illnesses

Mycobacterium Tuberculosis

Tuberculosis often refers to a range of clinical illnesses caused by *Mycobacterium tuberculosis* and less commonly *Mycobacterium bovis*. In 2014, TB killed 1.5 million people including 890,000 men, 480,000 women, and 140,000 children [67]. Infection with *M. tuberculosis* might be acquired at home or during travel. Risk of infection is determined by infectiousness of the source patient, frequency of exposure to a case, susceptibility of those exposed, and the duration of exposure. Whether travel may increase the underlying risk depends on country of origin, destination, and duration of travel. Tuberculosis incidence varies among locations [67], but also within a country [68]. A high level of attention has been given to the risk of tuberculosis transmission during air travel and the World Health Organization has published guidelines on tuberculosis and air travel [69]. Indoors, tubercule bacilli are expelled into a limited space and may remain viable and suspended in the air for long periods of time [70]. Outdoors, the tubercule bacilli disperse, decreasing risk of exposure to nearby individuals. Available evidence suggests that the risk of transmission of infection on short flights is minimal [71, 72]. However, longer flights (particularly greater than 8 h) involve increased risk of exposure and subsequently transmission of tuberculosis [73]. Long-term travelers also have an increased risk of exposure. In one study of long-term travelers from the Netherlands who were abroad for more than half the year largely visiting Africa, Asia, and Latin America, the risk of acquiring *M. tuberculosis* in the travelers was essentially the same as the risk as estimated for the general population in the destination country [74].

Pulmonary manifestations of *M. tuberculosis* are varied and can include a chronic cough, chest pain, and coughing up blood or sputum with chest radiography having normal results in some patients and others demonstrating a patchy or nodular infiltrate in the lung apices, occasionally with cavitation. Other nonspecific symptoms associated with TB include fatigue, anorexia, weight loss, fevers, night sweats, and chills. If concerned about potential diagnosis of pulmonary tuberculosis, then obtaining sputum culture for acid-fast bacillus testing is the gold standard for diagnosis with multiple specimens increasing sensitivity. Airborne isolation should be considered in the acute setting, while the diagnosis of pulmonary tuberculosis is being assessed. This is of particular importance as the incidence of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis is increasing globally with more than half the cases worldwide occurring in India, China, and the Russian Federation in 2014 [67].

Nontuberculous Mycobacteria

Nontuberculous mycobacteria (NTM) are a large group of acid-fast bacteria ubiquitous in the environment that present as lymphadenitis, skin and soft tissue infections, and occasionally also as a lung disease or a disseminated infection. Pulmonary infections are most commonly due to *Mycobacterium avium complex* (MAC), *Mycobacterium kansasii*, and *Mycobacterium abscessus*. Important differences in geographical distribution of these species have been observed. The prevalence of MAC pulmonary disease varies from approximately 1.3 cases per 100,000 persons in the United States [75] and Japan [76] to France where there are 0.2 cases per 100,000 persons [77]. Common risk factors associated with MAC include underlying lung disease, mainly previous history of tuberculosis, bronchiectasis, cystic fibrosis, or chronic obstructive pulmonary disease. Most patients with MAC present with clinical symptoms, commonly cough and fatigue, in addition to sputum samples smear positive for acid-fast bacilli [77]. In the United States, *M. kansasii* is the second most commonly recognized NTM after MAC, often seen in southern and central regions, and is often associated with HIV infection [78]. *M. abscessus* is the third most common cause of NTM in the United States, though geography varies with reports in Asia suggesting that *M. abscessus* has higher prevalence in South Korea than in other countries, including Japan [79]. Patients with NTM often present with chronic cough with or without sputum production, fatigue, and less frequently malaise, dyspnea, fevers, hemoptysis, and weight loss. Clinical studies should include sputum culture for acid-fast bacilli and chest radiography. It is important to note that a single sputum culture with NTM is not proof of disease with NTM, especially when the acid-fast bacilli are present in low numbers, and there are diagnostic criteria to determine lung disease caused by NTM [78]. Mainstay of transmission prevention for *M. tuberculosis* is airborne precautions and treatment of persons who have suspected or confirmed TB disease. For NTM, the agents are ubiquitous in soil, water, food, and animals and specific transmission precautions and treatment should be targeted for that organism.

In summary, the pulmonary manifestations of *M. tuberculosis* are chronic productive cough with sputum or blood and chest pain associated with the above nonspecific symptoms including weight loss, fevers, and night sweats. Transmission prevention is prompt airborne precautions and treatment with antituberculous therapy. If relapse or treatment failure occurs, early consultation with infectious diseases or pursuing specialty expertise is recommended. Pulmonary NTM disease presents similarly and initiation of therapy should be determined based on individual cases by a pulmonary or infectious disease specialist.

Parasitic Infection

Strongyloides stercoralis

The primary parasite that causes pulmonary infection is *Strongyloides stercoralis*, a parasite widely distributed in tropical or subtropical climates. *Strongyloides* spp. is endemic to Southeast Asia, Latin America, sub-Saharan Africa, and parts of the Southeast United States [80, 81]. Primary populations affected are commonly those of low socioeconomic status, institutionalized groups, and those who live in rural areas where it is often associated with agricultural activities. Global prevalence of *S. stercoralis* has been on the rise secondary to poor personal hygiene, insufficient access to drinking water, unsanitary conditions, and lack of knowledge in high-risk populations [80]. A number of studies have found an association with *Strongyloides* and infection with Human T-Cell Lymphotropic Virus-1 (HTLV-1) [80, 82].

The diagnosis of strongyloidiasis requires a high degree of suspicion as there are no distinct clinical features and lab and imaging studies are nonspecific. Clinical correlation of symptoms with travel and residence history should be considered in a patient who has been to endemic areas. Clinical presentation often includes a dry cough, wheezing, non-specific gastrointestinal complaints (stomach ache, bloating, diarrhea, constipation, and anorexia), seriginous urticarial eruption from larva currens where the worm has entered the skin, and an erythematous rash often along the thighs and buttocks. Laboratory results will show a serum eosinophilia. Hyperinfection syndrome is a phenomenon that results from the enormous multiplication of infective larvae into the respiratory and GI tract. Hyperinfection occurs commonly in the immunosuppressed state, but there have been some reports of it occurring in immunocompetent states [80, 83]. Most commonly, a stool smear is the mode of diagnosis as the larvae can be easily identified on the stool smear. However, reportedly a single stool exam is only about 50 % sensitive for making the diagnosis, and a negative result does not rule out the disease; therefore, it is essential to examine a series of samples which can increase sensitivity up to 70–80 % [80]. Peripheral eosinophilia is common in acute infection representing the body's immune response to the migration of larvae through the host tissue. However, in immunocompromised patients and in severe cases of strongyloidiasis peripheral eosinophilia can be absent [80]. The mainstay of transmission prevention is shoe wearing while walking on soil, avoidance of fecal matter or sewage, and proper sewage and fecal management. Anthelmintic should be initiated with ivermectin and/or albendazole.

Physicians should consider strongyloidiasis if the patient has traveled to a tropical or subtropical climate and presents with a dry cough, wheezing, seriginous

urticaria and labs studies showing serum eosinophilia. Specific attention should be made to identify an immunocompromised state as these patients are at risk for hyperinfection. A series of stool samples for testing is recommended for accurate diagnosis and treatment is with an anthelmintic. Transmission prevention includes footwear protection from soil and proper sewage and sanitation management.

Conclusion

Respiratory tract infections remain commonly reported illnesses in travelers. As the number of people who travel increases, the potential to create an epidemic or pandemic from a severe and newly emerging respiratory infection is more likely, such as in the cases of MERS or SARS. Preventing epidemics and pandemics is a public health concern and starts with the individual healthcare provider. A comprehensive yet focused travel history with a basic understanding of the epidemiology of various respiratory diseases can help build a differential diagnosis that is narrow enough for a clinical workup, but broad enough to prevent premature diagnostic closure.

A detailed travel history with the chronology of symptoms paired with the patient's medical risk factors and exposures will help create a clinical picture that considers both travel and nontravel-related respiratory diseases. It is of utmost clinical importance to focus on the patient's medical risk factors. Emphasis should be placed on comorbid medical conditions such as underlying pulmonary disease, renal failure, cardiac disease, advanced age, and an immunocompromised state as these populations are more susceptible, the presentation of the illness may be atypical, and the disease may become fulminant quickly. This framework will help create a broad, but appropriate differential diagnosis, as well as guide the physician's clinical workup, prevent delays in diagnosis, and facilitate patient care while preventing further transmission. Emphasis should be placed on calling an infectious disease consultant early in the hospital course to assist in early identification of a travel-related respiratory illness that is beyond the clinician's scope of practice as well as to aid in diagnosis, guide therapy, and implement appropriate infection precautions.

Compliance with Ethical Guidelines

Conflict of Interests Drs May & Okamoto declare no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain studies with human or animal subjects performed by the author.

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