WHITE PAPER

on

Determining the sources of Mucormycosis in the COVID 19 pandemic

by

Mucormycosis subcommittee under the Technical Advisory Committee to the COVID-19 Ministerial Task Force, Government of Karnataka

INTRODUCTION

Zygomycosis (Mucormycosis) is a rare fungal infection caused by moulds belonging to the order Mucorales.[1] The order Mucorales is divided into six families of significance in human or animal disease, but most cases of human infection are caused by members of the Mucoraceae. This includes the genera Absidia, Mucor, Rhizomucor, and Rhizopus.[2] Although these organisms are ubiquitous in nature and are present almost everywhere, predominantly in soil, their propensity to cause infections in human beings is low and is limited to people who are severely immunocompromised including those with diabetes mellitus, or those experiencing trauma. Risk factors for Mucormycosis include immunosuppression, with many infections seen in people who have had stem cell or solid organ transplant, hematologic malignancies, and long-term treatment with corticosteroids.[3] Because Mucormycetes grow best in acidic, high-glucose environments, diabetes, especially if poorly-controlled or complicated by ketoacidosis, is also an important risk factor.[4] Some evidence suggests that the number of invasive Mucormycosis infections has risen over time, in part because of better recognition and diagnosis, but also because advances in cancer treatment have increased the number of immunocompromised patients most vulnerable to infection.[5] Hospitalization and ambulatory care represent risk factors that are well known for infection caused by bacteria, yeasts, or Aspergillus species. However, the occurrence of Mucormycosis during healthcare procedures is not well documented and is probably underestimated. It's histopathological hallmark is the invasion of blood vessels, vasculotropism, leading to tissue infarction and necrosis

INCIDENCE OF MUCORMYCOSIS IN INDIA

Despite being the country reporting the largest number of cases of Mucormycosis in the world, the annual incidence of this disease in India is yet to be conclusively determined and remains unclear. The annual incidence reported per center varies from 9.5 cases to 24.5 cases.[6] The data indicates that the estimated prevalence of Mucormycosis in India, which is about 14 cases per 100,000, is nearly 70 times higher than the global data, which is estimated to be at 0.02 to 9.5 cases per 100,000 persons.[7] In India, the increase in incidence of Mucormycosis has been attributed predominantly to Diabetes Mellitus, Diabetic Ketoacidosis, organ transplantation, hematological malignancies and less so to nosocomial factors. The most common form of invasion into the human body is Rhino-orbito-cerebral Mucormycosis (ROCM), followed by pulmonary, gastrointestinal, cutaneous, disseminated and other miscellaneous forms.[7]

Figure 1: A COVID patient receiving oxygen in a healthcare facility

RISE IN MUCORMYCOSIS IN INDIA DURING THE 2ND WAVE OF THE COVID-19 PANDEMIC

While COVID-19-associated pulmonary aspergillosis (CAPA) has received much international attention, the Indian epidemiology has recorded over 12,000 cases of invasive Mucormycosis. As on May 26th 2021, India recorded 11,717 cases of Mucormycosis with Gujarat, Maharashtra, Andhra Pradesh, Madhya Pradesh and Telangana logging the highest number of the rare fungal infection, according to the latest government data. While Maharashtra has reported 2,770 cases, Gujarat, Andhra Pradesh, Madhya Pradesh, Telengana and Delhi have logged 2,859, 768, 752, 744 and 620 cases so far.[8] As of March 2021, 70% of worldwide Mucormycosis was reported in India itself. The Government of India declared it a notifiable disease on May 20, 2021 under the Epidemic Diseases Act 1897.

S.No.	State/UT	Patients under Treatment on 25th May 09:36 PM (As per Portal)	Draft Allocation 25th May	Draft Allocation Rounded off
1	A&N Islands	0	0	0
2	Andhra Pradesh	768	1950	1930
3	Arunachal Pradesh	0	0	0
4	Assam	0	0	0
5	Bihar	215	546	550
6	Chandigarh	83	211	210
7	Chhattisgarh	103	262	260
8	D&D & D&N		0	0
9	Delhi	119	302	300
10	Goa	10	25	50
11	Gujarat	2859	7260	7210
12	Haryana	436	1107	1110
13	Himachal Pradesh	3	8	50
14	J&K(UT)	5	13	0
15	Jharkahand	29	74	70
16	Karnataka	481	1221	1220
17	Kerala	36	91	100
18	Ladakh (UT)	0	0	0
19	Lakshdweep	0	0	0
20	Madhya Pradesh	752	1910	1910
21	Maharashtra	2770	7034	6980
22	Manipur	0	0	0
23	Meghalaya	0	0	0
24	Mizoram	0	0	0
25	Nagaland	0	0	0
26	Odisha	15	38	50
27	Puduchery	2	5	50
28	Punjab	141	358	360
29	Rajasthan	492	1249	1250
30	Sikkim	0	0	0
31	Tamil Nadu	236	599	600
32	Telangana	744	1889	1890
33	Tripura	1	3	0
34	Uttar Pradesh	701	1780	1780
35	Uttarakhand	124	315	320
36	West Bengal		0	0
37	Central Institutions	592	1000	1000
	TOTAL	11717	29250	29250

Figure 2: Total number of cases of Mucormycosis as on 25th May 2021 as per Government of India sources

LOOKING INTO THE POSSIBLE SOURCES OF INFECTION

The medical fraternity in India is considering and investigating varied patient factors such as hyperglycemia and acidosis, neutropenia, raised ferritin level, corticosteroid based immunosuppression, misuse of antibiotics and mutant strain of COVID-19 to be the reason for the disease. However, some questions remain unanswered. More common fungi like Candida and Aspergillosis have not seen a recent rise. Mucormycosis is being seen even in young healthy adults taking treatment for COVID-19. It is surprising to note that the same treatment strategies were followed during the first COVID-19 wave last year, and there was no surge of cases during first wave in contrast to rising number of cases in a short period of time during the current second wave. While Mucormycosis has been declared an epidemic in India, and it has not affected neighbouring countries in the subcontinent which have the same clinical milieu and socioeconomic factors. Almost 70% of the reported cases of Mucor in the world today is from India and barring our country, there has been practically no surge in cases elsewhere in the world.

The contributing factors to an epidemic is not an EITHER-OR situation. In every epidemic, there are host factors and a source factors. While the host factor in the present Mucor epidemic is being discussed widely and taking nothing away from the clinical aspects which need to be researched and taken care of therapeutically, there will be environmental factors that can be controlled with immediate effect which may bring down the numbers quickly. Investigating the source is the standard and natural SOP that is followed across the world in the advent of an epidemic. While in the west, Mucormycosis is very rare and almost purely a nosocomial infection, that India has a 70% higher baseline incidence of Mucormycosis than the rest of the world, itself is indicative of the fact that there are significant source related causes that beg to be investigated.

We investigated the potential sources of Mucormycosis in the current surge in cases in India, which can be described in the following categories:

PERSONAL PROTECTIVE EQUIPMENT (PPE) KIT MANUFACTURING & THE USAGE OF MASKS:

India has grown from being an importer of PPE kits before the pandemic broke out in 2020, to being the 2nd largest PPE kit manufacturing country, globally, second only to China. India is now producing close to 500,000 PPE suits daily and over 600 companies are certified to manufacture PPEs.[9,10] The number of NABH accredited laboratories equipped with Synthetic Blood Penetration Resistance Test facilities as well as the necessary approvals required for conducting tests and certification for Body Coveralls (PPE) required for COVID-19 has increased from nine laboratories in the country as of May 26, 2020 to 30 laboratories today including the Defence Research and Development Organisation (DRDO). Institute of Nuclear Medicine & Allied Sciences (INMAS), Delhi, under the DRDO has been authorized for laboratory testing of Personal Protective Equipment (PPE) Body Coverall samples for COVID-19, submitted by prospective manufacturers in India. A

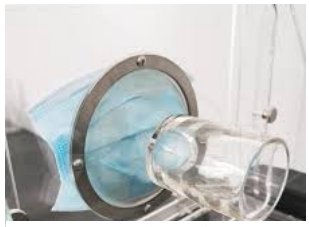
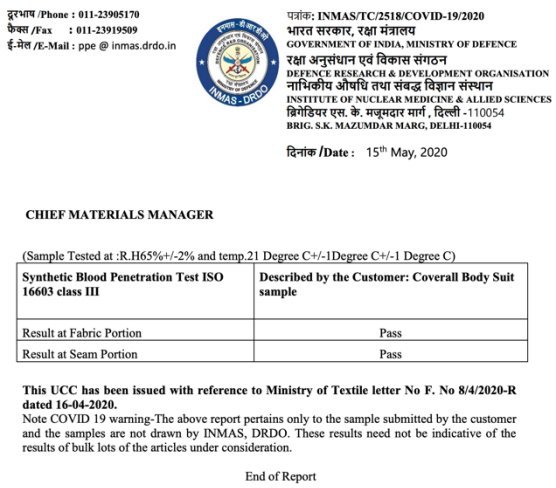


Figure 3: Mask synthetic blood penetration tester

laboratory test Synthetic Blood Penetration Resistance Test is conducted and a Test Report is issued for the same by INMAS.A Unique Certification Code (UCC-COVID19) is generated for each PPE kit, having a record of the type of fabric, type of garment, its date of testing, testing standard and other relevant information. UCC-COVID-19 certificate is given to prototype samples sent by respective manufacturers to labs. However, the certificate pertains only to the sample submitted by the customer and the samples are not drawn by INMAS, DRDO and a footnote on the certificate puts a caveat that these results need not be indicative of the results of bulk lots of the articles under consideration. Lack of periodic surprise on-site checks by agencies at the manufacturing factories may lead to complacency in adhering to strict cleanliness guidelines.



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पत्रांक: INMAS/TC/2518/COVID-19/2020
भारत सरकार, रक्षा मंत्रालय
GOVERNMENT OF INDIA, MINISTRY OF DEFENCE
रक्षा अनुसंधान एवं विकास संगठन
DEFENCE RESEARCH & DEVELOPMENT ORGANISATION
नाभिकीय औषधि तथा संबद्ध विज्ञान संस्थान
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दिनांक /Date : 15th May, 2020

CHIEF MATERIALS MANAGER

(Sample Tested at :R.H65%+/-2% and temp.21 Degree C+/-1Degree C+/-1 Degree C)

Synthetic Blood Penetration Test ISO 16603 class III	**Described by the Customer: Coverall Body Suit sample**
Result at Fabric Portion	Pass
Result at Seam Portion	Pass

This UCC has been issued with reference to Ministry of Textile letter No F. No 8/4/2020-R dated 16-04-2020.
Note COVID 19 warning-The above report pertains only to the sample submitted by the customer and the samples are not drawn by INMAS, DRDO. These results need not be indicative of the results of bulk lots of the articles under consideration.

End of Report

Figure 4: Foot note reads that the results need not be indicative of the results of bulk lots of the articles under consideration

> *"One of the key challenges was to educate people, including factory owners and workers, on what a PPE kit was and its purpose. There were several hits and misses on meeting quality standards with many manufacturers unable to meet the criteria initially….. Welspun India is largely into home textiles, so they had to set up a separate facility almost overnight to manufacture N-95 masks, respirators and overalls. They began with crude, fabricated, in-house equipment until the imported equipment to manufacture the gear could arrive. The government enabled all the permits, "an entire ecosystem was built", from knowledge transfer, sessions on R&D, setting up of testing facilities in every state—and all these things happened within no time." Gautam Nair, MD and CEO of Matrix Clothing* [9]

Most PPE manufacturing units in India today, are Micro, Small and Medium Enterprise (MSME) units employing people in the lower socioeconomic strata of society, and the Ministries of MSME and Textiles must educate the stakeholders regarding the importance of cleanliness and sterility of these products.

Figure 5: The MSME units must be educated regarding the importance of sterility of their products

Hygienic use of masks: A matter of concern is that the public are not aware of the regulations and guidelines on wearing mask and PPE kits. A survey conducted by us showed that due to the fact that the masks are considered expensive, many people use the same mask repeatedly over many days, even weeks. Wearing double masks has been widely practised in the second wave and this simply double the trouble. Mask conditions allow fungi to thrive.[11] The median particle emission rate during breathing, speaking and coughing is 0.31 particles/s, 2.77 particles/s and 10.1 particles/s respectively.[12] Another study showed that over the entire range of vocalization amplitudes, the particle emission rate increasing from 6 to 53 particles/s at the quietest and loudest vocalizations respectively.[13] In addition, heat, humidity, sweating and moisture accumulation on the inner surface of the masks, especially in those wearing the mask for long durations is a risk factor.

Figure 6: Unhygienic use of a mask

Recommendation of the committee:

1. Regulating agencies like NABL be directed by the Government to adopt stringent and periodic and continued checks on the quality of the PPE and ensure that manufacturers maintain sterility of products and standards during manufacturing.
2. Public advisories be issued by the health authorities and hospitals at all community levels to educate the public on how to wear masks, how long each mask can be used and how to reuse them. Mask have to be discarded or washed after 8 hours of use or earlier if they become wet or visibly soiled. Front portion of the mask should not be touched or handled during use. If the mask gets wet or dirty with secretions, it must be changed immediately.[14]

HOME CARE/ISOLATION & STEAM INHALATION:

Figure 8: Indoor molds on walls and AC vents can cause increase spore content indoors

With more than 80 per cent people developing mild-to-moderate Covid-19 infections that require no hospitalisation, in the second Covid- 19 wave in India, a large number of affected patients are opting to undergo home treatment – either due to paucity of hospitals beds or their own choice. In many places small hotels are being converted into home care centers.[15,16] Treating uncontrolled Diabetic-COVID patients at home may expose an immunocompromised patient to unhygienic indoor conditions. Also, Work-From-Home has become the norm since mid 2020, after the setting in of the COVID-19 pandemic, and will continue to be so for the rest of the year. In summer, indoor airborne fungi are approximately 20 times higher than the winter season. It is well known that substantial indoor dampness, mould odour, and visible mould exposure can trigger asthma, with an increased risk of 30–50% and many patients with asthma are sensitive to several fungi. Hot and dry temperatures are conducive for both the aerosolization, spread and even virulence of Fungi. Fungal colonization at home can be heightened due to temperate climate in India, unhygienic air conditioners, indoor plants, carpets & upholstery. Many opportunistic mucorales are typical inhabitants of natural composts, tropical soils, and other heated materials. Indoor sites particularly associated with these fungi, therefore, may be those where humid organic material is exposed to heat, most notably within poorly maintained heating ducts and attached humidifier structures, in soils of potted plants (especially those placed in warm locations), and in indoor composts. Due to loss of manpower during the pandemic, segregated waste from homes might not being collected as regularly as before. This means that homes contain decaying organic matter for longer periods, which is a potent medium for fungal growth, thereby leading to increased aerosolization of spores indoors.

Figure 7: Accumulated waste outside a home in India

The clinical course of zygomycosis is characterized by extremely rapid progression. In diabetic animal models inhalation of Mucorales spores resulted in rapidly progressive pulmonary Mucormycosis and death within 1–4 days. This suggests that onset of symptoms rapidly follows the inhalation of fresh spores in susceptible hosts. Since the pathogenesis of rhinocerebral and pulmonary Mucormycosis is thought to be due to inhalation of spores by a susceptible patient, the seasonal pattern of onset of symptoms may be due to fresh deposition of spores in affected tissue with an inoculum size proportional to peak

atmospheric concentration of airborne Mucorales spores during the late summer and autumn seasons.[17]

Steam Inhalation: Airborne fungal spores are almost ubiquitous and can be found on all human surfaces in contact with air, especially on the upper and lower airway mucosa. Inhalation of sporangiospores must be a daily occurrence. Surprisingly, members of the Mucorales are very rarely found in nasal mucus, suggesting that spores in the mucus of airway mucosa are cleared by mucociliary transport or that there is a low level of airborne contamination.[1] Hence the body has a robust first line of defence against fungal spores and hence the low levels of fungal infections in the upper airway.

Figure 9: Mass steam inhalation from cookers at a place in India

However, unwarranted use of steam inhalation with or without various herbal concoctions in the boiling water as advised and practiced by many in India is an important threat. During the pandemic, as a presumed preventive measure against the COVID-19 virus, people have adopted to doing steam inhalation using boiling water 1-4 times a day on a daily basis. Excessive steam inhalation can cause scalding of the nasal mucosa and provide a point of entry for fungi. The water quality too is suspect. Even if boiling water will destroy most of the spores and fungal elements in water at the surface, vapour condenses into water droplets as it cools off near the face and nose and it is these droplets that may carry spores on their surface into the nasal passages. Water vapour cannot transport organisms but water droplets can. Sporangiospores released by mucorales range from 3 to 11 microm in diameter, are easily aerosolized, and are readily dispersed throughout the environment. This is the major mode of transmission.[1] These sporangiospores can hitchhike on water droplets during steam inhalation leading to infection.

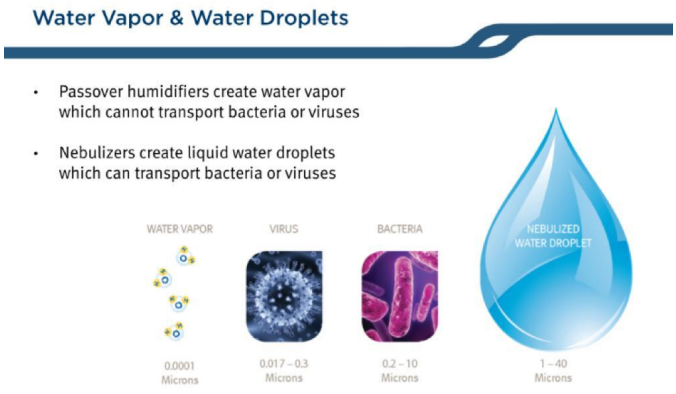


Figure 10: Sporangiospores released by mucorales range from 3 to 11 microm in diameter, are easily aerosolized by steam inhalation

In the Zygomycetes, the unit of dispersal is normally a sporangiospore from within a sporangium. Typically, a sporangium may contain up to 100,000 spores. Smaller sporangia may contain only a few hundred spores. Generally, mucoraceous moulds can produce aerial growth only when the surrounding air is extremely damp. In most mucorales, the wall of the sporangium eventually dissolves. Not only does the wall, except for a small collar around the base of the columella, break down, but water passes into the spore-mass through the columella. The result is that a 'sporangial drop' is formed; this is considerably larger than the original sporangium, and its spores are dispersed by 'splash dispersal'. Other species form dry, powdery spores. The sporangiospores dehisce, and the released sporangiospores can be dispersed by low-speed winds.[1] Steam inhalation can provide with both splash dispersal mechanism and low speed winds for spore distribution

Oxygen concentrators: The government has allowed imports of oxygen concentrators for personal use through post, courier or e-commerce portals under the gift category amid increasing demand for oxygen due to rising COVID-19 cases.[18] It is recommended that distilled water be used in the concentrators. Distilled water, if used beyond expiry dates, may be contaminated with Fungi because it does not contain a preservative. People may also not be using and practicing sterilisation of these types of medical equipment due to lack of knowledge regarding how it is to be done. The nasal cannula prongs often become contaminated when patients don't properly protect the cannula between uses (i.e., leaving the nasal cannula on the floor, furniture, bed linens, etc.). Then the patient puts the contaminated nasal cannula back in their nostrils and directly transfers potentially pathogenic organisms from these surfaces onto the mucous membranes inside their nasal passages, putting them at risk of developing a respiratory infection.

Figure 11: Oxygen concentrators must be used in a clinically sterile way

Recommendation of the committee:

1. COVID-19 positive patients with uncontrolled Diabetes Mellitus must not be kept in home care
2. Advisories must be issued to the public keep their indoor conditions hygienic: to dispose off bio-waste on a daily basis, clean air conditioning systems, avoid plants in the presence of Diabetic COVID 19 patients and near oxygen delivery apparatuses.
3. Avoid steam inhalation completely. Especially in Diabetic COVID-19 patients
4. Use Oxygen concentrators according to hygiene guidelines. Use fresh distilled water or sterile water

NOSOCOMIAL SOURCES:

Mucormycosis, a formerly community-acquired condition and often seen in the setting of diabetic ketoacidosis, is rapidly becoming a nosocomial infection in patients with malignancy or undergoing organ or hematopoietic cell transplantation.[19,20] Almost every Mucor outbreak has been not only associated with immunosuppression, but also diagnostic or therapeutic procedures such as Ventilators, ECHMO, biopsies, contaminated bandages, intravenous catheters, medical instruments and even tongue depressors. Air contamination is also linked to construction, water leaks, insufficient air filtration, non-sterile medical supplies, contaminated linen, contaminated food, and supplements has also been described as a source of infection.[4,19,21] Possibility of cross contamination of infection is also high in hospitals. Investigations about increased airborne fungal load should be conducted especially during hospital renovation and construction activities in the vicinity of the care units.[22] In emerging countries, some operating theaters are equipped with air conditioners but inefficient air filters, which may lead to a significant increased fungal risk.[23] Hospital water is also a potential reservoir for fungi.[24]

Figure 12: Wet and unhygienic areas in hospitals

Figure 13: Construction activities must be avoided or stopped in or near hospitals

To assess changes in infection rates over time, hospitals can begin by examining trends in all invasive mold infections, including Aspergillus, which causes infections more frequently than mucormycetes. Tracking Aspergillus infections may help to identify problematic exposures, because like mucormycosis, these molds are transmitted via airborne spores.[5] Infection Control Team in the hospital must meet weekly to investigate and trace possible sources of infection. Mucormycosis investigations require a multidisciplinary team. Optimally, the team should include those with clinical expertise, as well as those with expertise in case-finding, environmental assessment, and infection control. Effective response to a suspected outbreak thus requires early communication and close collaboration among infection prevention, facility maintenance, construction, environmental services, nursing, infectious disease, pathology, hospital administration, and media relations.[5]

Table 1. Published Outbreaks of Healthcare-Associated Mucormycosis

Reference	No. of Cases	Origin of Contamination	Microorganism	Localization	Underlying Condition	Death Attributable to Mucormycosis
[103]	17	Elastoplast	*Rhizopus microsporus* (8 of 17)	Skin	Surgery, corticosteroids, cancer, diabetes mellitus	Not available
[104]	5	Elastoplast	*Lichtheimia corymbifera*	Skin	Burn unit	3 (60%)
[72]	5	Wooden tongue depressors	*R. microsporus*	Digestive tract	ICU, steroids	3 (60%)
[105]	4	Wooden tongue depressors	*R. microsporus*	Skin	Premature infant	2 (50%)
[79]	2	Building construction	*Mucor indicus* (1 of 2)	Lungs	Premature infant	2 (100%)
[78]	3	Building construction	*Cunninghamella bertholletiae*	Lungs	Hematological malignancies	2 (66%)
[96]	2	Ostomy bags	*Rhizopus* species	Skin	Surgery, corticosteroids	1 (50%)
[60]	2	Water circuitry damage	*Rhizomucor pusillus* (1 of 2)	Rhinocerebral, disseminated	Hematological malignancies	0/2

Abbreviation: ICU, intensive care unit.

Figure 14: Published outbreaks of HAM

Table 2. Attributed or suspected healthcare exposures in published reports of mucormycosis.

Exposure Reported as Likely Cause of Infection	Number of Infections and Site(s)	Publication Year	Reference
Non-Sterile Products			
Bandages, patches, tape, and adhesives			
Elastic adhesive bandages	>20 cutaneous	1978–1980	[44–50]
Bandages	5 wounds; 3 necrotizing fasciitis	2005, 2011	[51,52]
Tape used to secure endotracheal tube	2 cutaneous	1998, 2002	[53,54]
Karaya gum adhesive used to secure ostomy bag	2 cutaneous infections of stomas	2006	[40]
Adhesive used to secure heart monitor and temperature probe in preterm infants	2 cutaneous	1997	[55,56]
Nitroglycerin patches applied at home	1 cutaneous	2003	[57]
Fabric under a cast	1 cutaneous	1993	[58]
Linen			
Contamination of linen and linen delivery bins	5 cutaneous	2014	[17]
Contamination of hospital laundry carts	4 cutaneous	2016	[59]
Poor ventilation, high humidity, and dust at company supplying hospital linen	3 pulmonary, 2 cutaneous, 1 pulmonary and cutaneous	2016	[18]

Figure 15: (Part 1) Attributed or suspected healthcare exposures in published reports of Mucormycosis

Table 2. *Cont.*

Exposure Reported as Likely Cause of Infection	Number of Infections and Site(s)	Publication Year	Reference
Wooden tongue depressors			
Wooden tongue depressors used to prepare oral medications given through nasogastric catheter	5 gastric	2004	[60]
Wooden tongue depressors used as splints	4 cutaneous	1996	[61]
Medications, supplements, and food			
Probiotic powdered supplement	1 gastrointestinal	2014	[43]
Probiotic oral supplement	1 hepatic	1996	[62]
Allopurinol tablets	17 intestinal	2009	[63]
Procedures, Devices, and Organs			
Catheters and tubes			
Permanent bladder catheter	1 bladder	2004	[64]
Periumbilical cutaneous catheter and chest tube	1 cutaneous; 1 chest wall and pulmonary	1998	[65]
Orogastric tube	1 gastrointestinal	2004	[66]
Catheter for continuous ambulatory peritoneal dialysis	4 peritonitis	1989, 1991, 2003, 2006	[67–70]
Dental procedures			
Unspecified dental procedure	2 rhino-orbital; 1 rhinocerebral	2006, 2009	[71,72]
Tooth extraction	1 mandible, 1 rhinocerebral, 1 maxilla, 1 jaw	1997, 2001, 2006, 2018	[73–76]
Cardiac surgery			
Explantation of left ventricular assist device	1 aortic	2008	[77]
Implantation of prosthetic valves	3 prosthetic valves	1972, 1987, 1999	[78–80]
Catheterization and bypass surgery	1 sternotomy wound	1994	[81]
Insulin pumps and finger sticks			
Insulin infusion pump insertion	1 cutaneous	1989	[82]
Daily insulin needle punctures	2 cutaneous	2004, 2017	[83,84]
Finger sticks for blood glucose self-monitoring	1 disseminated (initially cutaneous)	2005	[85]
Medical devices			
Deficiencies in sterilization of screws used in ligament reconstruction	3 bone	2016	[86]
Organ transplant			
Kidneys donated by near-drowning victim after motor-vehicle crash	2 renal	2010	[41]
Environmental Sources: Air, Dust, Water, Soil			
Air filtration and intakes			
Air filter insufficient to trap spores	4 mycotic endocarditis, including one with *Mucor* sp.	1992	[87]
Air intake close to the ground in outdoor yard	3 sinus	1993	[88]
Negative pressure room			
Use of negative-pressure isolation room for transplant surgery patients	1 disseminated, 1 cutaneous, 1 pulmonary	2015	[42]
Construction			
Inadequate barriers during renovation	2 pulmonary	1985	[89]
Leaks and water damage			
Shower leak that led to mold growth on wall in linen closet near patient rooms	1 brain and 1 cutaneous	2008	[90]
Plants			
Petal, stem, and leaf applied to skin for allergy test	1 cutaneous	2002	[91]

Figure 16:(Part 2) Attributed or suspected healthcare exposures in published reports of Mucormycosis

Table 3. Various Food Items Contaminated With Mucorales

Foodstuffs Known to Contain Mucorales [2]	Foodstuffs Containing Mucorales Found in Hematological Unit [147]
Barley	
Sorghum	
Wheat	
Corn	
Oat	
Rice	Regular tea
Onions	Biscuits
Cotton	Freeze-dried soup
Groundnuts	Pepper
Sweet potatoes	
Pecans	
Brazil nuts	
Oranges	
Honey	
Tomatoes	

Figure 17: Possible sources of food contamination in Mucormycosis

Most of the fungal outbreaks outside India have been traced to a source

The COVID-19 pandemic has led to loss of manpower among medical and non-medical staff and those remaining in the system are highly stressed. The patient turnaround time is very less due to high hospital footfalls. This has led to a situation wherein medical staff might not have the time or resources to effectively follow sterilization protocols. Many equipments such as oxygen masks and nebulizer chambers may be transferred from patient to patient several times daily but they may be seldom cleaned daily. This is especially true in the case of smaller and less resourceful hospitals. Preliminary data from our state also suggests that Mucormycosis cases have been initially treated in smaller hospitals from the peripheries where hospital sterility practices may not be optimally followed.

Humidifiers: Respiratory care equipment such as oxygen humidifiers, and nebulizers has been identified as a potential vehicle causing major nosocomial infections if colonized by fungi or bacteria.[25] In an Indian study, 75.71% samples showed fungal growth; out of which, 69.70% were from the ICU, 80% were from the wards and 85.71% were from the OPDs. 76.66% swabs from the central line humidifiers, 78.26% swabs from the O2 cylinder humidifiers and 47.5% swabs from the nebulizers grew bacteria. 86.79% swabs form O2 humidifiers & 41.17% swabs from Hudson's chambers grew fungi.[26,27] The oxygen and nebulizer chambers need to be cleaned frequently with disinfectants. Only distilled or sterile water must be used in humidifiers and nebulizers. It is also a myth that air/O2 flow is always unidirectional from humidifiers to patient. Contamination can take place due to opposite flow from the mask/canula to the humidifiers.

Figure 18: Humidifier must have a temperature regulator

High flow nasal oxygen therapy is considered in COVID-19 sepsis,[28] with unsterile contaminated oxygen inhalation for a long time could possibly breach the normal nasal mucosa and be a probable reason for increased ROCM cases. Increased workload, an inexperienced staff or lack of distilled/sterile water can lead to patients being provided with non-humidified oxygen. Humidifiers are sometimes used without a thermo-regulator or a filter as shown in the picture. Using cold, non-humidified air or oxygen for a long time can cause serious nasal mucosal damage leading to seeding of fungal spores. Using tap water instead of distilled/sterile water can be counterproductive as tap water can harbour organisms. A possible solution to this problem might be to use sterile disposable oxygen humidifiers with distilled or sterile water with proper disinfection.[29] Use of HepaShield pleated hydrophobic bacterial/viral mechanical filters can be used to minimize flow resistance and to reduce microbial contamination into the nose.

Usage of Methylene blue in the treatment of COVID-19 is under investigation[30] and it is also used in sub lingual and nebulised form or in humidifiers. It is proposed that it helps in clearing alveolar capillary blocks. However, we postulate that when methylene blue is mixed with oxygen and inhaled by the patients, it stains and create patches inside the lungs and creates more mucus thus worsening the situation. However, more studies are required to evaluate its efficacy.

Sr. no	Name of the species	Frequency of isolation	Predominate site	Predominant equipment
1	*Aspergillusfumigatus*	18 (33.96%)	• TB & Chest OPD (5/18) • SICU(3/18) • PICU(3/18) • Female Surgery Ward(2/18) • Casualty (2/18) • MICU (1/18) • Male Med Ward(1/18) • Male Surgery Ward (1/18)	• Central line humidifier 10/18 • O_2 cylinder humidifier 6/18 • Nebulizer 2/18
2	*Aspergillusniger*	10 (18.86%)	• Pediatric Ward(3/10) • PICU(3/10) • Pediatric OPD (2/10) • Female MedicineWard(1/10) • Surgical ICU(1/10)	• CentralLine Humidifiers(4/10) • O_2 Cylinder Humidifiers(4/10) • Nebulizers (2/10)*
3	*Fusarium spp.*	8 (15.09%)	• Pediatric Ward(3/8) • Pediatric ICU(2/8) • Female MedicineWard(1/8) • Male TB Chest Ward (1/8) • Surgery OPD(1/8)	• Central Line • Humidifiers(4/8) • O_2 Cylinder Humidifiers(3/8) • Nebulizer(1/8)
4	*Alternaria spp.*	7 (13.20%)	• Male TB Chest Ward (2/7) • Surgical ICU(2/7) • Female Medicine Ward(1/7) • Female Surgery Ward(1/7) • Surgery OPD(1/7)	• O_2 Cylinder Humidifiers(5/7) • Central Line Humidifiers(2/7)
5	*Chaetomium spp.*	5 (9.4%)	• Female medicine Ward (1/5) • MICU(1/5) • Male TB Chest Ward(1/5) • SICU(1/5) • TB & Chest OPD(1/5)	• Central Lines(3/10) • Cylinders(1/5) • Nebulizer(1/5)
6	*Aspergillus flavus*	3 (5.6%)	• FemaleMedicine W(1/3) • PICU(1/3) • Casualty (1/3)	• O_2 Cylinders(3/3)
7	*Aspergillusgalucus*	3 (5.6%)	• MICU(2/3) • Medicine OPD(1/3)	• O_2Cylinders(2/3) • Central Line(1/3)
8	*Chrysosporium spp.*	3 (5.6%)	• MICU(1/3) • SICU(1/3) • Pediatric OPD (1/3)	• Central Lines(2/3) • O_2 Cylinders(1/3)
9	*Streptomyces spp.*	3 (5.6%)	• SICU(2/3) • TB & Chest OPD (1/3)	• Central Line(1/3) • O_2 humidifiers(1/3) • Nebulizers(1/3)
10	*Candida spp.*	2 (3.7%)	• Casualty(1/2) • MICU(1/2)	• Central Line(1/2) • Nebulizers(1/2)
11	*Trichoderma spp.*	2 (3.7%)	• MICU(2/2)	• Central Line(2/2)
12	*Penicillium spp.*	2 (3.7%)	• MICU(2/2)	• Central Line(2/2)
13	*Curvularia spp.*	1 (1.8%)	• MICU(1/2)	• Central Line(1/2)

[Table/Fig-2]: Frequency of Various Fungal Isolates in Swab Samples out of a total of 53 positive samples

Figure 19: Site of fungal contamination in hospitals

Sr. no	Name of bacteria	Frequency of isolation	Predominate site	Predominant equipment
1	*Pseudomonas spp.*	15	• MICU(5/15) • SICU(5/15) • PICU(3/15) • OPD(2/15)	• Central Line(3/15) • O_2 humidifiers(8/3) • Nebulizers(4/3)
2	*Acinetobacter spp.*	10	• MICU(4/2) • PICU(4/10) • SICU(1/3) • OPD(1/3)	• Central Line(4/10) • O_2 humidifiers(4/10) • Nebulizers(2/10)
3	*E. coli*	8	• PICU(4/8) • MICU(2/8) • SICU(1/8) • OPD(1/8)	• Nebulizers(4/8) • Central Line(3/8) • O_2 humidifiers(1/8)
4	*Klebseilla spp.*	7	• PICU(4/7) • SICU(1/7) • MPICU(1/7) • OPD(1/7)	• Nebulizers(4/7) • Central Line(2/7) • O_2 humidifiers(1/7)
5	*Methicillinresistant Staphylococcus aureus (MRSA)*	5	• MICU(2/5) • PICU(1/5) • SICU(1/5) • OPD(1/5)	• Nebulizers(2/5) • Central Line(2/5) • O_2 humidifiers(1/5)
6	*Methicilin sensitive staphylococcus aureus (MSSA)*	6	• MICU(2/6) • SICU(2/6) • PICU(1/6) • OPD(1/6)	• Nebulizers(3/6) • Central Line(2/6) • O_2 humidifiers(1/6)
7	*Coagulase negative Staphylococcus aureus (CONS)*	8	• PICU(4/8) • MICU(2/8) • OPD(1/8) • S ICU(1/8)	• Central Line(4/10) • O_2 humidifiers(4/10) • Nebulizers(2/10)
8	*Stenotrophomonasmaltophila*	2	• SICU(1/2) • PICU(1/2)	• Central Line(1/2) • O_2 humidifiers(1/2)

[Table/Fig-3]: Frequency of Various bacterial Isolates in Swab Samples out of a total of 61 positive samples

Figure 20: Site of bacterial contamination in hospitals

Recommendation of the committee:

1. Formulate Mucor Cells in every hospitals. This should include ENT surgeon, Pulmonologist, Infectious Disease Control Specialist and an administrative staff. A telephonic helpline must be established in all hospitals
2. Infection Control Committees should be set up in all hospitals. This must include one member of the Management, one Microbiologist, one Physician, one Surgeon, one Anaesthesiologist/Intensivist, Nursing Superintendent, Biomedical Chief and Chief of Maintenance and supply.
3. This team must meet once a week during an epidemic and once a month during non-epidemic periods
4. In the present Mucormycosis outbreak
    a. Maintain a database of Mucormycosis patients that will be updated on a daily basis that is also made available to the MoHFW. This must include general patient data, demographic data, referral data, clinical symptoms & signs, treatment details, outcome of treatment and possible source of infection. Particularly, it must also include history of COVID 19 in the past, antibiotic use/abuse, steroid use/abuse, use of steam inhalation, Diabetes Mellitus
    b. Identify an in-house outbreak and if so, take immediate corrective measures
    c. Identify possible sources of Mucor contamination in ER, ICU, OT and wards by microbiological sampling techniques
    d. Investigating Gaseous supply chains from the point of entry of cylinders to the point of exit through nasal canulae/masks/nebulisers (that essentially includes all points in the entire gaseous transport chain)

e. Weekly microbiological sampling for Mucormycosis from various points in: OT, ICU, ER, wards, humidifiers, nasal canulae, gaseous outlets, oxygen generating chambers, gas cylinders (both inner and outers surface after use) and various points in air conditioning units
f. All cylinders and other medical supplies coming into a hospital must be sterilised according to SOPs (enclosed)
g. Close monitoring of sterilization of medical equipment in the hospitals by concerned staff
h. Ensure use of distilled or sterile water in humidifiers. Do not use methylene blue dye in humidifiers.
i. Ensure strict sterilization of masks, nasal canulae and other gas delivery equipment
j. Medical staff education regarding Mucormycosis
k. Public awareness outreach regarding Mucormycosis
l. All construction activities in and around hospitals must be ceased immediately
m. All air conditioning units in all parts of the hospitals to be serviced and optimized

HOSPITAL GASEOUS SUPPLY CONTAMINATION:

Air compressors: Insufficient air filtration and air intakes that are near the ground, outdoor construction, or exhaust, is also be associated with mucormycosis infections. A hospital investigating four cases of mycotic endocarditis among open-heart surgery patients in a single year, including one with Mucor sp., isolated Mucor sp. and Aspergillus sp. in dust from an air conditioner duct and in air samples. The team found that the air filter used was likely insufficient to trap spores.[5] The highest bacteria count was found in the ICU (Intensive Care Unit) Highest fungi count was found in the emergency room. Pipelines might be incriminated as source of microbial contamination of compressed and synthetic air for medical use. Contamination can be present in the compressed air from three sources These are namely: the atmosphere, the compressor & the distribution equipment.[31] Medical air is the result of compression of 8 cubic feet of atmospheric air into 1 cubic foot of compressed air; all contaminants in atmospheric air, including water and carbon monoxide, are, therefore, concentrated eightfold in compressed air. Our inspection of some hospital premises showed that air compression units and filtration units were stationed in unhygienic rooms. The compressed air is drawn into the hospitals pipe conduits after going through a three-stage filtration process for microbes. The filters are to be checked regularly and changed once in 6 months to ensure microbe free air. Also, air in critical areas must be regularly cultured for microorganisms. Hospital authorities must ensure that this is done on top priority.

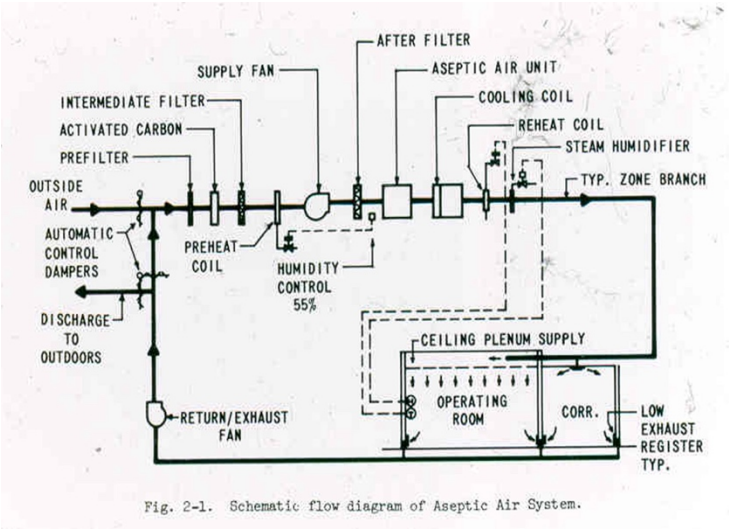


Figure 21: Schematic flow diagram of aseptic air system

Figure 22: In house air compressor in a tertiary care center

Figure 23: Dirty water accumulation in air compressor room

Figure 24: Unhygienic conditions near air compressor room

Air compressor unit in unhygienic conditions

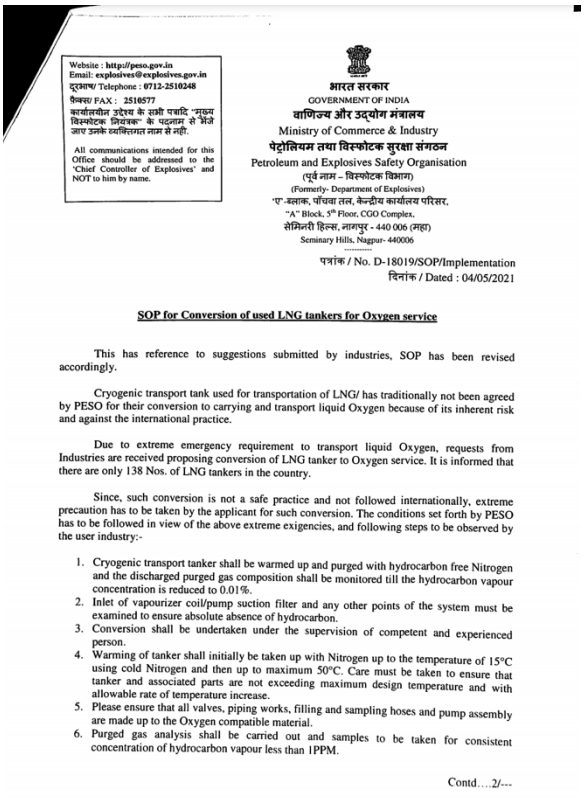
In addition to visual inspection, review of facility records can also help investigators identify possible sources of mold. Records to review include: Indoor air temperature and humidity logs, including any days when humidity exceeded 60%, Dates of air filter changes, HVAC system, filters, and fans maintained according to manufacturer instructions, Frequency and method of filter performance, Air flow monitoring records

Liquid & gaseous oxygen: It has been postulated that rise in Mucor is not linked to oxygen therapy, however insights into the oxygen therapy devices could probably lead to source of contamination and possible reasons for flaring up of Mucormycosis. Liquid Medical Oxygen (LMO) comes from the same source as industry grade oxygen (IGO). While medical grade oxygen needs to be very pure (>98% purity), industries may or may not require very pure oxygen (80% to 99.8%). The containers used to store LMO is often interchanged with that of IGO, especially in the last few months, due to the acute shortage of oxygen supplies in the wake of the second COVID-19 wave.

Industrial Usage – Core Industrial Usage and Medical Requirements (Pre-Covid & post)

CAPACTIY	PRE-COVID SCENARIO	POST-COVID SCENARIO	ASSUMPTIONS
TOTAL PRODUCTION CAPACITY	7200 MT	7200 MT	Data from submissions to Delhi HC
NEW CAPACITY ADDED *		3300 MT	Statement of PMO on 22-Apr 2021
TOTAL CAPACITY	7200 MT	10500 MT	
INDUSTRIAL USAGE			
(a) 'Core' Industries identified	2500 MT	2500 MT	Data from submissions to Delhi HC
(b) 'Non-core' Industries	1790 MT	700 MT	Impossible to stop fully other usage
Total Industrial	4290 MT	3200 MT	
MEDICAL USAGE			
a) Non-Covid usage	1210 MT	1210 MT	
b) Covid usage	0 MT	6790 MT	
Total Medical	1210 MT	8000 MT	Data from submissions to Delhi HC
Excess/ Short Capacity	1700 MT	-700 MT	
Available Buffer stock at April 1	50000 MT		

Figure 25: Massive increase in O2 production by GoI, post COVID, especially in the second wave



Website : http://peso.gov.in
Email: explosives@explosives.gov.in
दूरभाष/ Telephone : 0712-2510248
फैक्स/ FAX : 2510577
कार्यालयीन उद्देश्य के सभी पत्राचार 'मुख्य विस्फोटक नियंत्रक' के पदनाम से भेजे जाए उनके व्यक्तिगत नाम से नहीं.

All communications intended for this Office should be addressed to the 'Chief Controller of Explosives' and NOT to him by name.

भारत सरकार
GOVERNMENT OF INDIA
वाणिज्य और उद्योग मंत्रालय
Ministry of Commerce & Industry
पेट्रोलियम तथा विस्फोटक सुरक्षा संगठन
Petroleum and Explosives Safety Organisation
(पूर्व नाम – विस्फोटक विभाग)
(Formerly- Department of Explosives)
'ए'-ब्लाक, पाँचवा तल, केन्द्रीय कार्यालय परिसर,
"A" Block, 5th Floor, CGO Complex,
सेमिनरी हिल्स, नागपुर - 440 006 (महा)
Seminary Hills, Nagpur- 440006

पत्रांक / No. D-18019/SOP/Implementation
दिनांक / Dated : 04/05/2021

SOP for Conversion of used LNG tankers for Oxygen service

This has reference to suggestions submitted by industries, SOP has been revised accordingly.

Cryogenic transport tank used for transportation of LNG/ has traditionally not been agreed by PESO for their conversion to carrying and transport liquid Oxygen because of its inherent risk and against the international practice.

Due to extreme emergency requirement to transport liquid Oxygen, requests from Industries are received proposing conversion of LNG tanker to Oxygen service. It is informed that there are only 138 Nos. of LNG tankers in the country.

Since, such conversion is not a safe practice and not followed internationally, extreme precaution has to be taken by the applicant for such conversion. The conditions set forth by PESO has to be followed in view of the above extreme exigencies, and following steps to be observed by the user industry:-

1. Cryogenic transport tanker shall be warmed up and purged with hydrocarbon free Nitrogen and the discharged purged gas composition shall be monitored till the hydrocarbon vapour concentration is reduced to 0.01%.
2. Inlet of vapourizer coil/pump suction filter and any other points of the system must be examined to ensure absolute absence of hydrocarbon.
3. Conversion shall be undertaken under the supervision of competent and experienced person.
4. Warming of tanker shall initially be taken up with Nitrogen up to the temperature of 15°C using cold Nitrogen and then up to maximum 50°C. Care must be taken to ensure that tanker and associated parts are not exceeding maximum design temperature and with allowable rate of temperature increase.
5. Please ensure that all valves, piping works, filling and sampling hoses and pump assembly are made up to the Oxygen compatible material.
6. Purged gas analysis shall be carried out and samples to be taken for consistent concentration of hydrocarbon vapour less than 1PPM.

Contd....2/---

Figure 26: PESO circular for conversion of LNG tankers to oxygen service

- Due to an unprecedented second wave of COVID-19 infections, the country faced an acute shortage of medical oxygen in the months of March and April 2021. Apart from the shortage of oxygen, another problem the country is facing is the shortage of tankers suitable to transport and store oxygen, especially liquid oxygen. As a result, Liquid Nitrogen Gas Tankers have been converted to Liquid Oxygen Tankers. The Ministry of Commerce and Industry, Government of India, through the Petroleum and Explosive Safety Organisation (PESO) granted permission to convert the use of Nitrogen, Argon, Helium cylinders for transportation of oxygen purposes.[32] Safety standards followed for sudden conversion of industrial nitrogen storage facilities for medical use is questionable and needs detailed investigation for a source of primary microbial contamination.[33] Fungi play an important role in nitrogen role, thus conversion of nitrogen cylinders for medical purpose could be a risk factor[13]. Industrial oxygen is not fit for medical use and contamination of industrial gases is high.

PESO: "Since such conversion is not a safe practice and not followed internationally, extreme precaution has to be taken by the applicant for such conversion. The conditions set forth by PESO in view of the above extreme exigencies."[32]

Fungi occupy diverse environments where they are constantly challenged by stressors such as extreme pH, temperature, UV exposure, and nutrient deprivation. Nitrogen is an essential requirement for growth, and the ability to metabolize a wide variety of nitrogen sources enables fungi to colonize different environmental niches and survive nutrient limitations. It has also been proven that fungal spores can survive cryogenic temperatures and such containers are in fact used to store spores. Frozen ampoules were thawed in a water bath at 38 to 40 C. Viable and unmutated cultures were developed from reactivated specimens after storage for as long as 5 years.[34] Could oxygen supply chains contaminated with Nitrogen be potential sources of fungal spores?

In gas production processes there are no sterilization treatments. The conditions in which gases are produced, including temperature, pressure, and lack of humidity and nutrients, does not allow microorganism to proliferate. Gases are manufactured in completely closed systems, supplied under pressure, and with no contact with ambient air, humans or animals. Where gas is exposed to process water as part of the manufacturing process, the water quality is controlled using validated methods.

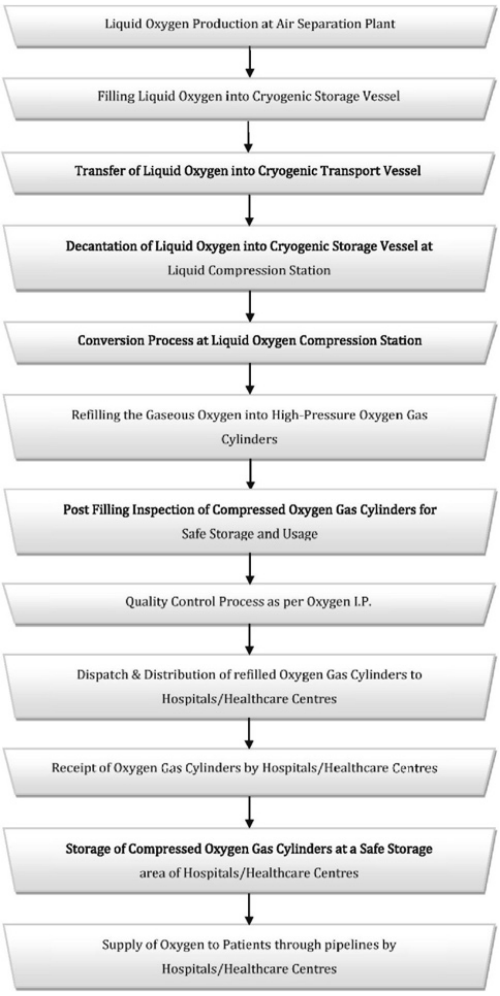


Figure 27: Steps in the LMO supply chain

However, there are some rare microorganisms able to thrive in extreme environments. These extremophiles include, for example, pressure-phile, anhydrobiotic and low pH-phile microbes. The International Organization for Standardization (ISO) publishes world-class standards for products, services and systems, to ensure quality, safety and efficiency.[35] ISO 8573 is an available standard addressing compressed air quality. It consists of nine parts that address purity classes, specifications, and procedures. ISO 8573-7:2003, the most current version, can be utilized across all industries' compressed air microbial monitoring plans. In European studies,[36] the choice of parameters to be investigated in the gas supply chain, is based on the acceptance criteria of the microbiological quality of non-sterile products for pharmaceutical use of the European Pharmacopoeia 10.0 in chapter 5.1.4, where the maximum criteria indicated for products for inhalation use is: Total Aerobic Microbial Count: (102) 200 CFU/ml or CFU/g Total Yeasts Microbial Count: (101) 20 CFU/ml or CFU/g. In another European study, the microbiological aspects of gases for food and pharmaceutical use were presented with the related data from sampling to analytical activity. Different sampling methods have been tested and, to date, the best is the impaction method, validated with recovery tests with different American Type Culture Collection (ATCC) strains. The data collected, based on more than one thousand analyses, reveal an average microbial load of the order of approximately 10 CFU/Nm3 with maximum values of 100 CFU/Nm3 and 50 CFU/Nm3, respectively for bacteria and fungi, and an absence of pathogens and opportunistic microorganisms. The results refer both to liquid bulk and package gas production processes and considers the possible microbial contribution of the cylinder surfaces content. Data confirms that the microbiological quality of gases in Europe complies with the European Pharmacopeia

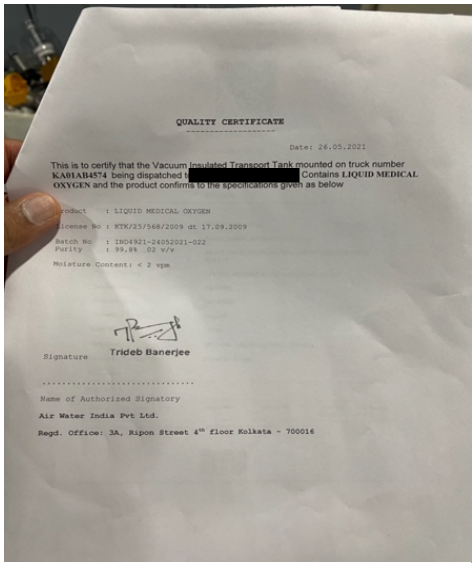
Figure 28: LMO container in a tertiary care center

Figure 29: Evaporation unit

Figure 30: Gas control chain

acceptance criteria for inhalation use.[36] In the technical paper 'Life in extreme environments', authors investigated if micro-organisms survive in compressed gas system, and if they survive, what appropriate methods are applied in order to collect and enumerate them.[36] Recovery tests have been done on compressed air in cylinders at pressures from 10 bar to 170 bar, on 13 microorganisms with impaction and filtration sampling. The tested microorganisms were cultivated on Tryptone Soy Agar (TSA) and on Sabouraud Dextrose Agar (SDA). Results indicated that microorganisms can be collected and grow from compressed gas with recovery of 85% at 10 bar and 0% at 170 bar. Up to 10 bar, 11 of the 13 microorganisms survived and grew.

When gas outlets are certified, concentration or purity of the gases or medical air is documented. However, this purity of oxygen (80% to 99.8%) is only chemical gas purity vis-à-vis CO or CO2 gases. This does not ensure microbial purity. Particulate, foreign bodies, and bacteria are not the usual part of a certification of medical gases. The medical air system, because of moisture, is the most common site of bacterial contamination. However, culturing of medical gas is rarely performed. While Indian gas manufacturers are guided by the Indian Pharmacopoeia 2018 (Under Ministry of Health and Family Welfare, Government of India), there is NO microbiological sampling of the gaseous supply chain mandated by any governmental licensing organization. Our investigation also revealed that the certification of purity of gases is a self-regulated process by the companies and no periodic checking or testing by any governmental agency.


QUALITY CERTIFICATE

Date: 26.05.2021

This is to certify that the Vacuum Insulated Transport Tank mounted on truck number KA01AB4574 being dispatched t[redacted] Contains LIQUID MEDICAL OXYGEN and the product confirms to the specifications given as below

Product : LIQUID MEDICAL OXYGEN
License No : KTK/25/568/2009 dt 17.09.2009
Batch No : IN04921-24052021-022
Purity : 99.8% 02 v/v
Moisture Content: < 2 vpm

Signature
Trideb Banerjee
.....
Name of Authorized Signatory
Air Water India Pvt Ltd.
Regd. Office: 3A, Ripon Street 4th floor Kolkata - 700016

Figure 31: LMO purity certificate is provided by the agency supplying it and not by a regulator

The medical air system, because of moisture, is the most common site of bacterial contamination. However, bacteria can grow in spaces left in improperly joined pipes. Culturing of medical gas is rarely performed. Documented contamination of pipelines includes dirt, sand, gravel, cement, rust, vermin, cigarette butts, and wood. Contamination with these substances results from the pipes and bulk gas containers being opened and exposed to construction debris and to the atmosphere. While ventilators and respiratory care systems are a known source of infection due to bacterial contamination, the idea that the source could be beyond the walls in the pipe systems is not easily accepted by owners or administrators, possibly due to liability issues and the need to clean the systems once the contamination is identified.[33]

Figure 32: Pipings may contain particulate matter

Oxygen supply chain and cylinders: Most of the oxygen production capacity was concentrated in Eastern India, while Delhi in the North and Maharashtra and Gujarat in the West were the worst affected and had the most pressing need for oxygen. The Railways are now running RO-RO rakes of truck mounted cryogenic tankers. Empty ones are ferried to oxygen production plants, filled and transported to high demand centres before being offloaded and driven the last mile to the final destination. The Indian Air Force is using its giant cargo planes to airlift oxygen cylinders. India Inc has swung into action, with many business houses organising the import of cryogenic containers of oxygen. Other countries too, have airlifted oxygen to India, while the Centre placed emergency orders to airlift 23 oxygen generation plants from Germany, to be set up at the worst-hit hospitals. At all the steel plants in the country, be it private or public sector, industrial grade oxygen is being converted into medical grade oxygen on a war footing. Oxygen Express is plying on railway tracks.

> *"The main issue was in supply chain as liquid medical oxygen has to be transported in cryogenic tankers, which normally cater to a 200 kilometer radius. With the increased demand even in remote areas, now tankers have to cater to over 1,000 kilometer radius. India had only 1,200 such tankers before the current crisis and permission was given recently to convert another 1,200 nitrogen and argon carrying tankers to transport medical oxygen. Besides, some 40 plus such tankers have been imported. With the point-to-point green corridor 'Oxygen Express' trains shuttling between most affected areas, and with Airforce, Navy helping with the transport, the logistics issues are more or less resolved. Now, we can cater to even remotest areas even if the wave spreads to non-affected states," Siddharth Jain, Director, INOX Air Products.*

Due to oxygen cylinder shortages, almost every cylinder available is being used. The life span of a cylinder is 10-12 years after which they have to be discarded. However, the cylinders are subjected to hydraulic and NRV tests every 5 years. Old cylinders are now being used without undergoing any tests. Due to shortage of cylinders industrial cylinders are being used for medical usage. Industrial cylinders are being purchased by the public from local vendors and the same is being used for medical purposes. Every cylinder that is not routinely used in the medical chain has to be cleaned and purged. This may not be done due to the low turn over time and due to the prevailing chaos. All cylinders, once they come back for a refill, have to be vacuum cleaned. However, right now only new cylinders are being treated so. It is also brought to our notice that, due to the emergent situation, some of the patient attenders get their cylinders refilled by industrial oxygen suppliers. While cleaning cylinders, water

Figure 33: AIGA guidelines that are not followed in most supply chains and hospitals

is used and if not dried properly this can grow fungus. Purity of oxygen (99% and above) is a concern. Despite the assurances from the vendors, there is no evidence for the same. Quality checks are done by in house teams randomly on a batch basis. No regulatory body is involved in the checking process, at least not at this time. There are no government authorised/accredited laboratories involved in checks and balances. There is a filter inside the converter of the humidifier that prevents microbial infiltration, which needs to be changed regularly, but it is conveniently ignored.

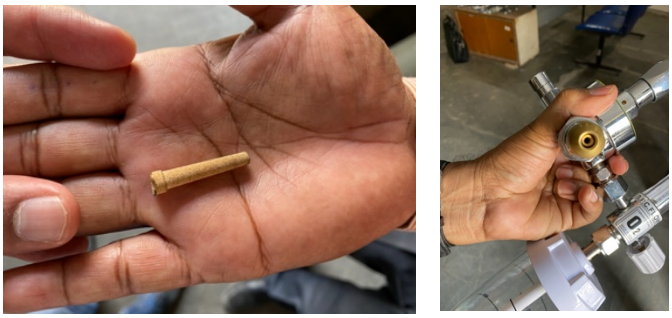


Figure 34: Metallic filter inside the humidifier connector valve

Cylinders must be stored in clean areas with proper ventilation, which prevents dust and other contaminants accumulating on the cylinder. However, most hospitals allot the dingiest part of the building as the cylinder manifold room. Once the B-type cylinders come to manifold from patient ward/room for refilling it is the duty of the hospital to disinfect the cylinder before sending it back to the supplier. However, very few hospital biomedical staff take this seriously. The Asian Industrial Gas Association has issued guidelines in this regard but our investigation reveals that no hospital/supplier follows these guidelines. All cylinders must be cleaned with antiseptic solutions in the manifold room of the hospital. This is not being done and the only point that the cylinders are (supposedly) cleaned is when they are brought in empty to the supplier for a refill. However, the cylinders go from the supplier's premises through mud and muck to reach the hospitals. Sometimes the unclean cylinders are sent right up to the patient bed to supply oxygen. The patients or the para medical staff may contaminate themselves by touching the outer surface of the cylinder and then by touching their face, nose or masks. Refillable oxygen cylinders for medical use are made of steel, aluminum/alloy, other composite material which may rust. Due to improper handling of the cylinders and not following proper sterilization techniques, microbial pathogens are harbored in them and acts a medium in spreading the pathogen.

Figure 35: Cylinder manifold rooms are usually not well ventilated

Figure 36: Cylinders travel widely and often to very unhygienic places

Figure 37: The same cylinders reach patient's bedside sometimes without any form of external disinfection

Oxygen concentrators: Oxygen concentrators are taking atmospheric air and separates oxygen and

supplies to the patient. The purity levels of concentrators is 90+3 or -3. if it is -3 then the purity level will be 87%. Oxygen concentrator/cylinders are available on rental basis and due to short turnover time often kept next to patients. Unless they are cleaned hygienically after each use, they could be a source of infection.

Recommendation of the committee:

1. Micro Testing of Compressed Air or Bioburden Testing per ISO 8573-7 must be made mandatory. Compressed air and process gases can be sampled using specialized samplers that use contact plates to capture any microorganisms present. Micro testing is imperative to avoid microbial contaminants inside controlled environments including production areas and clean rooms.
2. There is a lack of an accountable authority to coordinate and enforce the many codes and standards now in place for medical gas manufacturers. There should be an organizational chart with a specific agency at the top. Included in the structure should be the education and credentialing of those involved in medical gas and vacuum system (MGVS) construction, from design architects to plumbers.
3. Anesthesiologists must involve themselves during the construction phase of their MGVS
4. Anesthesiologists should not hesitate to don a hardhat and enter the construction area. They are the end users of the MGVS and should understand the complexity of this life-support system of their hospitals.
5. The Asian Industrial Gas Association recommendations for cleaning and sterilization of gas cylinders has to be strictly followed by all suppliers and hospitals
6. Preventive steps such as regular checks of fittings and connections, cleaning exterior, ensuring identification of externally contaminated cylinders with clear marking or labelling, cylinder pick up area to be located away from the patient wards and infection area of the hospital, disinfecting the cylinders with 70% Iso Propyl Alcohol (IPA) or Ethyl Alcohol or diluted Bleach/Water Solution ⎪ 0.1% Sodium Hypochlorite Solution ⎪ 0.5% Hydrogen Peroxide Solution can reduce the causes for this factor of possible contamination.
7. Government accredited agencies and relevant authorities must increase vigilance and ensure strict adherence to gas supply chain protocols.

CONCLUSION

From less than 100 cases a year, Mucormycosis has grown to over 11,000 cases in just a few months and declaring it as an epidemic is crucial for India's health infrastructure not to collapse. Diabetes, COVID-19 and immunosuppression are a concoction for disaster, and these exist in massive numbers in Indian patients at the moment. However, if we ignore source-based infection, it will be at our own peril. Unless this is tackled on a war footing and coordinated effectively, we will have a prolonged epidemic. More people will start getting affected by Mucor over a longer time, long after COVID-19 has been contained with the vaccine. This disaster can be averted with timely interventions.

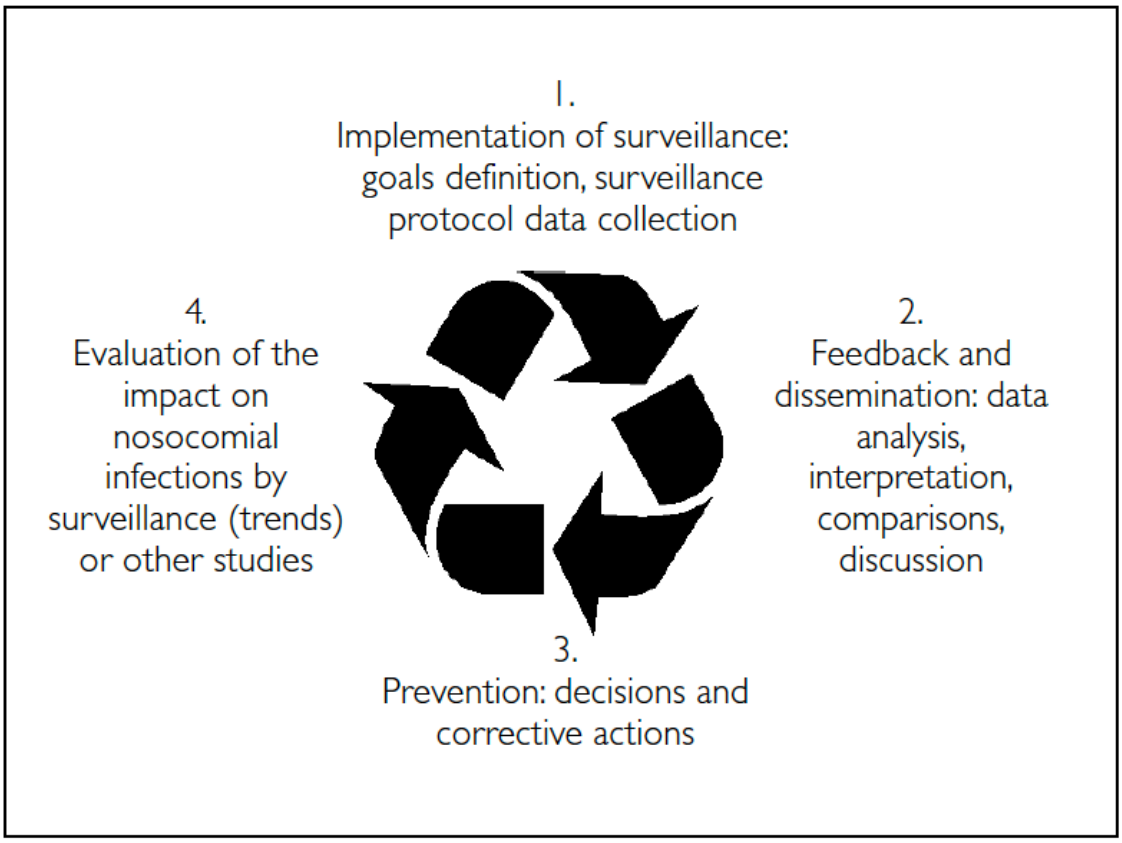


Figure 38: SURVEILLANCE IS A CIRCULAR PROCESS

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