

Review Article

Laboratory-Acquired Fungal Infections: A Review

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Abstract

Laboratory-acquired infections (LAIs) are defined as infections acquired through laboratory or laboratory-related activities. Whether the infected host remains asymptomatic or becomes symptomatic with overt illness depends on many unpredictable factors. A variety of microorganisms, viz. bacteria, viruses, rickettsiae, fungi and parasites cause LAIs. These infections are a hazard in personnel engaged in clinical research laboratories. An intensive search of literature through several search engines revealed that dimorphic fungi, viz. *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Histoplasma capsulatum* are responsible for the maximum number of laboratory-acquired (LA) mycoses. Coccidioidomycosis caused by *C. immitis* and dermatophytosis caused by *Trichophyton mentagrophytes* are the commonest laboratory acquired (LA) fungal infections. The aim of this

study is to give an update of the present state of our knowledge on LA fungal infections and suggest preventive measures.

Keywords: Fungus-infection; Laboratory-acquired; A review

List of abbreviations: LAIs: Laboratory acquired infections; LA: laboratory acquired; BSC: Biological Safety Cabinet

1. Introduction

Laboratory-acquired infections (LAIs) are defined as all infections symptomatic or asymptomatic acquired through laboratory or laboratory-related activities [1]. When a pathogenic microorganism is studied in the laboratory, it is possible that sooner or later some laboratory workers will become infected with that agent. Many unpredictable

factors involving the interaction of the host and the agent will determine whether or not the host has overt illness, or none, and the nature of the signs, symptoms, and clinical course [2]. Infectious diseases acquired in a laboratory were reported first at the time of Pasteur and Koch in 1890 [3]. Several decades passed before the connection between human diseases and the handling of pathogenic microorganisms was understood [4, 5], and the implementation of protective measures against biological risks in humans was reported in the literature [4, 6]. The first safety measures in microbiology laboratories that work with pathogenic microorganisms were implemented in North America and the United Kingdom at the beginning of the 1970s [6]. LAIs are an occupational hazard, especially in personnel engaged in clinical and research laboratories. Such infections occur due to a variety of microorganisms, viz. bacteria, viruses, rickettsiae, fungi and parasites [7].

Bacteria are the commonest causes of LAIs. The precise risk of infection after an exposure is, however, not defined. Laboratory workers become infected through unexpected modes of transmission [4, 7]. An analysis of 3291 LAIs [8] showed that 9% of these infections are caused by fungi. Dermatophytes as well as dimorphic fungi can be involved in laboratory acquired infections. Cutaneous infections due to dermatophytes and some other fungi occur by accidental inoculation. A review in 2009 [9] reported that dimorphic fungi are responsible for the greatest number of LA fungal infections. Aerosols of these fungi produced in various ways are probably the most frequent causes of laboratory-associated infections [2]. Accidental infections have also resulted while pipetting, and from the spills by the use of a needle and syringe [2, 10]. The aim of this review is to provide an update on the occurrence of laboratory acquired infections world-wide due to different fungi and to suggest preventive measures.

2. Materials and Methods

An intensive search was made for literature in fungal infections through several search engines, viz. PubMed, MEDLINE, Biomed Lib, Med Facts using different sets of keywords, viz. Lab-acquired fungi, fungal infections, mycoses, USA, Europe, South America, Asia. A major source of data known till 1965 was the manual: Laboratory-Acquired Infections published by the US Department of Army in 1967 [3].

3. Infections due to systemic pathogenic fungi

Dimorphic fungi, viz. *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Histoplasma capsulatum* are responsible for the maximum number of laboratory-acquired fungal infections in the United States [8-10]. Most of these infections are caused by inhalation of infectious conidia from the mold form, resulting in pulmonary infection. The updated information on different systemic fungal pathogens and dermatophytes is described below.

3.1 *Coccidioides immitis*

Coccidioides immitis is the most virulent and infectious fungus posing an occupational hazard to laboratory workers and other personnel in the immediate vicinity, and also maintenance staff as well as visitors. The first authentic case of laboratory acquired *C. immitis* infection was reported in 1913 [11]. A total of one hundred and forty-two and five suspected cases of laboratory-associated coccidioidomycosis were documented till 1967 [3]. Additional 93 cases of coccidioidomycosis with two deaths were documented based on the data for the years 1976 and 1978 [9]. Another review [12] listed two more cases of LA coccidioidomycosis from the data for the years 2002-2004. Although cutaneous infections from accidental inoculation are known, most laboratory-associated infections are caused by inhalation of highly infectious arthroconidia. The

risk is a serious one, owing to the large numbers of arthroconidia produced by most isolates in culture [13]. The aerosol amount to which these workers may be exposed while examining culture plates, or making slide preparations or subcultures is likely to be much greater than would be encountered in natural environment. The mere removing the lid of a petri dish culture is often sufficient to cause the release of large numbers of conidia, and should a sporulating culture be dropped, millions of conidia would be dispersed [13].

Coccidioidomycosis has been recognized as the tenth most frequent laboratory acquired infection [9]. The risk of working with *Coccidioides* in the laboratory is only slightly higher than the risk of infection in the general population [13]. A further search of the literature revealed a case report of laboratory acquired coccidioidomycosis in a 65-year-old Indian male employed as laboratory technician working mostly with *Coccidioides immitis* in research projects [14].

3.2 *Histoplasma capsulatum*

The first report of laboratory-acquired histoplasmosis was documented in 1952 [15]. In this study of 56 employees at the U.S. Public Health Field Station, Kansas City, Kansas, pulmonary histoplasmosis was diagnosed in seven persons who had influenza-like illness and tested positive for histoplasmin skin test and had X ray findings compatible with histoplasmosis. The infection rate among these employees based on positive histoplasmin test was 2.5 times greater than that for school children in Kansas, an area endemic for histoplasmosis. The authors of this report [15] concluded that laboratory is apparently an ideal environment for human infection. Subsequent to this report, 35 cases of LA histoplasmosis were described between the period 1953 to 1966 [3].

3.3 *Blastomyces dermatitidis*

The first report of laboratory acquired blastomycosis was in 1903 [16]. The author of this paper, a physician accidentally pricked the palmar surface of his left index finger with a needle while performing an autopsy on a patient who had died of systemic blastomycosis. Diagnosis was made by microscopic examination of culture of pus from a pustule that developed at the site of needle injury [16]. Subsequently eight cases of LA cutaneous blastomycoses following accidental parenteral inoculation and pulmonary infections following presumed inhalation of conidia have been reported between the period 1924 to 1967 [3]. Another case of LA primary blastomycosis was reported in 1970 in a 36-yr-old laboratory worker exposed to a culture of *B. dermatitidis* [17]. No further case of LA blastomycosis has been reported subsequently. The risk to laboratory personnel is related to accidental inoculation and infectious aerosols.

3.4 *Sporothrix schenckii*

The first case of a laboratory infection with *S. schenckii* occurred in France [18], while the author of this report was injecting rabbits with the fungal suspension by a syringe and a part of the suspension sprayed into his eyes. Within a period of two weeks, pustules developed in both the eyes, and *S. schenckii* was cultured from the pus. He recovered completely after 75 days of potassium iodide treatment [18]. Six more cases of LA *S. schenckii* infection were reported between the period 1909 to 1954 [3].

3.5 *Talaromyces (Penicillium) marneffeii*

The first known case of human *Talaromyces marneffeii* infection was laboratory acquired, when a researcher [19] accidentally pricked his own finger with a needle filled with *Talaromyces marneffeii* that was being used to inoculate hamsters. A small nodule developed at the site of needle prick, followed by axillary lymphadenopathy. This accidental infection was

cured by intensive treatment with oral nystatin for 30 days [20]. No case of laboratory-acquired *Talaromyces marneffeii* infection has been reported subsequently.

A further intensive search of the literature including a review of laboratory acquired infections in the Asia Pacific did not reveal any additional case of LA systemic mycoses [21].

3.6 Dermatophytes

The first report of laboratory acquired dermatophytic infection was *Microsporum (Trichophyton) gypseum* infection in three laboratory attendants who were in daily contact with infected mice in a colony of 2500 mice; one of attendants' boy contact also got infected [22]. Subsequent to this report, numerous cases of laboratory acquired dermatophytic infections were described between the period 1951-1965 [3]. These included 37 cases caused by *T. mentagrophytes*, three by *Microsporum canis* and one due to *M. aoudouinii*, and additional 40 cases of dermatophytoses including 18 animal attendants, and two physicians during a 10-year period [3]. The causative agents of these 40 cases were *T. mentagrophytes*, *T. rubrum*, *M. audouinii*, and *M. canis* from hamsters, guinea pigs, rats, mice, rabbits, dogs, and a cat. An analysis of 3291 cases of LAIs worldwide mentioned (4%) cases of infection due to *T. mentagrophyte* [8]. A subsequent review of reports of LAI in the Asia Pacific published between 1982 and 2016 revealed two cases due to *Athroderna benhalmaiae (Trichophyton mentagrophyte)* including one in scientist in 2001 and the another one in a research worker in 2002 in Japan [21].

4. Discussion

The risk of infection in the modern mycology laboratory is probably low, since handling of specimens is done in laminar-flow Biological Safety Cabinet (BSC). It is assumed that the BSC

fully protects the worker from the organisms while working in the BSC. The limited available data on the protective power of BSCs is not very reassuring, because the cabinets are likely not being used correctly [13]. Among the systemic mycosis, coccidioidomycosis is the commonest laboratory acquired mycosis and is the tenth in order of frequency among all the LAIs [9]. Further, a greater risk of infection is likely from an aerobic culture set-up, because colonies of *B. dermatitidis* and *C. immitis* can grow fast on routine media and may be visible within 2–3 days [13]. Since systemic mycotic infections may be subclinical and many laboratories do not maintain a periodic skin testing program, it is probable that many laboratory-acquired infections are not discovered [23]. An acute febrile influenza-like illness in a person working with these fungi should be investigated to rule out the possibility of mycotic infection [23]. The systemic pathogenic fungi must be considered as high-risk microorganisms.

5. Conclusion

It cannot be overemphasized that clinicians who suspect a dimorphic fungal infection should immediately alert the microbiology laboratory. Also, all procedures that involve manipulation of cultures of dimorphic fungi, viz. *C. immitis*, *B. dermatitidis* and *H. capsulatum* should as far as possible be conducted in a biological safety cabinet [6]. It should be ensured that culture plates are secured with shrink seal to prevent accidental opening and cultures be disinfected and discarded immediately after identification [6]. Further all laboratory personnel should be skin-tested before their initial exposure, and a program of periodically repeated skin tests in negative personnel should be established. Laboratory workers and infectious disease specialists and other appropriate officials should be trained on the use of safety equipment and aseptic precautions in all procedures, All cases of laboratory acquired infections should be notified to infection control staff [23, 24].

References

1. www. bch.cbd.int > database > record Biosafety and Biotechnology Unit, Wttenschappelijk Instituut Volksgezondheid. Editor : Dr John Peeters, General Director, Wytzmanstraat Brussels, Belgium December 14 (2012):1015.
2. Wedum AG. History & Epidemiology of Laboratory-Acquired Infections (in relation to the cancer research program). Journal of the American Biological Safety Association 2 (1997): 12-29.
3. Hanel E. Laboratory-acquired mycoses. Department of the Army, Fort Detrick (1967).
4. Sulkin SE. Laboratory-acquired infections. Bacteriological Reviews 25 (1961): 203.
5. Traxler RM, Lehman MW, Bosserman EA, et al. A literature review of laboratory-acquired brucellosis. Journal of Clinical Microbiology 51 (2013): 3055-3062.
6. Collins CH. Laboratory-acquired infections: history, incidence, causes and prevention. Butterworth & Co (Publishers) Ltd (1988).
7. Pike RM. Past and present hazards of working with infectious agents. Archives of Pathology & Laboratory Medicine 102 (1978): 333-336.
8. Pike RM. Laboratory-associated infections: summary and analysis of 3921 cases. Health Laboratory Science 13 (1976): 105-114.
9. Weinstein RA, Singh K. Laboratory-acquired infections. Clinical Infectious Diseases 49 (2009): 142-147.
10. Sewell DL. Laboratory-associated infections and biosafety. Clinical Microbiology Reviews 8 (1995): 389-405.
11. MacNEAL WJ, Hjelm CE. Note on a mold, *Coccidioides immitis*, found in a case of generalized infection in man. Journal of the American Medical Association 61 (1913): 2044.
12. Weinstein RA, Singh K. Laboratory-acquired infections. Clinical Infectious Diseases 49 (2009): 142-147.
13. Baron EJ, Miller JM. Bacterial and fungal infections among diagnostic laboratory workers: evaluating the risks. Diagnostic Microbiology and Infectious Disease 60 (2008): 241-246.
14. Mattar ZR, Abugiazia A, Totok N, et al. Laboratory-acquired coccidioidomycosis Chest October Meeting 2009, Abstracts.
15. Furcolow ML, Guntheroth WG, Willis MJ. The frequency of laboratory infections with *Histoplasma capsulatum*: their clinical and x-ray characteristics. The Journal of Laboratory and Clinical Medicine 40 (1952): 182-187.
16. Evans N. A Clinical Report of A Case of Blastomycosis of The Skin From Accidental Inoculation. Journal of the American Medical Association 40 (1903): 1772-1775.
17. Baum GL, Lerner PI. Primary pulmonary blastomycosis: a laboratory-acquired infection. Annals of Internal Medicine 73 (1970): 263-265.
18. Fava A. Un cas de sporotrichose conjonctivale et palpebrale primitives. Ann Ocul (Paris) 141 (1909): 338-343.
19. Segretain G. *Penicillium marneffei* n. sp., agent d'une mycose du systeme reticulo-endothelial. Mycopathologia et Mycologia Applicata 11 (1959): 327-353.
20. Drouhet E. Penicilliosis due to *Penicillium marneffei*: a new emerging systemic mycosis in AIDS patients travelling or

living in Southeast Asia: review of 44 cases reported in HIV infected patients during the last 5 years compared to 44 cases of non AIDS patients reported over 20 years. *Journal de Mycologie Médicale (Paris)* 3 (1993): 195-224.

21. Siengsan-Lamont J, Blacksell SD. A review of laboratory-acquired infections in the Asia-Pacific: understanding risk and the need for improved biosafety for veterinary and zoonotic diseases. *Tropical Medicine and Infectious Disease* 3 (2018): 36.

22. Parish HJ, Craddock S. A ringworm epizootic in mice. *British Journal of Experimental Pathology* 12 (1931): 209.
23. Hearn T. Addressing the Continuing Threat of Laboratory-Acquired Infections. NCPDC.2007; <ftp.cdc.gov>. [≥PDF≥ addenda≥Liac0908≥](#)
24. HHS Publication No. (CDC) 21-1112, U.S. Department of Health and Human Services Biosafety in microbiological and biomedical laboratories. 5th Edn, 2018.



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