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Exposure to Microbiological Agents in Indoor and Occupational Environments

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Foreword

Microorganisms are indispensable companions to human life.

We have always been faced with the galaxy of microorganisms in our environment, and the science developments during the last decades have unequivocally shown that our "internalized" microorganisms referred to as the microbiome are determining our health and disease.

The new measuring techniques next generation sequencing has opened a whole new area of research, and much is still to be learnt about the interface between humans and their surrounding microorganisms.

Modern living is associated to the movement of people at an unprecedented high level. Such a high mobility leads to new threats in society and new tools to handle these. These issues call for a constant vigilance in the focus on microorganisms in different areas and purposes. The current volume is a great companion for the many people responsible for the management of public health in connection to the diverse effects of microorganisms, from surveillance of moulds in occupational settings to the handling of the microbial environment in hospitals.

This book provides a valuable companion to all who are concerned with diseases, related to microbial exposure at the workplace. The content covers a very diverse turf, from infections and noninfectious effects of microorganisms to the different measuring strategies and special occupational environments with high levels of microorganisms and their endo- and exotoxins.

Whether the reader is concerned with infections, allergies, or with other potential adverse health effects, this book will give valuable background information. By bringing together what is currently known about these conditions, together with the latest information on their detection, monitoring and control, the authors have provided a comprehensive resource for all those concerned with this increasingly important and diverse field of health effects related to microbial exposures. Increased awareness of this field will be needed in order to develop new strategies for intervention and prevention. Given the potential for public health benefit as well as burden of these exposures the book can be highly recommended.

June 17, 2017 Torben Sigsgaard

List of Abbreviations

15-Ac-DON	15-acetyl-deoxynivalenol
16HBE140	human bronchial epithelial cell line
2'R-OTA	2'R-ochratoxin A
3-AcDON	3-acetyl-deoxynivalenol
4R-OH-OTA	4'R-hydroxy-ochratoxin A
A549	human alveolar epithelial type II cell line
AIHA	American Industrial Hygiene Association
AdV	human adenovirus
AFB_1	aflatoxin B_1
AFB1	aflatoxin B1
AFB_1-N^7-guanine	aflatoxin B_1-N^7-guanine
AFB_1-NAC	aflatoxin B_1-N-acetyl-cysteine
AFB_2	aflatoxin B_2
AFG_1	aflatoxin G_1
AFG_2	aflatoxin G_2
AFLP	amplified fragment length polymorphism
AFM_1	aflatoxin M_1
AIDS	acquired immune deficiency syndrome
AM	alveolar macrophages
APS	aerodynamic particle sizer
ASHRAE	American Society of Heating, Refrigerating and Air-Conditioning Engineers
BEAS-2B	human bronchial epithelial cell line
BEN	Balkan endemic nephropathy
Calu3	human airway epithelial cell line
CAM	chorioallantoic membrane
CD14	cluster of differentiation 14 gene
CDC	Centers for Disease Control and Prevention
CFS	chronic fatigue syndrome
CFU	colony forming unit

CMV	cytomegalovirus
CoNTC	concentration of no toxicologic concern
COPD	chronic obstructive pulmonary disease
DBS	dried blood spot
DGGE	denaturizing gradient gel electrophoresis
DGGE	denaturing gradient gel electrophoresis
DMI	sterol dimetilation inhibitors
DNA	deoxyribonucleic acid
DOM-1	deepoxy-deoxynivalenol
DON	deoxynivalenol
DON-15-GlcA	deoxynivalenol-15-O-β-glucuronide
DON-3-GlcA	deoxynivalenol-3-O-β-glucuronide
dsDNA	double strained DNA
ECDC	European Center for Disease Prevention and Control
ECRHS	European Community Respiratory Health Survey
EDC	electrostatic dustfall collector
EDX	energy dispersive X-ray spectroscopy
EF	enhanced Fujita scale
EFSA	European Food Safety Authority
EIA	enzyme immunoassay
ELISA	enzyme linked immunosorbent assay
ELPI	electrical low pressure impactor
EM	electron microscopy
EPS	extracellular polysaccharides
EPSS	electrostatic precipitator with superhydrophobic surface
ERMI	environmental relative moldiness index
EU	endotoxin units
EU	European Union
EU/m^3	endotoin unit per cubic meter
EVs	enteroviruses
FB_1	fumonisin B_1
FDA	Food and Drug Administration
FLD	fluorescence detector
FSSST	fungal spore source strength tester
FUS	fusarenon x
G-	gram negative bacteria
G+	gram positive bacteria
GC	gas chromatography
HAI	hospital acquired infection
HAI	healthcare-associated infections
HBM	human biomonitoring
HBROEL	health-based recommended occupational exposure limit
HCW	healthcare workers
HEPA	high-efficiency particulate arrestance
HEPA	high efficacy particulate airfiltration

HIV	human immunodeficiency virus
HMPV	human metapneumovirus
HPIV	human parainfluenza virus
HPLC	high performance liquid chromatography
HRV	human rhinovirus
HSCT	allogeneic hematopoietic stem cell transplantation
HVAC	heating, ventilation and air conditioning
IA	invasive aspergillosis
IAC	immuno-affinity chromatography
IARC	International Agency for Research of Cancer
IFI	invasive fungal infection
IgA	immunoglobulin A
IgE	immunoglobulin E
IgG	immunoglobulin G
IL	interleukin
INAS	intra-nasal air sampler
IOM	Institute of Medicine
ISO	International Organization for Standardization
ITS	internal transcribed spacer regions
IV	influenza virus
JEFCA	Joint FAO/WHO Expert Committee on Food Additives
LAI	laboratory-acquired infection
LAL	limulus amebocyte lysate
LIF	laser induced fluorescence
LOD	limit of detection
LOQ	limit of quantification
LPS	lipopolysaccharide
LPSN	list of prokaryotic names with standing in nomenclature
m3	cubic metre
MALDI	matrix-assisted laser desorption/Ionization
MALDI-TOF	matrix-assisted laser desorption/ionization time-of-flight
MALDI-TOF-MS	matrix assisted laser desorption/ionization-time of flight mass spectrometry
MDR	multidrug resistance
MEA	malt extract agar
MERS	middle east respiratory syndrome
MERS-CoV	middle east respiratory syndrome coronavirus
MGE	mobile genetic elements
mm	millimetres
Mrna	messenger RNA
MRSA	methicillin-resistant *Staphylococcus aureus*
MS	mass spectrometry
MS/MS	tandem mass spectrometry
MSQPCR	mold-specific quantitative PCR
MSSA	methicillin-resistant *Staphylococcus aureus*

MTT	(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
MVOCs	microbial volatile organic compounds
MWF	metalworking fluids
NADPH	nicotinamide adenine dinucleotide phosphate
NAHA	N-acetylhexosaminidase
NCID	National Center for Infectious Diseases
ng/m^3	nanogram per cubic meter
NGS	next generation sequencing
NIOSH	National Institute for Occupational Safety and Health
NIV	nivalenol
NLVs	norwalk-like viruses
NoVs	noroviruses
ODTS	organic dust toxic syndrome
OEL	occupational exposure limit
OPCs	optical particle counters
OTA	ochratoxin A
PBOA	primary biogenic organic aerosols
PCR	polymerase chain reaction
PFGE	pulse field gel electrophoresis
P-FLEC	particle-field and laboratory emission cell
PM	particulate matter
PM10	particulate matter 10 micrometres or less in diameter
PM10	particulate matter
PMN	polymorphonuclear cells
PPE	personal protective equipment
qPCR	quantitative PCR
rDNA	ribosomal DNA
REL	recommended exposure limit
rFC	recombinant factor C
RFLP	restriction fragment length polymorphism
RH	relative humidity
RNA	ribonucleic acid
ROS	reactive oxygen species
rRNA	ribosomal RNA
RSV	respiratory syncytial virus
RT – PCR	reverse transcription polymerase chain reaction
RT-PCR	real time PCR
RV	rhinovirus
RWI	recreational water illness
SARS	severe acute respiratory syndrome
SARS-CoV	severe acute respiratory coronavirus
SAX	anion exchange resin
SCF	scientific committee for food
SEM	scanning electron microscopy
SPE	solid phase extraction

SPP.	species
SRM	single reaction monitoring
ssDNA	single stranded DNA
TCID50	median tissue culture infectious dose
TDI	tolerable daily intake
TGGE	temperature gradient gel electrophoresis
Th cells	T-helper cells of either type 1 (Th1) or type 2 (Th2)
Th-2	type 2 helper cells
TLR	toll-like receptors
Tm	melting temperature
TMC-120A	mycotoxin furo[3,2-h]isoquinoline
TMV	tobacco mosaic virus
TOF	time off light
T_{reg}	regulatory T cells
TRFLP	terminal restriction fragment length polymorphism
TSA	tryptone soy agar
TTC	threshold of toxicological concern
UVAPS	ultra violet aerodynamic particle sizer
VOC	volatile organic compound
VRE	vancomycin-resistant enterococci
VZV	varicella-zoster virus
WGS	whole-genome sequencing
WHO	World Health Organization
XTT	2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide
ZAN	zearlanone
ZEN	zearalenone
ZEN-14-GlcA	zearalenone-14-O-β-glucuronide
α-ZAL	α-zearalanol
α-ZEL	α-zearalenol
β-ZAL	β-zearalanol
β-ZEL	β-zearalenol
Δ	difference
μm	micro molar

Contents

Part I
Indoor Exposure to Microorganisms with Emphasis on Occupational Environments

Chapter 1
Occupational Fungal Exposure in the United States

Brett J. Green

Abstract The objective of this book chapter is to provide a review of recent advances in our understanding of fungal exposures encountered in United States occupational environments and the impacts that these exposures have on worker health. Occupational exposure can occur to a broad diversity of fungal bioaerosols that include spores, conidia, hyphae, yeasts, chlamydospores, and submicron fragments. Pulmonary exposure to fungal bioaerosols in the work environment can lead to some respiratory morbidities. In some cases, exposure to dimorphic fungal conidia can also result in a symptomatic pulmonary infection that can disseminate and become life threatening. Transcutaneous penetrating injuries sustained while handling vegetation may additionally implant fungal spores or hyphae and result in a subcutaneous infection. Workers may also be susceptible to dermatophytes that can proliferate in occluded regions of the skin such as interdigital spaces and cause a cutaneous infection. Occupational environments and work related tasks that can lead to fungal exposure are reviewed. Strategies to avoid worker fungal exposures including engineering and administrative controls as well as personal protective equipment are additionally provided.

Keywords Exposure assessment · fungus · dermatophytes · gene sequencing · occupational hazards

1.1 Introduction

Fungi are eukaryotic organisms that lack chlorophyll. Many species are saprophytic and obtain nutrients from live or dead organic material in the environment. Based on these properties, fungi can proliferate within a number occupational settings in the United States, including non-industrial indoor environments that

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contain cellulose-based building materials, agricultural settings, or other occupational environments in which contaminated organic material or soil are handled or disturbed. Fungi are a diverse kingdom, and 1.5 million species are estimated to exist (Hawksworth 2001). Compared to prokaryotes described in independent chapters, fungi contain a membrane-bound nucleus, mitochondria, centrioles, and 80S ribosomes (Cannon et al. 2006). The fungal cell wall is rigid and composed of mannose proteins, (1→3)-β-d-glucan, chitin and the sterol, ergosterol (Cannon et al. 2006). Fungi are larger in size than bacteria and produce a variety of structures that range from unicellular yeasts to filamentous hyphae that can include arrangements of sexual spores or asexual conidia. These reproductive particles range in size from as small as 2 μm to greater than 120 μm in size. Biotic or abiotic disturbance can result in the release of spores in concentrations that can exceed 10^8 colony forming units per cubic meter in some industrial environments (Eduard 2009).

Workers can be exposed to a variety of fungal phyla, but three predominate and include the Ascomycota, Basidiomycota, and Zygomycota. Recent metagenomic studies suggest that the Ascomycota and Basidiomycota are the most common fungal phyla detected in indoor, outdoor, and occupational environments (Green et al. 2016; Rittenour et al. 2014). In contrast, some workers may only be exposed to a homogenous fungal source, such as processing workers in a mushroom production facility in which spore concentrations can be as high as 10^6 spores per cubic meter (Sastre et al. 1990). Some of the particles that the U.S. workforce can be exposed to include spores or conidia, unicellular yeasts, chlamydospores, and even fragments of each of these reproductive structures. Hyphae or microscopic structures of the cell wall can also fragment and aerosolize into the breathing zone of a worker (Green et al. 2011).

Fungi can be monomorphic and consist of either a unicellular yeast or a multicellular hyphal form. Dimorphic fungi are a unique group of fungi placed in the phylum Ascomycota and include the primary endemic pathogens that grow in the environment as multicellular filamentous fungi and produce spores that when inhaled by a host, convert into a budding yeast (Gauthier 2015; Klein and Tebbets 2007). Polymorphic fungi include endogenous flora, such as the yeast species *Candida albicans*, that produce budding yeast, pseudohyphae, true hyphae and chlamydospores. Worker exposure to asexual or sexual spores derived from monomorphic fungi such as yeasts or filamentous hyphal forms is the predominant fungal particle exposure in occupational settings. In some cases that involve disturbance to the soil, workers can inhale the spores of dimorphic fungal pathogens that are endemic to specific regions of the U.S., although cases outside of these geographical boundaries have been reported (Marsden-Haug et al. 2012). Exposure to these types of fungi can cause pulmonary or disseminated infection in immunocompetent and immunocompromised hosts. Workers that sustain transcutaneous injuries while handling organic material may also acquire a subcutaneous fungal infection following implantation of fungal spores or hyphae. Worker exposure to infectious dermatophyte arthroconidia in combination with wearing occluded footwear or clothing can result in a fungal infection restricted to the skin, hair or nails. Respiratory morbidity such as hypersensitivity pneumonitis, allergy, and asthma following exposure to fungal particles is also widely reported among working populations (Eduard 2009). Exposure to these

particles occurs in a variety of occupational environments especially those that handle or disturb organic material or whose work environment is within a fungal contaminated damp indoor environment.

The objective of this book chapter is to provide a review of recent advances in our understanding of fungal exposures encountered in U.S. occupational environments and the impacts that these exposures have on worker health. Dimorphic fungal pathogens are reviewed, and updates on endemic areas and affected working populations are presented. Fungi that are associated with subcutaneous and cutaneous fungal mycoses in the U.S. workforce are also reviewed. New insights into the diversity of fungi a worker can be exposed to are additionally evaluated. This book chapter will also provide information about preventive and protective measures to avoid each of these fungal hazards in U.S. occupational environments.

1.2 Dimorphic Fungal Pathogens

Most fungi grow as saprophytes in the environment, but some are considered harmful to human health and cause disease in immunocompetent and immunocompromised individuals (Gauthier 2015; Klein and Tebbets 2007). Dimorphic fungi cause endemic mycoses and are considered primary pathogens, placed in a limited group of six phylogenetically related Eurotiomycetes in the Ascomycota order, Onygenales (Thompson and Gomez 2015). Dimorphic fungi can switch between a filamentous hyphal and a yeast phase (Gauthier 2015; Klein and Tebbets 2007). Thermal or non-thermal mechanisms govern this morphological change, a process recently reviewed by Gauthier (Gauthier 2015). In the environment, dimorphic fungi grow as a filamentous hyphal form in soil and organic debris at ambient temperatures and produce infectious spores (Gauthier 2015; Klein and Tebbets 2007). Members of this phylogenetically related group produce unicellular aleuroconidia or arthroconidia (Thompson and Gomez 2015). Abiotic and biotic disturbance to soil results in the aerosolization and inhalation of the infectious spores into the host's lungs. Upon deposition, the spores convert to into a budding yeast as part of the pathogenic phase (Klein and Tebbets 2007).

Dimorphic fungal pathogens are restricted to specific geographic regions and account for several million infections each year (Klein and Tebbets 2007). Three dimorphic fungal pathogens are endemic to the U.S. and include *Histoplasma capsulatum* (Histoplasmosis), *Blastomyces dermatitidis* (Blastomycosis), and *Coccidioides immitis* (Coccidioidomycosis). Histoplasmosis and Coccidioidomycosis are the most frequently encountered endemic mycoses in the U.S., whereas Blastomycosis is less common. Exposure to the infectious fungal conidia derived from these fungi can result in an infection that is often asymptomatic or self-limited, or can present as a symptomatic pulmonary infection that can disseminate and impact multiple organs. Although exposure can occur during recreational activities, there are some recent examples in the published literature where U.S. workers can be exposed to infectious spores while performing work-related tasks.

1.2.1 Histoplasmosis

H. capsulatum is the causal agent of Histoplasmosis, also known as Darlings disease. The species is placed in the Ascomycota order, Onygenales. This species is thermally dimorphic and grows in the soil at ambient temperature (Gauthier 2015; Klein and Tebbets 2007). *H. capsulatum* produces septate hyphae, and two types of asexual spores termed tuberculate macroconidia and microconidia (Fig. 1.1). Tuberculate macroconidia are ornate, and range in size from 8 to 15 μm (Fig. 1.1a), whereas

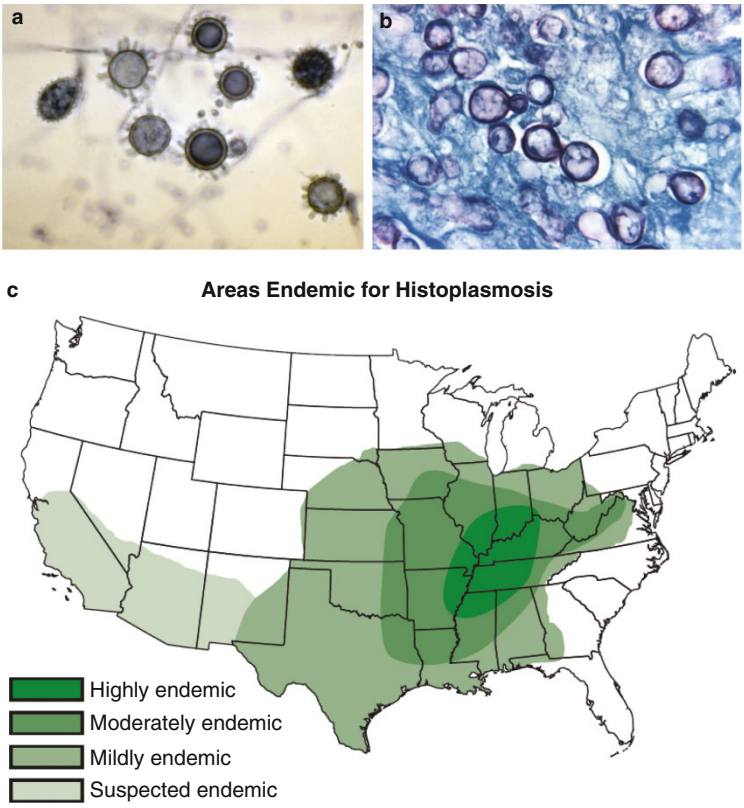

Fig. 1.1 Histoplasmosis, an endemic mycosis, is caused by the inhalation of *Histoplasma capsulatum*. The habitat of the fungus includes nitrogen rich soil that contains large amounts of bird or bat droppings. *H. capsulatum* is a dimorphic fungal pathogen and grows in the environment as a filamentous hyphal form producing tuberculate macroconidia and microconidia (**a**; Photo courtesy of CDC; CDC Public Health Image Library (PHIL) ID#: 299). Inhalation of microconidia results in the conversion to a budding yeast that can proliferate within the reticuloendothelial system (**b**; Photo courtesy of CDC/Dr. Libero Ajello; CDC Public Health Image Library (PHIL) ID#: 4221). Endemic regions of histoplasmosis include central and eastern states, especially areas around the Ohio and Mississippi River valleys (**c**). The endemic regions were determined from histoplasmin skin response surveys and outbreak cases (Map courtesy of the Centers for Disease Control and Prevention). It is important to note that cases can occur outside endemic areas

microconidia are respirable in size (Fig. 1.1b, 2–5 μm) and considered infectious. Biotic or abiotic soil disturbance events within endemic regions aerosolizes microconidia that are then inhaled by the host. Introduced to a higher temperature, suboptimal nutrients, and reduced oxygen, the microconidia then convert to a budding yeast. The yeast can modulate and proliferate within the phagolysosome of macrophages and become an intracellular pathogen within the reticuloendothelial system (Klein and Tebbets 2007). The mechanisms associated with yeast conversion and *H. capsulatum* pathogenesis are reviewed by Klein (Klein and Tebbets 2007) and Gauthier (Gauthier 2015).

Half a million Histoplasmosis cases are reported annually in the U.S. (Gauthier 2015; CDC 2016c). Inhalation of infectious microconidia can result in a lung infection that can be asymptomatic and self-limited, or can present as a symptomatic pulmonary infection that can disseminate and become life threatening. Estimates as high as 45% of hosts are not even aware of an infection and do not seek medical treatment (Lenhart et al. 1997). In symptomatic cases, mild flu-like symptoms with chest radiography resolving patchy pneumonitis that can calcify are experienced within an average of 20 days (Lenhart et al. 1997). Chronic histoplasmosis resembles tuberculosis and can last for extended durations. Disseminated histoplasmosis is the rarest and most severe form of the disease as it can affect multiple organs (Lenhart et al. 1997). Histoplasmosis can occur in both immunocompetent and immunocompromised workers and following infection, the organism can remain latent and may reactivate if the host becomes immunocompromised (Klein and Tebbets 2007). Methods to identify cases of histoplasmosis in clinical samples include viable culture, serological tests, detection of *H. capsulatum* polysaccharide antigen and the histoplasmin skin test. More detailed information related to these methods of detection are presented in detail elsewhere (Lenhart et al. 1997).

Histoplasmin skin test surveys conducted on U.S. Navy recruits in the 1950s (Manos et al. 1956) and outbreak cases are datasets used to map the continental distribution of histoplasmosis (Benedict and Mody 2016). The map presented in Fig. 1.1c outlines endemic areas of Histoplasmosis but it is important to note that cases can occur outside endemic areas. Recently, Benedict and Mody (Benedict and Mody 2016) reviewed U.S. outbreak cases of histoplasmosis between 1938 and 2013. Of the 105 reported outbreaks that included 2, 850 individual cases, over 50% of the cases were localized in Indiana, Ohio, and Iowa and onset occurred between May and November (Benedict and Mody 2016). *H. capsulatum* grows in the soil with high nitrogen content especially in soils enriched with bird droppings or bat guano. Endemic regions occur in eastern states along the Ohio and Mississippi River Valleys (Fig. 1.1c) (Lenhart et al. 1997). Areas of highest contamination include soil of various bird roosting sites, manure, and habitats of pigeons, bats and poultry (Lenhart et al. 1997).

Working environments where bird droppings or bat guano were present were estimated to account for 33% of the reported outbreaks (Benedict and Mody 2016). Other reported workplace sites included buildings, chicken coops, and farms (Benedict and Mody 2016). Occupational tasks performed during the work-related

outbreaks included construction, demolition, and maintenance (Benedict and Mody 2016). Disturbance or excavation of soil in areas with bird or bat droppings are additional risk factors for aerosolizing *H. capsulatum* infectious microconidia (Lenhart et al. 1997). In addition to disturbance mediated exposures, laboratory-acquired infections in laboratorians handling *H. capsulatum* cultures have also been reported in North America. A list of occupations at risk of *H. capsulatum* exposure is presented in Table 1.1.

Although personal exposure to microconidia is the source of exposure to *H. capsulatum*, the dose of infectious spores required to elicit symptomatic disease has not been reported. However, the higher the inoculum burden, longer duration of exposure, as well as the immune status and age of the individual are variables that can increase a worker's susceptibility to acquiring symptomatic histoplasmosis (Lenhart et al. 1997). Workers that engage in disturbance activities of nitrogen rich soils containing bird droppings or bat guano, within endemic regions are additional variables that can lead to worker exposures (Huhn et al. 2005). The National Institute for Occupational Safety and Health (NIOSH) and the National Center for Infectious Diseases (NCID) have published a guidance document aimed to increase employer and worker awareness of Histoplasmosis. The guidelines provide strategies to protect workers from occupational exposure to infectious *H. capsulatum* microconidia (Lenhart et al. 1997), particularly in workplaces where bird or bat droppings are present and environmental disruption occurs (Benedict and Mody 2016; Huhn et al. 2005). A similar list of strategies to prevent exposures are published on the Centers for Disease Control and Prevention (CDC) website (CDC 2016c). Listed below are best work practices adapted from the NIOSH/NCID guidance document that aims to prevent worker exposure to *H. capsulatum* in endemic regions.

- Remove bat colonies and birds from buildings.
- Provide health risk warnings and signage in workplaces.
- Suppress dust generation and soil disruptive activities.
- Disinfect areas identified to harbor *H. capsulatum*.
- Workers should wear personal protective equipment (PPE) presented in Table 1.1.

1.2.2 Blastomycosis

Inhalation of infectious spores derived from *B. dermatitidis* (Klein and Tebbets 2007; Klein et al. 1986) can result in Blastomycosis, otherwise referred to as Gilchrist's disease (Saccente and Woods 2010) or Chicago disease (Thompson and Gomez 2015). *B. dermatitidis* is an endemic dimorphic fungal pathogen placed in the phylum Ascomycota. This species grows as septate hyphae in the soil at ambient temperature and is thought to break down leaves and wood. Infectious spores are produced that aerosolize following abiotic or biotic disturbance of the soil (Fig. 1.2a). Compared to the other North American dimorphic fungal pathogens, the natural habitat of *B. dermatitidis* is not as well understood.

Table 1.1 Occupations at risk of exposure to dimorphic primary pathogens and fungi that can cause subcutaneous and cutaneous mycoses. Administrative, engineering, and personal protective controls that are adapted from NIOSH and CDC guidance documents are presented with the aim to minimize worker fungal exposure

Fungal species	Mycosis	Exposure	Detection methods	Occupational exposure	Avoidance strategies	PPE
Histoplasma capsulatum	Histoplasmosis	Microconidia	Viable culture Direct microscopy ITS Gene Sequencing LAMPPCR Serological assays	Bridge inspector/ painter Chimney cleaner Construction worker Demolition worker Poultry worker Farmer Gardener HVAC technician Pest controller Building restoration Roofer Prison Guard Laboratorian	• Avoid bird or bat colonies in endemic regions • Minimize dust generation activities • Disinfect soil • Worksite training • Ventilation systems • Educate and train employees safe work practices	• NIOSH-approved respirator • Disposable protective clothing • Shoe coverings • Gloves
Blastomyces dermatitidis	Blastomycosis	Conidia	Viable culture Direct microscopy ITS Gene Sequencing PCR Serological assays	Forestry worker Construction worker Excavator Rail road worker Diver Laboratorian	• Minimize dust or soil disturbance activities in endemic regions • Educate and train employees safe work practices	• NIOSH-approved respirator • Disposable protective clothing • Shoe coverings • Gloves

(continued)

Table 1.1 (continued)

Fungal species	Mycosis	Exposure	Detection methods	Occupational exposure	Avoidance strategies	PPE
Coccidioides immitis	Coccidioidomycosis	Arthroconidia	Viable culture Direct microscopy Whole genome sequencing ITS Gene Sequencing PCR Serological assays	Geologist Textile Worker Agriculture worker Farmer Construction worker Excavator Military Personnel Archeologist Healthcare worker Oil and Gas worker Telecommunication worker Prison Guard Wildland firefighters Television crew	• Minimize dust or soil disturbance activities • Avoid peak seasons • Wash equipment • Excavate using heavy machinery • Educate and train employees safe work practices • Wet soil during soil disturbance activities	• NIOSH-approved respirator • Disposable protective clothing • Shoe coverings • Gloves
Sporothrix schenckii	Sporotrichosis	Conidia	Viable culture Direct microscopy Fluorescence microscopy ITS Gene Sequencing PCR Serological assays Sporotrichin skin test	Farmer Landscaper Gardener Nursery worker Forestry worker Flower vendor Animal husbandry worker Laboratorian	• Educate and train employees safe work practices • Avoid transcutaneous injuries • Use alternative packaging materials	• Protective clothing that covers lower extremities • Shoe coverings • Gloves • NIOSH-Approved respirator (Laboratorians)

(continued)

Table 1.1 (continued)

Fungal species	Mycosis	Exposure	Detection methods	Occupational exposure	Avoidance strategies	PPE
Fonsecaea pedrosoi *Fonsecaea monophora* *Phialophora verrucosa* *Cladophialophora carrionii*	Chromoblastomycosis	Conidia (muriform or sclerotic cells)	Viable culture Direct microscopy	Farmer Rural worker	• Educate and train employees safe work practices • Avoid transcutaneous injuries	• Protective clothing that covers lower extremities • Shoe coverings • Gloves
Alternaria spp. *Exserohilum* spp. *Exophiala jeanselmei* *Wangiella dermatitidis* *Bipolaris* spp.	Phaeohyphomycosis	Yeast Conidia Hyphae	Viable culture Direct microscopy ITS Gene Sequencing PCR	Farmer Rural worker Boat builder	• Educate and train employees safe work practices • Avoid transcutaneous injuries	• Protective clothing that covers lower extremities • Shoe coverings • Gloves
Mucor spp. *Rhizopus* spp. *Apophysomyces trapeziformis* *Apophysomyces* spp.	Mucormycosis	Sporangiospores Hyphae	Viable culture Direct microscopy ITS Gene Sequencing PCR	First responders – natural disasters Emergency preparedness and response worker	• Educate and train employees safe work practices • Avoid transcutaneous injuries • Minimize dust or soil disturbance activities	• NIOSH-approved respirator • Protective clothing that covers lower extremities • Shoe coverings • Gloves

(continued)

Table 1.1 (continued)

Fungal species	Mycosis	Exposure	Detection methods	Occupational exposure	Avoidance strategies	PPE
Trichophyton spp. *Microsporum* spp. *Epidermophyton* spp.	Dermotophytosis	Arthroconidia	Viable culture Direct microscopy ITS Gene Sequencing PCR	Manual laborer Farmer Miner Military personnel Meat processor Dairy processor Poultry processor Forestry worker	• Educate and train employees safe work practices • Minimize indirect or direct contact with infectious arthroconidia (shared occupational change room facilities) • Minimize wet skin and clothes • Wear non-occluding footwear • Wash hands after handling livestock	

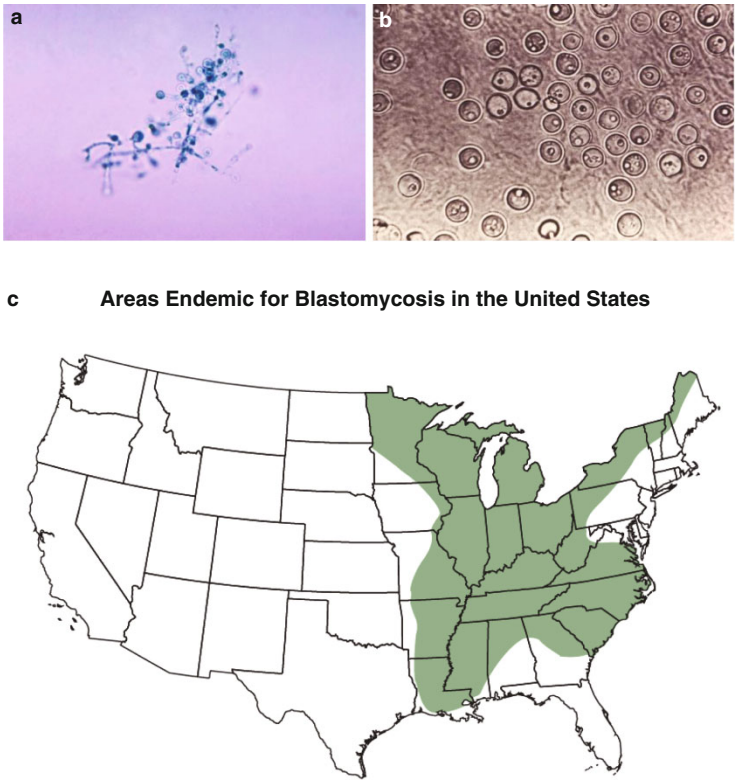

Fig. 1.2 Blastomycosis, an endemic mycosis, is caused by the inhalation of *Blastomyces dermatitidis* conidia. The habitat of the fungus is less well described compared to *H. capsulatum* and includes damp soil near bodies of water such as rivers or lakes. *B. dermatitidis* is a dimorphic fungal pathogen that decomposes organic matter such as leaves and wood as a filamentous hyphal form producing conidia (**a**; Photo courtesy of CDC/Dr. Leanor Haley; CDC Public Health Image Library (PHIL) ID#: 3768). Inhalation of conidia results in the conversion to a large budding yeast with thick refractive walls (**b**; Photo courtesy of CDC/Dr. Lucille K. Georg; CDC Public Health Image Library (PHIL) ID#: 14882). Blastomycosis is sporadic and occurs in southeastern U.S. regions especially the Mississippi and Ohio River valleys as well as the Canadian provinces of Ontario, Quebec, and Manitoba (**c**; Map courtesy of the Centers for Disease Control and Prevention). It is important to note that cases can occur outside endemic areas

Inadequate skin test reagents and serology methods have limited the research community's understanding of Blastomycosis, and much of our knowledge of endemic regions has been based on reported outbreaks (Saccente and Woods 2010). The saprophytic habitat of *B. dermatitidis* includes wet earth and organic debris associated with bodies of waters such as rivers, streams, and lakes (Saccente and Woods 2010). One study located in Northern Wisconsin showed that Blastomycosis cases were related to soil disturbance surrounding a beaver lodge (Klein et al. 1986). Cases of Blastomycosis are sporadic and occur in southeastern U.S. regions,

especially the Mississippi and Ohio River valleys, as well as the Canadian provinces of Ontario, Québec, and Manitoba (CDC 2016a). Fig. 1.2c presents the geographic distribution of Blastomycosis cases.

Epidemiological studies suggest that the mode of infection includes the inhalation of conidia following soil disturbance activities (Fig. 1.2a) (Klein et al. 1986). Conversion of the conidia into a broad based-budding yeast cell (8–10 μm) follows respiratory deposition (Fig. 1.2b) (Klein and Tebbets 2007). Exposure to *B. dermatitidis* can result in pulmonary, cutaneous or disseminated Blastomycosis (Klein and Tebbets 2007). Pulmonary infections are predominant, and 50% are reported to be asymptomatic and self-limited (Klein and Tebbets 2007). In symptomatic cases, symptoms appear anywhere from 3 weeks to 3 months following exposure (CDC 2016a). Primary cutaneous blastomycosis has also been reported following a penetrating injury (CDC 2016a).

As *B. dermatitidis* is restricted to wet earth and organic debris, workers that handle or disturb soil within endemic regions are at risk of being exposed to infectious spores. The incidence of Blastomycosis is low compared to the other dimorphic fungal pathogens. The disease is reportable in Arkansas, Louisiana, Michigan, Minnesota, and Wisconsin (CDC 2016a). In a recent study, the annual incidence of Blastomycosis in Quebec, Canada was 0.133 cases per 100,000 individuals (Litvinov et al. 2013), whereas in a Wisconsin country the annual incidence was 40 cases per 100,000 individuals (Saccente and Woods 2010). Occupations at risk of exposure to *B. dermatitidis* in endemic regions are presented in Table 1.1 and include workers that disturb the soil such as professional divers (Kroll and Grossman 2013) and railroad workers (Siemieniuk et al. 2015). In addition to environmental sources of exposure, laboratorians that handle culture specimens can inadvertently aerosolize infectious *B. dermatitidis* spores and acquire blastomycosis (Cote et al. 1997; Saccente and Woods 2010). Based on the low incidence of Blastomycosis in the U.S., methods to prevent exposure are presented by the CDC and are available online (CDC 2016a). Based on the available peer-reviewed literature, the following methods can minimize and help protect workers from exposure in endemic regions.

- Awareness and worksite training before soil disturbance occupational tasks (construction, excavation, and manual digging) in endemic regions.
- Minimize soil disturbance and dust generation on work sites.
- Wear PPE described in Table 1.1.

1.2.3 Coccidioidomycosis

Inhalation of *C. immitis* and *C. posadasii* infectious arthroconidia can result in Coccidioidomycosis or Valley Fever (CDC 2016b). *C. immitis* is thermally dimorphic, and optimal growth occurs in the southwest of the U.S. in the Lower Sonoran Life Zone. Growth is optimal in warm, dry climates with alkaline soil containing salt and borates (Ampel 2009, 2011). The species also extends into