Chapter

Healthcare-Associated Meningitis Caused by *M. tuberculosis* and Non-Tuberculous Mycobacteria

Ashit Bhusan Xess, Kiran Bala and Urvashi B. Singh

Abstract

Meningitis can be acquired in the community setting or secondary to invasive procedures or head trauma. The latter group has been classified as health-care-associated meningitis because the etiologic agents belong to a different spectrum of microorganisms, including *Staphylococcus aureus*, Coagulase negative staphylococcus Gram negative bacilli, Aspergillus, *Candida albicans*, *Cryptococcus neoformans*. IDSA Clinical Practice guidelines for Healthcare-associated ventriculitis and meningitis does not include *M. tuberculosis* and NTM, but in the last decade infections caused by these organisms are on a rise. These infections are mostly associated with cerebrospinal fluid shunts, cerebrospinal fluid drains, intra-thecal drug therapy, deep brain stimulation hardware, neurosurgery and head trauma. Most commonly these are introduced during surgical procedures. Another important pathogenic factor is biofilm formation that increases the persistence and resistance to antibiotic therapy, hence the survival. A high index of suspicion aids early diagnosis but preventive measures such as care of the devices introduced into sterile spaces is essential. Sterilization of the critical items is recommended by treating with different chemical sterilizing agents but most importantly meticulous cleaning must precede any high-level disinfection or sterilization process. A course of multidrug therapy is required for prolonged period of time depending on mycobacterial species.

Keywords: non-tuberculous mycobacteria, *Mycobacterium tuberculosis*, hospital acquired infections, iatrogenic infections

1. Introduction

Healthcare-associated CNS infection mostly includes meningitis, ventriculitis, subdural empyema and brain abscess. With increased use of intracranial devices and increase in number of patients requiring neurosurgery, the risk of acquiring these infections has increased. While these devices generally being sterile, they can provide a route for microorganism during placement, handling or maintenance. The most common causative agents are Staphylococcus aureus, coagulase negative staphylococcus, Gram-negative bacteria, candida species, Cryptococcus neoformans, etc. In the last decade, Mycobacterium tuberculosis and non-tuberculous mycobacterium are gaining prominence in causing healthcare-associated CNS infections. These organisms especially non-tuberculous mycobacterium are found in environment which once find entry into CNS can cause infections. No approved treatment guidelines are present for the treatment of non-tuberculous mycobacterium. So one must take utmost care

in maintaining these intracranial devices from not acquiring these infections. These devices and neurosurgical devices come under critical category as per Spaulding classification, so stringent decontamination and sterilization procedures have to be followed to render them sterile.

2. Meningitis

Meningitis is an acute inflammation of the protective membranes covering the brain and spinal cord known collectively as the meninges which consists of duramater, arachnoid mater and pia mater [1].

The patient with meningitis usually presents with fever, headache, altered sensorium, behavioral changes, focal neurological signs or seizures. There are various signs that can be elicited in meningitis patients such as nuchal rigidity, Kernig's sign and Brudzinski's sign. Nuchal rigidity or neck rigidity is elicited when neck resists passive flexion. Kernig's sign is elicited on a supine position where knees are flexed onto the abdomen. Any attempt to extend the knee from this position causes pain in the patient. Brudzinski's sign is also elicited in supine position where trying to flex the neck causes flexion at the knee and hip joints. These signs indicate there is meningeal irritation in the patient. But both these tests are uncertain in some cases such as in very young or old patients, immunocompromised or patients with depressed mental status.

Meningitis can be divided into acute, subacute and chronic meningitis. Acute meningitis is mostly caused by bacteria whereas subacute and chronic also include viral, fungal and parasitic causes. In cases of acute meningitis most common causes are Neisseria meningitides, *Streptococcus pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, Staphylococcus species, *Listeria monocytogenes*, *Haemophilus influenzae*, *Streptococcus agalactiae*, *Bacteroides fragilis* and *Fusobacterium* species. Viral causes include Enteroviruses, Herpes Zoster virus, Herpes Simplex viruse 2, Epstein Barr virus, Human Immunodeficiency virus (**Table 1**).

Organisms causing subacute meningitis consists of *Mycobacterium tuberculosis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Coccidioides immitis* and *Treponema pallidum*. Bacterial agents causing chronic meningitis are *Mycobacterium tuberculosis*, *Borrelia burgdorferi* and *Treponema pallidum*. Fungal agents comprises of *Cryptococcus neoformans*, *Coccidiodes immitis*, *Candida* species, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Aspergillus* species and *Sporothrix schenckii*. Helminthic causes are *Taenia solium*, *Gnathostoma spinigerum*, *Angiostrongylus cantonensis* [2].

2.1 Healthcare-associated meningitis

Meningitis can be acquired in community settings or in hospital settings via invasive procedures performed or through head trauma. In hospital settings the causative agents are totally different from those acquired in community settings. In many of the cases the symptoms appear after discharge from the hospital. There are many ways in which a patient can acquire meningitis in a hospital settings which are as follows [3]:

- CSF shunts
- CSF drains
- Intrathecal infusion pumps
- Deep brain stimulation hardware
- Neurosurgery

ACUTE MENINGITIS	SUBACUTE MENINGITIS	CHRONIC MENINGITIS
Neisseria meningitides	Mycobacterium tuberculosis	Mycobacterium tuberculosis
Streptococcus pneumonia	Treponema pallidum	Borrelia burgdorferi
Escherichia coli	**Fungal causes**	Treponema pallidum
Pseudomonas aeruginosa	Cryptococcus neoformans	**Fungal causes**
Staphylococcus species	Histoplasma capsulatum	Cryptococcus neoformans
Listeria monoocytogenes	Coccidioides immitis	Coccidioides immitis
Haemophilus influenzae		Candida species
Streptococcus agalactiae		Histoplasma capsulatum
Bacteroides fragilis		Blastomyces dermatitidis
Fusobacterim species		Aspergillus species
Viral causes		Sporothrix schenkii
Enteroviruses		**Helminthic causes**
Herpes zoster virus		Taenia solium
Herpes simplex virus 2		Gnathostoma spinigerum
Epstein barr virus		Angiostrongylus cantonensis
Human immunodeficiency virus		

Table 1.
Causative agents of meningitis.

2.1.1 Cereberospinal fluid shunts

CSF shunt is a system in which the proximal part of it is in the cerebral ventricle, subdural space, intracranial cyst or lumbar arachnoid space whereas the distal end is in the peritoneal, pleural or vascular space. A part of the system has a pressure regulating valve which usually is present just outside the skull or in the distal part of the system. Additional connecting systems may be present which facilitates connection of more catheters or devices [4].

The incidence of CSF shunt infections may show huge variations in various studies but it usually ranges from 4 to 17% [5, 6]. Factors associated with CSF shunt infections can be divided into preoperative and operative causes. Preoperative causes includes premature birth associated with intraventricular hemorrhage, younger age, previous shunt infections, hydrocephalus caused by purulent meningitis, hemorrhage or myelomeningocele. Operative causes are inexperienced neurosurgeon, movement of people during procedure, perforated surgical gloves, neuroendoscope use, longer duration of procedure, insertion of catheter below T7 vertebral body in case of ventriculoarterial shunting, improper patient skin

preparation, shaving of skin, large areas of skin exposed during procedure and repeated shunt revision surgeries [7, 8].

There are 4 possible mechanisms by which CSF shunts can get infected. First and most frequent mechanism is colonization of the shunt during surgery. The second mechanism is retrograde infection from the distal end of the shunt. This can be due to bowel perforation or surgeries being conducted in gastrointestinal tract or genitourinary tract. Due to the breach in the GI tract there is a possibility of retrograde infections by microbial flora of GI tract. Third mechanism is through skin after injection of drug into ventricular reservoir or assess potency. Fourth mechanism is through haematogenous seeding in cases of ventriculoarterial shunts wherein bacteremia is the cause of retrograde infections [3].

2.1.2 Cerebrospinal fluid drains

CSF drains are temporary catheters used to divert CSF externally into a collecting bag. These are used in the temporary management of elevated intracranial pressure due to acute hydrocephalus secondary to intracranial hemorrhage, neoplasm, obstruction of the CSF circulation or trauma. The proximal end of the catheter is usually situated in the cerebral ventricle, subdural space, intracranial cyst or lumbar subarachnoid space. The distal end is connected to a collecting system which consists of a drip chamber, ports for measuring intracranial pressure, ports for sampling and collecting bag. Studies have shown the incidence rates may range from 0 to 22%. In a study by Ramanan et al., the overall external ventricular drain related infection was found to be 11.4 per 1000 catheter days [9].

Factors associated with increased risk of infections in external CSF drains are intraventricular or subarachnoid hemorrhage, cranial fracture with CSF leak, catheter irrigation, craniotomy and duration of catheterization. Mechanisms generally include introduction of microorganism during the procedure, by retrograde infections through exit ports and during flushing of the tubings to maintain patency [3].

2.1.3 Intrathecal infusion pumps

Intrathecal infusion pumps are used as drug delivery systems in conditions such as cerebral palsy, multiple sclerosis, trauma, hereditary spastic paraplegia to deliver baclofen in order to relieve the spasticity. Through these delivery systems opiates are administered in management of intractable pain usually in cases of malignancy. The catheter of these pumps are inserted at the lumbar region and passed intrathecally to the point where drug has to be delivered. Generally these pumps are placed subcutaneously in the abdomen region but in pediatric patients these devices are placed under the abdominal fascia. These pumps have to be refilled from time to time transcutaneously with the desired drug [3].

Majority of the cases who get infected or contract meningitis consists of pediatric patients [10, 11]. Majority of the infections occur within 2 months of surgery but it can happen anytime in the next 3–6 months where drug is refilling is being done. Infection rates may vary from 3.6% in subfacially placed pumps to 20% in subcutaneously placed pumps [12]. In many studies it is seen that it is difficult to distinguish meningitis from local infections. In a study out of 207 children with infusion pumps 25 had suspected superficial infections, 13 had deep seated infections and only 2 of them had meningitis [13]. Route of entry for these infections are during surgery or during refilling of the pumps.

2.1.4 Deep brain stimulation hardware

Deep brain stimulation is used in cases of parkinsonism, dystonia, essential tremors and obsessive-compulsive disorders. This whole set up consists of intracranial lead, connector and a pulse generator implanted in infraclavicular area. In cases of intractable focal epilepsy cortical and depth electrodes are placed which not only detects abnormal electroencephalographic activity but also delivers patterned electrical stimuli to interrupt seizures.

The infections can occur during initial surgery or following surgery performed in order to replace the battery. The infection of pulse generator is the most common infection. There might be a retrograde infection from the pulse generator which can cause meningitis. The incidence of infection may vary from 0.62 to 14.3% and may involve all the 3 components of the device [14].

2.1.5 Neurosurgery

In cases of neurosurgery there is higher risk of ventriculitis and meningitis since there is direct manipulation of central nervous system. So the infections can be introduced during surgical procedure through various instruments or even surgeons themselves. The instruments may be at fault if they are not sterilized. Surgeons on the other hand if are not following proper hand washing practices might be the source of infection. In a study conducted in Taiwan the incidence of bacterial meningitis in a tertiary care hospital was 48% [15].

According to 2017 IDSA Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis all the above organisms mentioned in **Table 2** are common agents of healthcare-associated meningitis. *Mycobacterium tuberculosis* and non-tuberculous mycobacterium does not find mention in the above list. But there are adequate number of cases wherein *Mycobacterium* species especially non-tuberculous mycobacterium are causative agents of nosocomial meningitis.

2.2 *Mycobacterium tuberculosis* and non-tuberculous mycobacterium (NTM)

Traditionally *Mycobacterium* species has been classified according to phenotypic characteristics (**Table 3**) but with the advent of molecular studies characterization

Gram Positive Agents	Gram Negative Agents	Fungal Agents
• Coagulase Negative Staphylococcus (e.g. Staphylococcus epidermidis) • Staphylococcus aureus • Propionibacterium acnes	• Escherichia coli • Enterobacter species • Citrobacter species • Serratia species • Pseudomonas aeruginosa • Acinetobacter species	• Candida species • Exserohilum species

Table 2.
Causative agents of healthcare acquired meningitis.

Mycobacterium tuberculosis Complex	Nontuberculous Mycobacteria			
	Photochromogens	Nonphotochromogens	Scotochromogens	Rapid Growers
M.tuberculosis	M.kansasii	M.avium complex	M.schulzai	M.fortuitum
M.bovis	M.asiaticum	M.intercellulare	M.scrofulaeceum	M.chelonae
M.bovis BCG	M.marinum	M.ulcerans	M.interjectum	M.abscessus
M.africanum		M.celatum	M.gordonae	M.smegmatis
M.caprae		M.gastri	M.cookii	M.peregrinum
M.canetti		M.genavense	M.hiberniae	M.immunogenum
M.microti		M.haemophilum	M.lentiflavum	M.goodii
M.pinnepedii		M.malmoense	M.conspicuum	M.septicum
		M.shimoidei	M.heckeshornense	M. houstonense
		M.xenopi	M.tusciae	M.mucogenicum
		M.heidelbergense	M.kubicae	M.neworleansense
		M.branderi	M.ulcerans	M.brisbanense
		M.simiae	M.bohemicum	M.senegalense
		M.triplex		
		M.conspicuum		

Table 3.
Classification of genus Mycobacterium.

of these organisms are done at genetic level. The organisms belonging to genus *Mycobacterium* are aerobic, non-spore forming, non-motile, thin, slightly curved or straight rods. *Mycobacterium* species have a cell wall comprising of N-glycolylmuramic acid which has a very high lipid content. Because of this property it creates a hydrophobic permeability barrier. The growth rate of these organisms is very slow because of their hydrophobic cell surface. Because of the hydrophobicity these organisms tend to clump with each other which results in reduced diffusion of nutrients into the cell. The generation time for mycobacterium is about 20–36 h [16].

2.3 *Mycobacterium tuberculosis* and healthcare-associated infections

M. tuberculosis is the major cause of infectious health burden in the whole world. In the developing countries tuberculosis is a major concern in the population. Tuberculosis not only involves the respiratory system but also every system in the body. This is why tuberculosis is not only a health burden but also a social burden and economic burden on any nation.

M. tuberculosis becomes more lethal because of its latency. It is capable of going into a phase of latency wherein there are no symptoms at all to suggest the patient is infected. When the patients' immune system weakens these organisms find an opportunity to reactivate and affect any organ system in the body. Patients who come for different conditions to the hospital have weakened immune system. So it might so happen that these organisms may reactivate and affect the patient.

A study has shown that *M. tuberculosis* has been majorly involved in prosthetic joint infections [17]. In this study 53% of the cases were hip joint infections, 40.9% cases involved knee joint and rest were other joints. One reason could be that in patients with latent infections the infected monocytes migrate towards sites of inflammation i.e. surgical sites and cause prosthetic joint infections [18, 19]. Another reason could be that surgical trauma could break down old granulomas and hence reactivation of tuberculosis in the joints [20, 21].

Another site that *M. tuberculosis* is known to infect is the pacemaker implantation site. In a study by Al-Ghamdi it was found out of 25 cases of pacemaker implantation site infection 8 cases comprised of *M. tuberculosis* infection and others were NTM [22]. These sites were infected via haematogenous route.

2.4 Non-tuberculous mycobacteria and healthcare acquired infections

The NTM group consists of more than 172 different species implicated in different clinical conditions (http://www.bacterionet/mycobacterium.html). NTM are important environmental opportunistic pathogens of humans and animals including poultry and fish. The NTM are ubiquitous in nature and are found in various habitats. In the past few years NTM are isolated from natural sources like water, soil, animals, milk, food products and from artificial resources such as water distribution systems and sewer [23, 24].

Unlike *Mycobacterium tuberculosis*, notification of NTM is not mandatory because of which accurate knowledge of impact of NTM on public health is unknown. The impact of NTM is significantly seen in immunocompromised patients e.g. AIDS and transplant patients as life-threatening opportunistic infections [25, 26]. Off late there has been a surge in pulmonary infections and hospital acquired infections (HAI) in immunocompetent patients suggesting the importance of NTM on human health [27–30]. NTMs are implicated in medical device related infections because of their biofilm capabilities [31]. Their ubiquitous nature allows them to cause persistent infection in the patients in healthcare settings [32].

2.4.1 Non-tuberculous mycobacterium and biofilms

In the early days of Mycobacteriology Lowenstein and Calmette described the phenomenon of mycobacterial cells forming aggregates and pellicles [33, 34], whereas Robert Koch described these cells pressed together and arranged in bundles [35]. These were the earlier days when we see description which are similar to the picture of biofilm formation in the present day. The first report of modern concept of biofilms was published by costerton [36]. A decade later articles began to appear about environmental mycobacterial biofilms [37, 38].

Biofilm formation by mycobacteria are no different from the process by which other bacteria form biofilms. It starts with bacterial adhesion goes through stages of surface attachment, sessile growth, matrix synthesis and dispersion. Intercellular communication happens through quorum sensing [39]. However mycobacterial biofilms can form on air-liquid interface. This happens because of composition of extracellular matrix. The extracellular matrix consists of short mycolic acid which are hydrophobic in nature and because of this property biofilms are formed at the air-media interface [40]. In a study it has been shown maximum thickness for *M. fortuitum* and *M. chelonae* biofilm was detected by 72 h but other non-pigmented RGM reach maximum thickness by 96 h. *M. chelonae*

covers smaller surface area than *M. abscessus*, but greater area than *M. fortuitum* and *M. margeritense*. *M. chelonae* forms a biofilm which grows vertically whereas *M. fortuitum* covers the entire surface with thinner growth. Extensive cording is seen in *M. abscessus* and *M. chelonae* [41].

NTM are considered as etiological agents of healthcare-associated infections (HAI), which is a major public health concern. These are responsible for colonization of respiratory tract, infections related to medical procedures and disseminated infections in immunocompromised. Earlier *M. avium* used to be the main cause but RGMs like *M. fortuitum*, *M. abscessus* and *M. chelonae* are growing into prominence [42–44]. The main reason is biofilm formation by NTM. NTM organized in biofilms are hard to eradicate by common disinfection process and disinfectants such as chlorine, organomercurials, alkaline glutaraldehydes [43, 45–47]. Biofilms are also highly resistant to antimicrobial drugs and are able to modulate the host immune response [48]. This is due to physical barrier formed by the biofilm itself and also due to horizontal gene transfer between cells [49]. Bacteria also can switch their phenotypic stages causing a slower growth rate hence the effect of drugs acting on replicating organisms is nullified. These bacteria are known as persisters [50].

It has been proved in studies that NTM form biofilms on medical devices which in turn causes persistent infections. In a study it has been shown NTM form biofilms on silicone which are used to coat medical devices e.g. endoscopes, catheters and air-liquid interface. Biofilms formed by *M. fortuitum* and *M. abscessus* have higher bacterial load than *M. chelonae*. *M. fortuitum* is considered as a good biofilm assembler [51].

2.5 Non-tuberculous mycobacteria and healthcare-associated meningitis

In the review of spectrum of CNS disease caused by RGM by Talati et al., [52] 19 cases of primary and secondary CNS infections were reported, fourteen cases were caused by *M. fortuitum*. Most common clinical presentation in the study was subacute meningitis, with symptom duration ranging from 3 days to 5 months. There are other isolated reports, where *Mycobacterium fortuitum* is the cause of CNS infections. **Table 4** summarizes cases isolated from CNS after VP shunt insertion. There are two other reported cases of VP shunt infection due to *M. abscessus*, a 30 yr. old male with hydrocephalus [53] and a 59-year-old man with hydrocephalus [54] (reported by us previously). Post insertion of VP shunt, the patients presented with meningeal signs and symptoms; but time duration for onset of symptoms varied from 8 days to months and in two cases, 16 and 30 years [55–58]. Other reports of cases of CNS infections due to *M. fortuitum* associated with intra-thecal pump infections, epidural catheter, balloon mitral valvotomy, chronic suppurative otitis media, mastoiditis, sacral trauma, meningioma resection have been published [59–61]. Literature reveals, only 6 cases of VP shunt due to *M. fortuitum* and *M. abscessus* (4, 2 cases respectively), causing CNS infections worldwide.

A 14 year old girl with high grade fever and altered sensorium was received in the emergency department of our institution. She had a past history of persistent headache and seizures. CT scan revealed posterior fossa glioma but could not be operated on since it was very near to the vital parts of the brain. So V-P shunt was placed in order to relieve the ventricular obstruction. After 3 years she underwent appendicectomy after which she started to have frequent convulsions. CT scan revealed dilated ventricles for which a revision shunt surgery was performed. But the symptoms were not relieved. Therefore shunt surgeries were performed without any improvement in the symptoms. In our institution we received the csf sample

S. no.	Authors	Country	Age/Sex	Underlying disease	Mode of acquisition	Mycobacterial spp	Treatment	Duration of therapy	Outcome
1.	Chan et al (1991) [57]	Hong Kong	60yr/F	Cerebral haemorrhage	V-A shunt	M. fortuitum	IV amikacin, ofloxacin	2.5 months	Alive
2.	Midani et al (1999) [56]	USA	13yr/ F	Spina bifida	V-P shunt	M. fortuitum	IV amikacin, cotrimoxazole	7.5 months	Alive
3.	Vishwanathan et al (2004) [58]	India	60 yrs/M	Traumatic Brain injury	Ventriculo arterial shunt	M. fortuitum	IV Kanamycin, ciprofloxacin	6 months	Alive
4.	Cadena et al (2014) [55]	USA	14 yrs/M	Congenital hydrocephalus	V-P shunt	M. fortuitum	IV meropenem, oral cotrimoxazole, oral moxifloxacin		Alive
5.	Baidya A, Singh U B (2016) [54]	India	59yrs/M	Tubercular Meningitis/ hydrocephalus	V-P shunt	M. abscessus	IV amikacin, clarithromycin, meropenem Shunt removal	One week	Died
6.	Montero et al (2016) [53]	USA	30yrs/M	Hydrocephalus	V-P shunt	M. abscessus	IV Azithromycin, Imipenem,amikacin Shunt removal	Two years	Alive
7.	Present case	India	14yrs/F	Glioma/ Hydrocephalus	V-P shunt	M. fortuitum	IV Linezolid, ofloxacin, clofazimine, clarithromycin.	continuing	Alive

Table 4.
World reports of Rapidly growing mycobacteria isolated from Central Nervous System after insertion of VP shunt.

and AFB was seen in ZN smear. On culturing on both MGIT and LJ media growth was seen within 7 days. MALDI-TOF identified the isolate as *Mycobacterium fortuitum*. The VP shunt was removed and she was started on Linezolid 10 mg/kg BD, Ofloxacin 20 mg/kg OD, Clofazimine 5 mg/kg OD, Clarithromycin 15 mg/kg BD according to IDSA guidelines on Diagnosis, Treatment and Prevention of Non-tuberculous Mycobacterial Diseases. The patient started improving and her GCS scale improved.

The source of infection in such cases can be nosocomial, trauma, abscess, revision of shunt surgery, and any other surgery performed even after 30 years of VP shunt insertion [53].

NTMs form biofilms on silicone, stainless steel, polyvinyl chloride and polycarbonate of which mostly the present day surgical equipments, catheters and prosthesis comprise of [51, 62]. These come under critical items that enter the sterile space and vascular system. Sterilization of these critical items is recommended by treating with different chemical sterilizing agents but most importantly meticulous cleaning must precede any high-level disinfection or sterilization process.

2.6 Sterilization of medical devices

Spaulding classified the medical instruments as critical, semi-critical and non-critical items (**Table 5**). Non-critical items consists of items which come in contact with patients' intact skin for which surface disinfectants are enough for cleaning. As per critical, semi-critical items which come in contact with sterile spaces and mucous membranes thorough cleaning and disinfection is advised. Though sterilization is the ideal procedure recommended for these items, it is not always possible due to the composition of some of the items e.g. polypropylene. Hence high level disinfection is recommended for these items.

In cases of implants such as VP shunt, venous catheters, orthopedic implants etc. needs to be removed completely. Other than these all critical and semi-critical items are supposed to be treated with high level disinfectants to render it safe for reuse in the next patient (**Table 6**).

Critical items	• Surgical instruments • Cardiac and urinary catheters • Implants • Ultrasound probes
Semi-critical items	• Respiratory therapy and anaesthesia equipment • Endoscopes • Laryngoscope blades • Esophageal manometery probes • Rectal manometery catheters
Non-critical items	• Bedpans • Blood pressure cuffs • Crutches • Bed rails • Bedside tables • Patient furniture

Table 5.
Spaulding classification.

Instruments Used In Hospitals	Sterilization/High Level Disinfection
• Ventriculoperitoneal shunt • Ventriculoarterial shunt • Dental implants	• Removal of implants [63].
• Cardiac /Urinary Catheters • Implants • Ultrsound Probes In Sterile Body Cavities	• Initial manual cleaning with a detergent (soak for 30 min)/enzyme. • Rinse with sterile water. • Blow completely dry with compressed air. • Repackage in sealed envelope. • Sterilize with Ethylene Oxide • Aerate catheters for at least 14 days at room temperature [64, 65].
• Laproscopes • Arthroscopes • Cystoscopes	• Initial manual cleaning with detergent/enzyme. Or • Automated washer/disinfector containing peraccetic acid as liquid disinfectant. • Soak in 2% Glutaraldehyde for 15-20 mins. Or • Orthophthaldehyde (low vapour pressure). Or • Gas plasma technology [66, 67]. • Use of *sterile water* for terminal rinsing.
• G.I. endoscopes • Bronchoscopes • Nasopharyngoscopes	• Clean mechanically internal and external surfaces with detergent/enzymes • Soak in 2% Glutaraldehyde for 15-20 min Or Orthophthaldehyde for 12 min Or 2% Glutaraldehyde @ 25°C ×45 min Or Ethylene Oxide sterilization [68–71]. • Rinse with sterile water. • Dry and rinse the insertion tube and inner channels with alcohol and dry with forced air after disinfection.

Table 6.
Sterilization Procedures for Instruments Used In Hospitals

3. Conclusion

Non-tuberculous mycobacteria may be rare causes of VP shunt-associated infections but should always be considered as a differential diagnosis. However, NTM does not find a mention as an offending organism nor any treatment protocols in the present IDSA guidelines for healthcare-associated ventriculitis and meningitis and management of ventriculo-peritoneal infections in adults. A high index of suspicion based on clinical presentation is essential to diagnose such rare pathogens.

Acknowledgements

I am thankful to Dr Urvashi B. Singh for being a constant support and inspiration for all the members of Tuberculosis laboratory. I am grateful to the technical staff of the laboratory whose tireless efforts have saved patients lives on a daily basis.

Conflict of interest

No conflict of interest.

IntechOpen

Author details

Ashit Bhusan Xess*, Kiran Bala and Urvashi B. Singh
All India Institute of Medical Sciences, New Delhi, India

*Address all correspondence to: drurvashi@gmail.com

References

[1] Sáez-Llorens X, McCracken GH. Bacterial meningitis in children. Lancet. 2003;**361**(9375):2139-2148

[2] Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J. Harrison's Principles of Internal Medicine. 19th ed. New York: McGraw Hill Education; 2015

[3] Tunkel AR, Hasbun R, Bhimraj A, Byers K, Kaplan SL, Scheld WM, et al. Infectious Disease Society of America's Clinical Practice guidelines for healthcare-associated ventriculitis and meningitis. Clinical Infectious Diseases. 2017:1-32

[4] Edwards RJ, Drake JM. Cerebrospinal fluid devices. In: Winn HR, editor. Youmans & Winn Neurological Surgery. 7th ed. New York: Elsevier; 2017. pp. 1638-1643

[5] Conen A, Walti LN, Merlo A, Fluckiger U, Battegay M, Trampuz A. Characteristics and treatment outcome of cerebrospinal fluid shunt-associated infections in adults: A retrospective analysis over an 11-year period. Clinical Infectious Diseases. 2008;**47**:73-82

[6] Vinchon M, Dhellemmes P. Cerebrospinal fluid shunt infection: Risk factors and long-term follow-up. Child's Nervous System. 2006;**22**:692-697

[7] van de Beek D, Drake JM, Tunkel AR. Nosocomial bacterial meningitis. The New England Journal of Medicine. 2010;**362**:146-154

[8] Simon TD, Butler J, Whitlock KB, et al. Risk factors for first cerebrospinal fluid shunt infection: Findings from a multi-centre prospective cohort study. Journal of Pediatrics. 2014;**164**:1462-1468 e2

[9] Ramanan M, Lipman J, Shorr A, Shankar A. A meta-analysis of ventriculostomy-associated cerebrospinal fluid infections. BMC Infectious Diseases. 2015;**15**:3

[10] Fjelstad AB, Hommelstad J, Sorteberg A. Infections related to intrathecal baclofen therapy in children and adults: Frequency and risk factors. Journal of Neurosurgery. Pediatrics. 2009;**4**:487-493

[11] Vender JR, Hester S, Waller JL, Rekito A, Lee MR. Identification and management of intrathecal baclofen pump complications: A comparison of pediatric and adult patients. Journal of Neurosurgery. 2006;**104**:9-15

[12] Motta F, Antonello CE. Analysis of complications in 430 consecutive pediatric patients treated with intrathecal baclofen therapy: 14-year experience. Journal of Neurosurgery. Pediatrics. 2014;**13**:301-306

[13] Hester SM, Fisher JF, Lee MR, Macomson S, Vender JR. Evaluation of salvage techniques for infected baclofen pumps in pediatric patients with cerebral palsy. Journal of Neurosurgery. Pediatrics. 2012;**10**:548-554

[14] Stenehjem E, Armstrong WS. Central nervous system device infections. Infectious Disease Clinics of North America. 2012;**26**:89-110

[15] Tsai MH, Lu CH, Huang CR, et al. Bacterial meningitis in young adults in Southern Taiwan: Clinical characteristics and therapeutic outcomes. Infection. 2006;**34**:2-8

[16] Tille PM. Diagnostic Microbiology. 13th ed. St. Louis, Missouri: Elsevier;

[17] Veloci S, Mencarini J, Lagi F, Beltrami G, Campanacci DA, Bartoloni A, et al. Tubercular prosthetic joint infection: Two case reports

and literature review. Infection. 2018;**46**(1):55-68. DOI: 10.1007/s15010-017-1085-1

[18] Barr DA, Whittington AM, White B, Patterson B, Davidson R. Extra-pulmonary tuberculosis developing at sites of previous trauma. The Journal of Infection. 2013;**66**:313-319

[19] Mahale YJ, Aga N. Implant-associated *Mycobacterium tuberculosis* infection following surgical management of fractures: A retrospective observational study. Bone & Joint Journal. 2015;**97-B**:1279-1283

[20] Kadakia AP, Williams R, Langkamer VG. Tuberculous infection in a total knee replacement performed for medial tibial plateau fracture: A case report. Acta Orthopaedica Belgica. 2007;**73**:661-664

[21] Neogi DS, Kumar A, Yadav CS, Singh S. Delayed periprosthetic tuberculosis after total knee replacement: Is conservative treatment possible? Acta Orthopaedica Belgica. 2009;**75**:136-140

[22] Al-Ghamdi B, Widaa HE, Shahid MA, Aladmawi M, Alotaibi J, Sanei AA, et al. Cardiac implantable electronic device infection due to Mycobacterium species: A case report and review of the literature. BMC Research Notes. 2016;**9**(1):414

[23] Tsuyuguchi K, Suzuki K, Sakatani M. Epidemiology of infection by nontuberculous mycobacteria. Respiration and Circulation. 2004;**52**(6):561-564

[24] Falkinham JO III. Surrounded by mycobacteria: Nontuberculous mycobacteria in the human environment. Journal of Applied Microbiology. 2009;**107**(2):356-367

[25] Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: Diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. American Journal of Respiratory and Critical Care Medicine. 2007;**175**(4):367-416

[26] Tortoli E. Clinical manifestations of nontuberculous mycobacteria infections. Clinical Microbiology and Infection. 2009;**15**(10):906-910

[27] Piersimoni C, Scarparo C. Pulmonary infections associated with non-tuberculous mycobacteria in immunocompetent patients. The Lancet Infectious Diseases. 2008;**8**(5):323-334

[28] Horsburgh CR Jr, Gettings J, Alexander LN, Lennox JL. Disseminated *Mycobacterium avium* complex disease among patients infected with human immunodeficiency virus, 1985-2000. Clinical Infectious Diseases. 2001;**33**(11):1938-1943

[29] Esteban J, García-Pedrazuela M, Muñoz-Egea MC, Alcaide F, Current treatment of nontuberculous mycobacteriosis: An update. Expert Opinion on Pharmacotherapy. 2012;**13**(7):967-986

[30] Shamaei M, Marjani M, Farnia P, Tabarsi P, Mansouri D. Human infections due to *Mycobacterium lentiflavum*: First report in Iran. Iranian Journal of Microbiology. 2010;**2**(1):27-29

[31] Al-Anazi KA, Al-Jasser AM, Al-Anazi WK. Infections caused by non-tuberculous mycobacteria in recipients of hematopoietic stem cell transplantation. Frontiers in Oncology. 2014;**4**:article 311, 12 p

[32] El Helou G, Viola GM, Hachem R, Han XY, Raad II. Rapidly growing mycobacterial bloodstream infections. The Lancet Infectious Diseases. 2013;**13**(2):166-174

[33] Löwenstein E. Vorlesungen über Bakteriologie, Immunität, spezifische

Diagnostik und Therapie der Tuberkulose. Jena: Fischer; 1920

[34] Calmette A. L'Infection Bacillaire et la Tuberculose. Paris: Masson et Cie; 1936

[35] Koch R. Classics in infectious diseases. The etiology of tuberculosis: Robert Koch. Berlin, Germany 1882. Reviews of Infectious Diseases. 1982;**4**:1270-1274. DOI: 10.1093/clinids/4.6.1270

[36] Costerton JW, Gessey GC, Cheng KJ. How bacteria stick. Scientific American. 1978;**238**:86-95. DOI: 10.1038/scientificamerican0178-86

[37] Wallace RJ Jr. Nontuberculous mycobacteria and water: A love affair with increasing clinical importance. Infectious Disease Clinics of North America. 1987;**1**:677-686

[38] Schulze-Robbecke R, Fischeder R. Mycobacteria in biofilms. Zentralblatt für Hygiene und Umweltmedizin. 1989;**188**:385-390

[39] Ojha AK, Baughn AD, Sambandan D, Hsu T, Trivelli X, Guerardel Y, et al. Growth of *Mycobacterium tuberculosis* biofilms containing free mycolic acids and harbouring drug-tolerant bacteria. Molecular Microbiology. 2008;**69**:164-174. DOI: 10.1111/j.1365-2958.2008.06274.x

[40] Richards JP, Ojha AK. Mycobacterial biofilms. Microbiology Spectrum. 2014;**2**(5). DOI: 10.1128/microbiolspec.MGM2-0004-2013

[41] Muñoz-Egea MC, García-Pedrazuela M, Mahillo I, García MJ, Esteban J. Autofluorescence as a tool for structural analysis of biofilms formed by nonpigmented rapidly growing mycobacteria. Applied and Environmental Microbiology. 2013;**79**:1065-1067. DOI: 10.1128/AEM.03149-12

[42] Phillips MS, von Reyn CF. Nosocomial infections due to nontuberculous mycobacteria. Clinical Infectious Diseases. 2001;**33**:1363-1374

[43] De Groote MA, Huitt G. Infections due to rapidly growing mycobacteria. Clinical Infectious Diseases. 2006;**42**:1756-1763

[44] Hoefsloot W, van Ingen J, Andrejak C, Angeby K, Bauriaud R, Bemer P, et al. The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples: A NTM-NET collaborative study. The European Respiratory Journal. 2013;**42**:1604-1613

[45] Carson LA, Petersen NJ, Favero MS, Aguero SM. Growth characteristics of atypical mycobacteria in water and their comparative resistance to disinfectants. Applied and Environmental Microbiology. 1978;**36**:839-846

[46] Le Dantec C, Duguet JP, Montiel A, Dumoutier N, Dubrou S, Vincent V. Chlorine disinfection of atypical mycobacteriaisolated from a water distribution system. Applied and Environmental Microbiology. 2002;**68**:1025-1032

[47] Selvaraju SB, Khan IUH, Yadav JS. Biocidal activity of formaldehyde and nonformaldehyde biocides toward *Mycobacterium immunogenum* and *Pseudomonas fluorescens* in pure and mixed suspensions in synthetic metalworking fluid and saline. Applied and Environmental Microbiology. 2005;**71**:542-546

[48] Bryers JD. Medical biofilms. Biotechnology and Bioengineering. 2008;**100**:1-18

[49] Casadevall A, Pirofski LA. Virulence factors and their mechanisms of action:

The view from a damage-response framework. Journal of Water and Health. 2009;**7**:S2-S18

[50] Kostakioti M, Hadjifrangiskou M, Hultgren SJ. Bacterial biofilms: Development, dispersal, and therapeutic strategies in the dawn of the post antibiotic era. Cold Spring Harbor Perspectives in Medicine. 2013;**3**:a010306-a010319

[51] Sousa S, Bandeira M, Carvalho PA, Duarte A, Jardao L. Nontuberculous mycobacteria pathogenesis and biofilm assembly. International Journal of Mycobacteriology. 2015;**4**(1):36-43

[52] Talati NJ, Rouphel N, Kuppalli K, Franco-Paredes C. Spectrum of CNS disease caused by rapidly growing mycobacteria. The Lancet Infectious Diseases. 2008;**8**:390-398

[53] Montero JA, Alrabaa SF, Wills TS. *Mycobacterium abscessus* ventriculoperitoneal shunt infection and review of literature. Infection. 2016;**44**:251-253

[54] Baidya A, Tripathi M, Singh UB, Pandey P. *Mycobacterium abscessus* as a cause of chronic meningitis: A rare clinical entity. American Journal of the Medical Sciences. 2016;**351**(4):437-439

[55] Cadena G, Wiedman J, Boggan JE. Ventriculoperitoneal shunt infection with *Mycobacterium fortuitum*: A rare offending organism. Journal of Neurosurgery. Pediatrics. 2014;**14**:704-707

[56] Midani S, Rathore MH. *Mycobacterium fortuitum* infection of ventriculoperitoneal shunt. Southern Medical Journal. 1999;**92**:705-707

[57] Chan KH, Mann KS, Seto WH. Infection of a shunt by *Mycobacterium fortuitum*: Case report. Neurosurgery. 1991;**29**:472-474

[58] Vishwanathan R, Bhagwati SN, Iyer V, Newalkar P. Ventriculo-peritoneal shunt infection by *Mycobacterium fortuitum* in an adult. Neurology India. 2004;**52**:393-394

[59] Alibadi H, Osenbach RK. Intrathecal drug delivery device infection and meningitis due to *Mycobacterium fortuitum*: A case report. Neuromodulation. 2008;**11**:311-314

[60] Madaras-Kelly KJ, Demasters TA, Stevens DL. *Mycobacterium fortuitum* meningitis associated with an epidural catheter: Case report and a review of the literature. Pharmacotherapy. 1999;**19**:661-666

[61] Uche C, Silibovsky R, Jungkind D, Measly R. Ventruloperitoneal shunt associated *Mycobacterium goodie* infection. Infectious Diseases in Clinical Practice. 2008;**16**:129-130

[62] Esteban J, Garcia-Coca M. Mycobacterium biofilms. Frontiers in Microbiology. 2018;**8**:2651. DOI: 10.3389/fmicb.2017.02651. e Collection 2017

[63] Pelegrin I, Lora-Tamayo J, Gomez-Junyent J, Sabe N, Garcia-Somoza D, Gabarros A, et al. Management of ventriculoperitoneal shunt infections in adults. Analysis of risk factors associated with treatment failure. Clinical Infectious Diseases. 2017;**64**(8):989-997

[64] Mayhall CG. Hospital Epidemiology and Infection Control. 3rd ed. Baltimore, Maryland: Lippincott Williams and Wilkins; 2004

[65] Ferrell M, Wolf CE, Ellenbogen KA, Wood MA, Clema HF, Gilligan DM. Ethylene oxide on electrophysiology catheters following resterilization: Implications for catheter reuse. The American Journal of Cardiology. 1997;**80**(12):1558-1561

[66] Rutala WA. 1994, 1995 and 1996 Guideline Committee: APIC guidelines for selection and use of disinfectants. American Journal of Infection Control. 1996;**24**:313-342

[67] Rutala WA, Weber DJ, Committee HICPA Guidelines. Disinfection and sterilization in healthcare facilities: What clinicians need to know. Clinical Infectious Diseases. 2004;**39**(5):702-709

[68] Vesley D, Melson J, Stanley P. Microbial bioburden in endoscope reprocessing and an in-use evaluation of the high level disinfection capabilities of Cidex PA. Gastroenterology Nursing. 1999;**22**(2):63-68

[69] Chu NS, McAlister D, Antonoplos PA. Natural bioburden levels detected on flexible gastrointestinal endoscopes after clinical use and manual cleaning. Gastrointestinal Endoscopy. 1998;**48**(2):137-142

[70] Kruse A, Rey JF. Guidelines on cleaning and disinfection in GI endoscopy. Update 1999. The European Society Of Gastrointestinal Endoscopy. Endoscopy. 2003;**35**:878-881

[71] Hulka JF, Wisler MG, Bruch C. A discussion: Laproscopic instrument sterilization. Medical Instrumentation. 1977;**11**:122-123