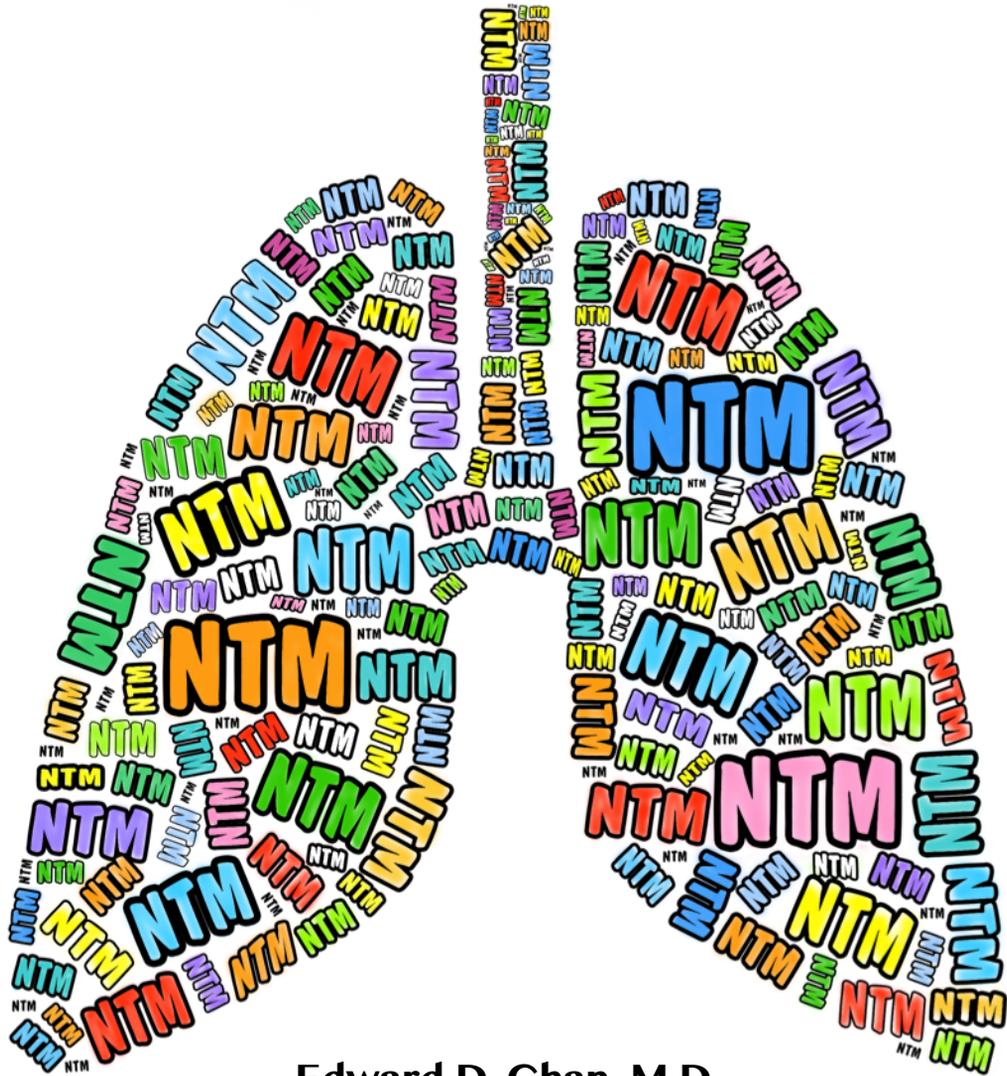


A Physician's View: Guide for Patients with NTM Infections



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What are non-tuberculous mycobacteria (NTM)?

NTM are cousins of the bacteria that cause tuberculosis & leprosy but there are many types of NTM

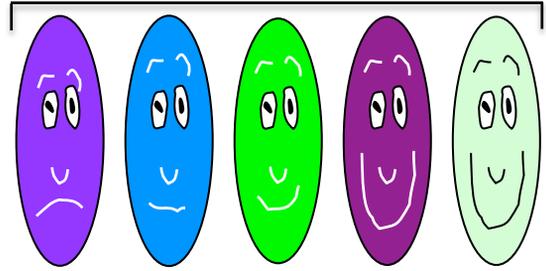
Mycobacterium tuberculosis



Mycobacterium leprae



NTM

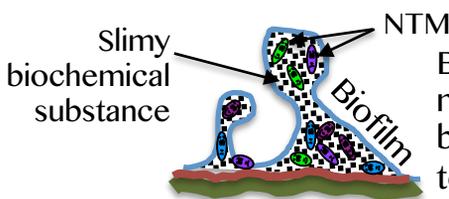
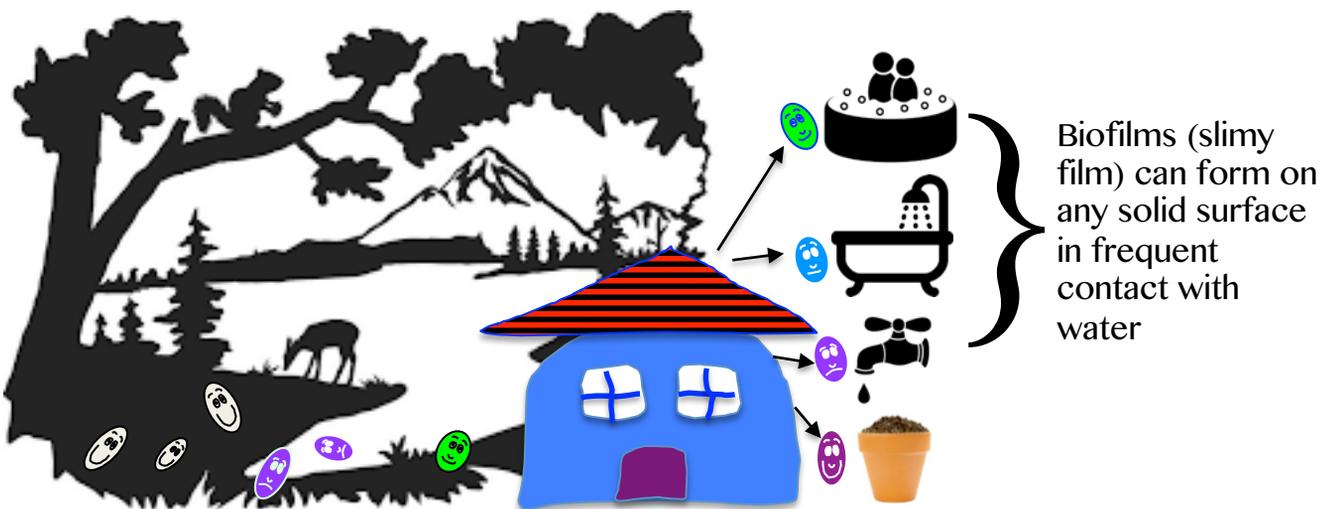


More virulent:
harder to treat

Less virulent: not
as hard to treat

Where are NTM lurking?

Soil, water, and biofilms in both natural & man-made niches

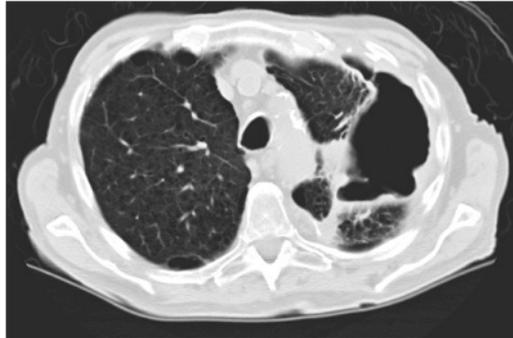


Biofilms are like cities for microbes, consisting of a slimy biochemical substance (buildings) teeming with bacteria (people).

Diseases caused by NTM

(can be classified into three main types)

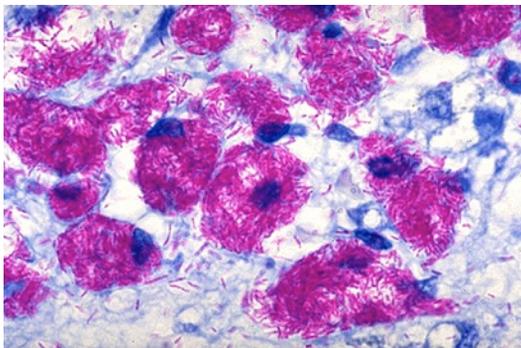
- Isolated lung disease



- Skin and soft tissue infections



- Internal organs other than the lungs



White blood cells in an internal organ filled with live *M. intracellulare* (magenta color organisms) in a patient with advanced AIDS. But with AIDS therapy, this severe form of NTM infection is rare now.

NTM lung disease

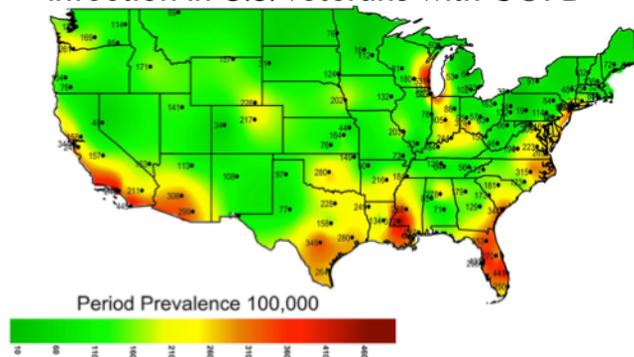
Epidemiology – how common is it?

- NTM are everywhere...but some parts of the country have more cases.



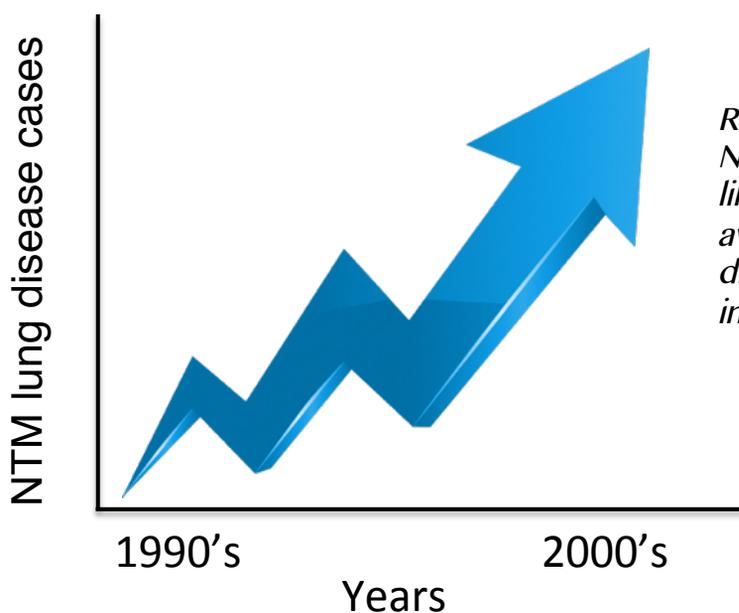
Adjemian J et al. Am J Respir Crit Care Med 2012

Period prevalence (2001-2015) of NTM infection in U.S. veterans with COPD



Pyrali FF et al. Front Med 2018

- Prevalence of NTM lung disease is increasing by 8% per year in the elderly population.



Rise in the number of NTM lung disease is due likely to both increased awareness of the disorder and a bona-fide increase.

Zheng C and Fanta CH. Q J Med 2013; Strollo SE et al. Ann Am Thorac Soc 2015.

What environmental “risk” factors are associated with NTM lung disease?

- Warm and humid environment.



- Living near bodies of water (lakes, oceans), especially turbid water.



- Occupational and recreational exposure to soil.
- Lower pH in soils, especially peat-rich soil.
- Higher copper and sodium & lower manganese in soil.
- Households with hot water heater temperature set at $\leq 125^{\circ}\text{F}$ ($\leq 50^{\circ}\text{C}$).

NTM lung disease

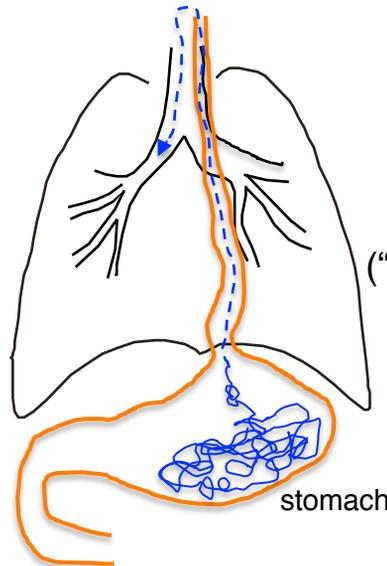
How do we acquire it?

- Inhalation of water, soil, and biofilm aerosols that contain NTM.



- Aspiration of NTM-containing secretions from “above” (swallowing dysfunction) or “below” (gastroesophageal reflux).

Swallowing difficulties causing aspiration (“from above”)

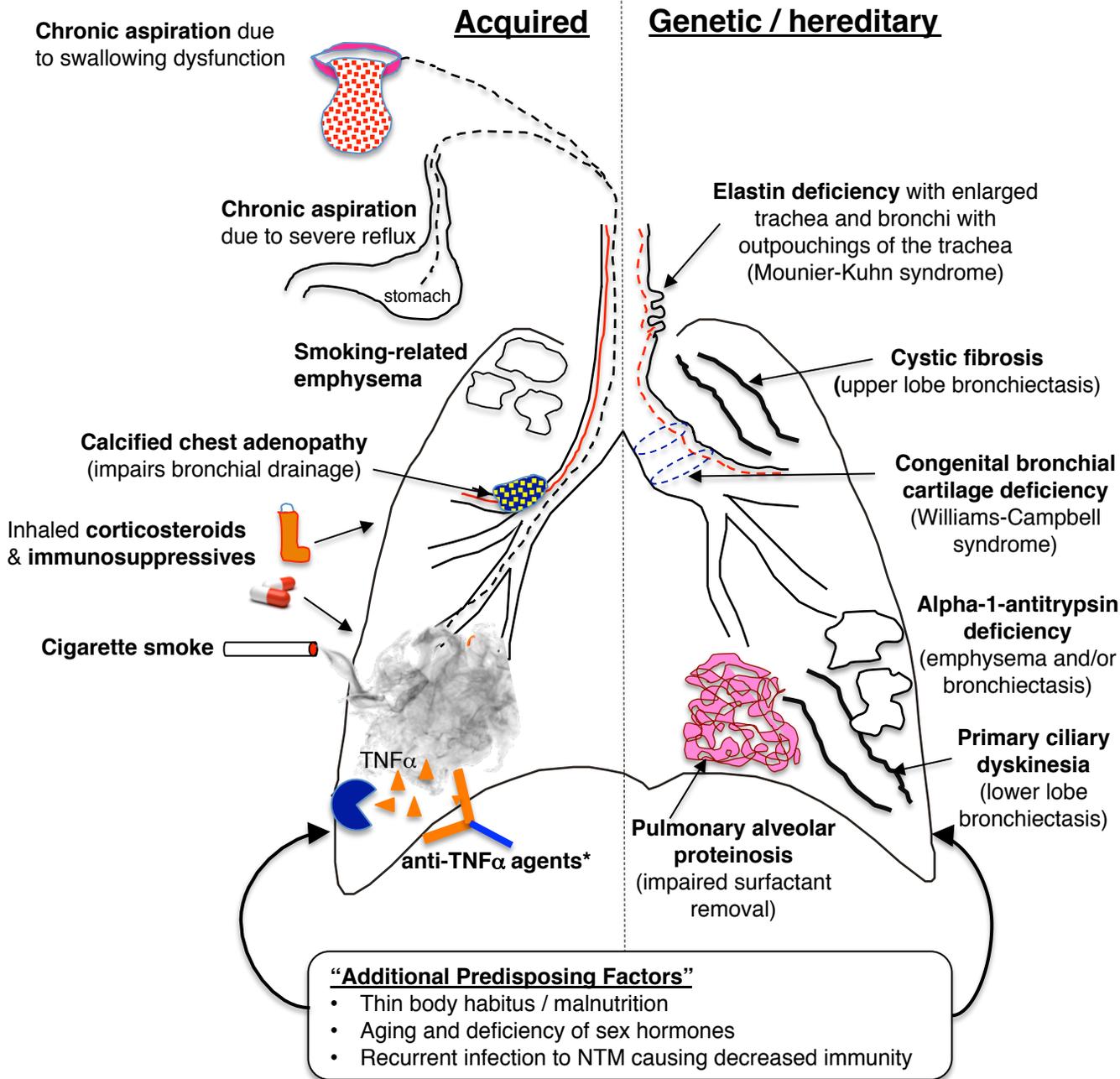


High reflux causing aspiration (“from below”)

NTM lung disease

Predisposing medical conditions

Risk factors for NTM-lung disease



*Anti-TNF α agents are used to treat various inflammatory / autoimmune conditions such as rheumatoid arthritis and inflammatory bowel disease.

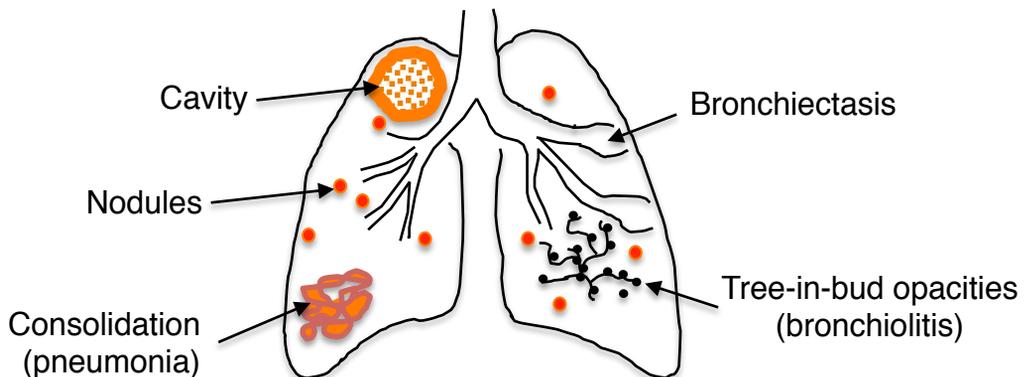
NTM lung disease

Three main components required for diagnosis

1. Clinical symptoms: Fever, cough, sputum, fatigue, night sweats, chest pain, and/or shortness of breath.

2. CT findings compatible with NTM lung disease:

- Bronchiectasis.
- Nodules, consolidation, tree-in-bud opacities, and/or cavities.



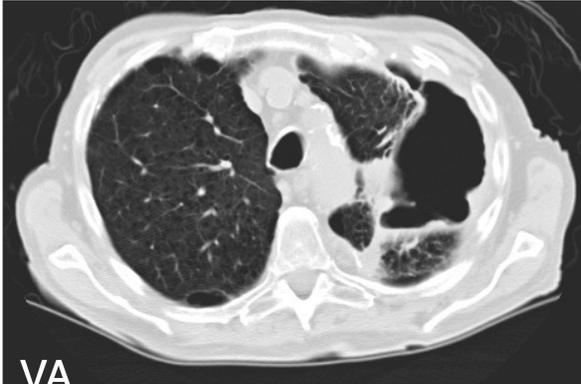
3. Microbiological findings:

- Two or more NTM positive sputum cultures *or*
- One positive bronchoscopy culture *or*
- Lung biopsy consistent with NTM lung pathology or a positive NTM culture from the biopsy.

NTM lung disease

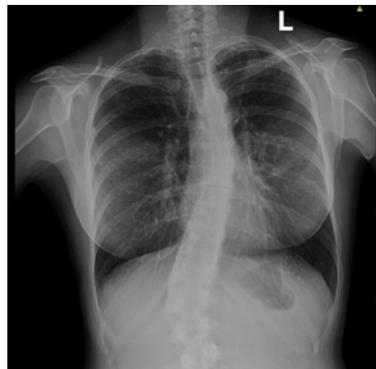
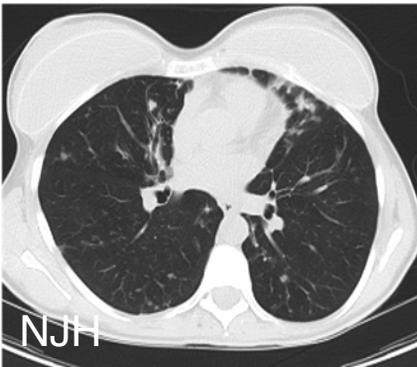
Radiographic manifestations

- Upper lobe fibrocavitary disease



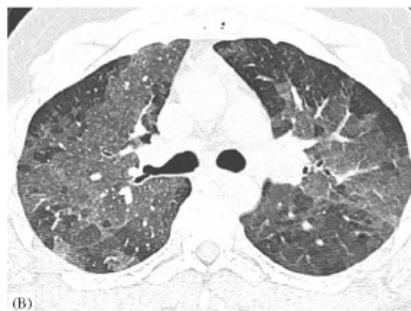
72 yo man
Underlying emphysema

- Nodular-bronchiectasis



41 yo previously healthy woman with “life-long” slender body habitus & severe scoliosis

- Hypersensitivity pneumonitis (“hot tub lung”)



Hanak V et al.
Respir Med 2006

Treatment of NTM lung disease

What to consider when deciding if and when to treat

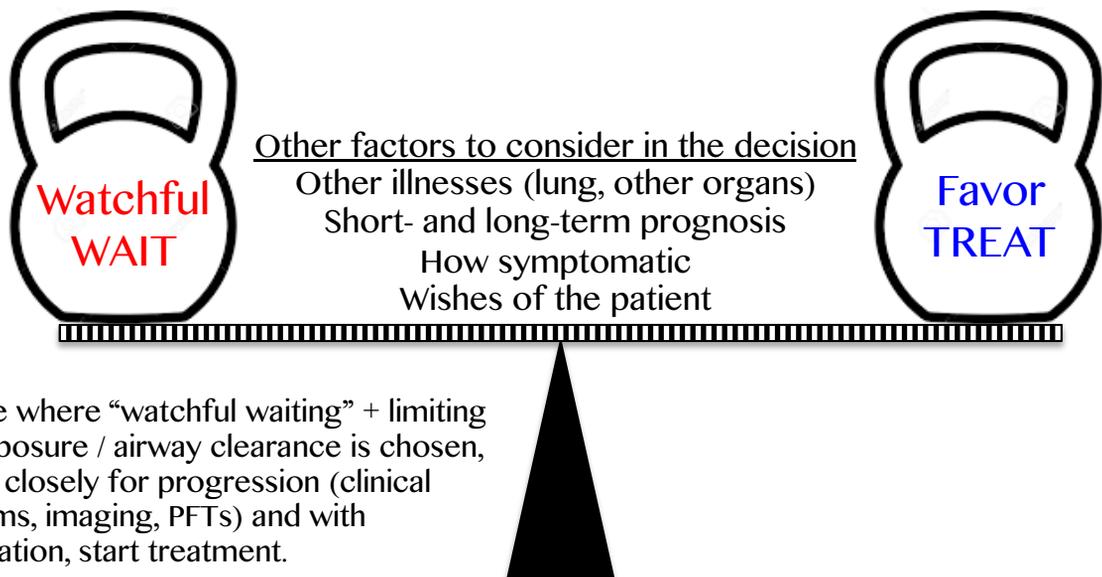
- When treating any illness, patients / clinicians have to weigh the risk and benefits of the treatment.
- Avoidance of potential sources of NTM exposure plus good airway clearance MAY result in the disappearance of NTM from the sputum in ~10-15% of subjects. Thus, careful consideration should be undertaken in deciding whether and when to treat for NTM lung infection.
- Below is a diagram on factors that favor antibiotic treatment vs. a watchful-waiting strategy.

Consider watchful waiting*

- Mild nodular-bronchiectasis
- Negative acid-fast stain of sputum
- High body mass index

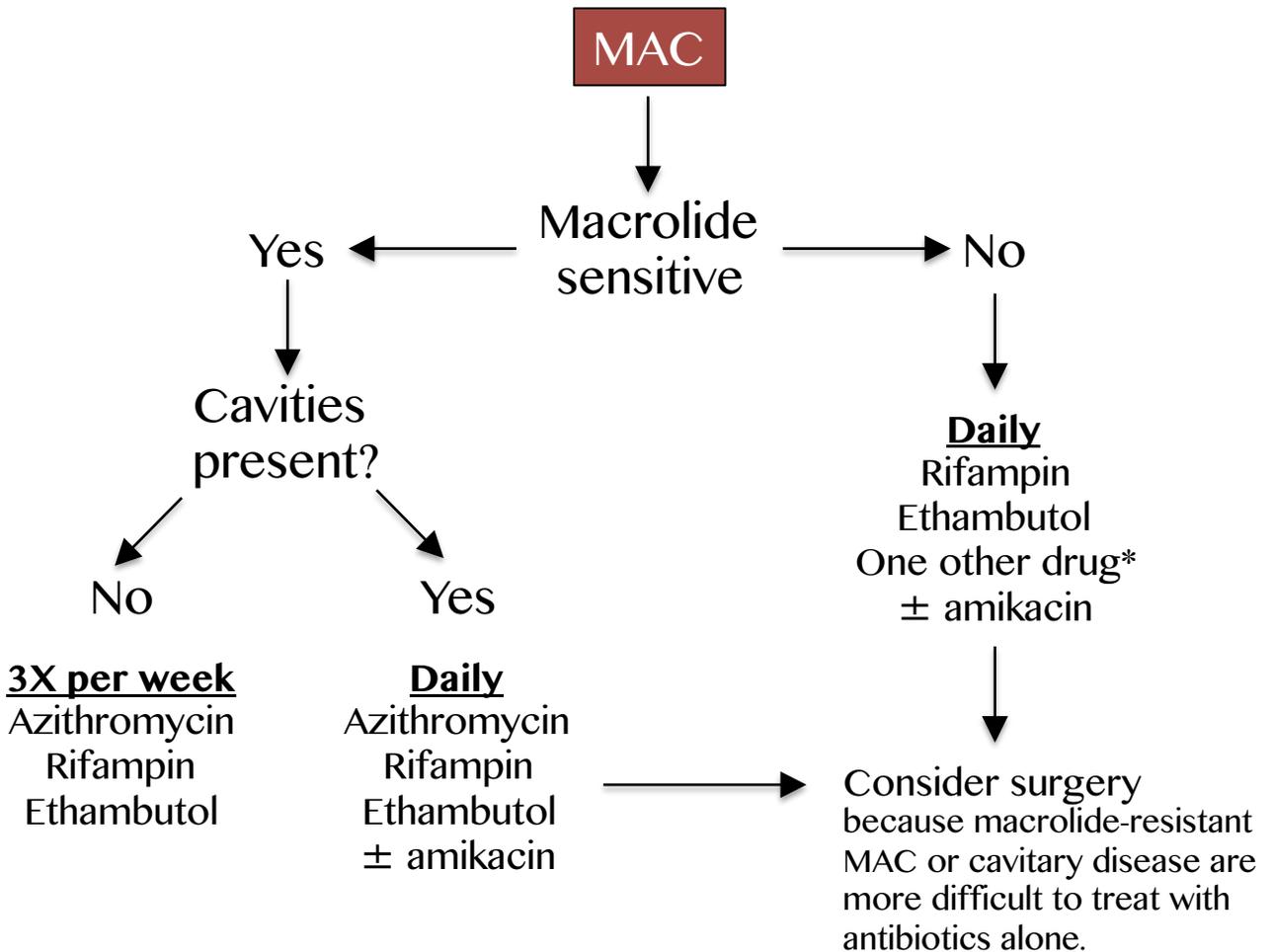
Consider treatment

- Cavitory or severe bronchiectasis
- Persistent microbiologic positivity
- Radiographic deterioration
- Decline in lung function



*In those where “watchful waiting” + limiting NTM exposure / airway clearance is chosen, monitor closely for progression (clinical symptoms, imaging, PFTs) and with deterioration, start treatment.

MAC Treatment Algorithm



Alternatives to ethambutol:
amikacin (IV or liposomal inhaled-Arikayce®)

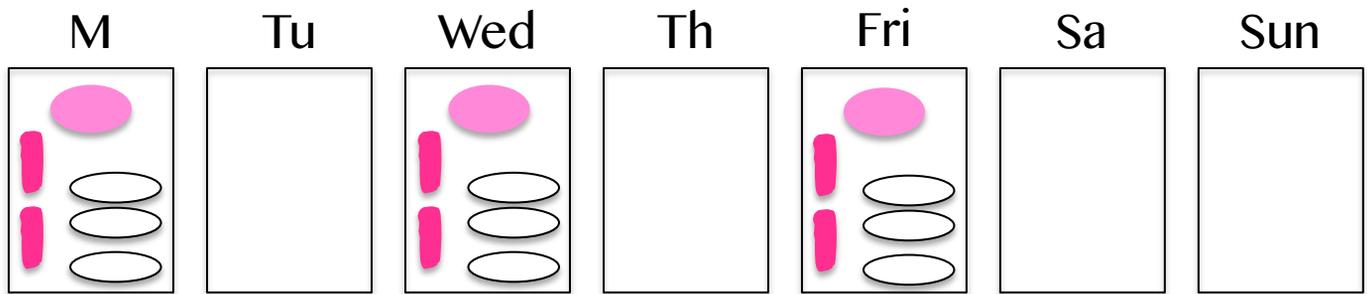
Alternatives to rifampin:
rifabutin, clofazimine

*Clofazimine
*Linezolid / tedizolid
*Bedaquiline
*Moxifloxacin (not favored by some)
*Ciprofloxacin (not favored by some)

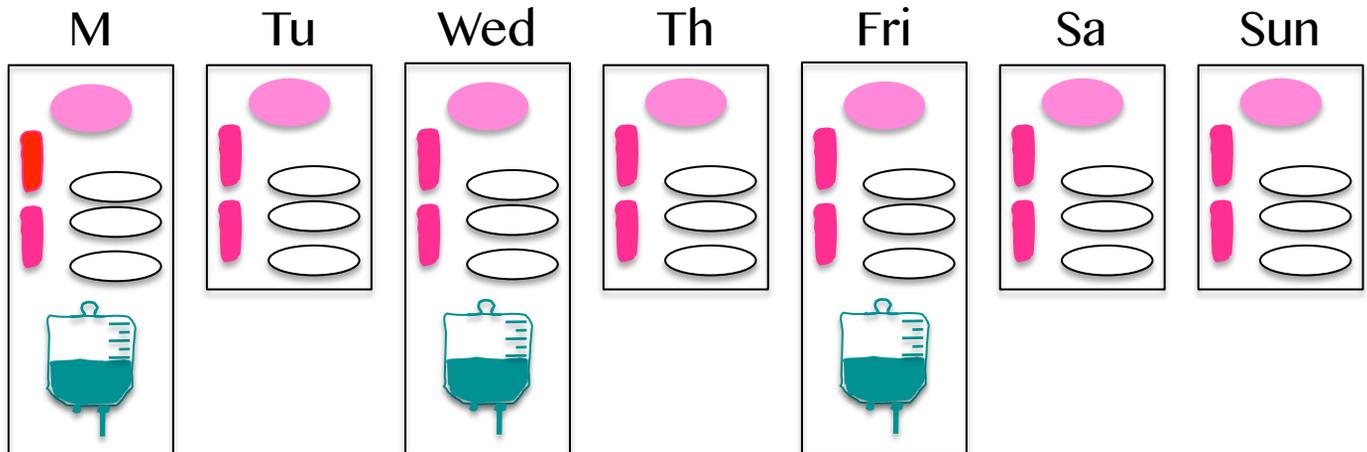
Treatment of MAC lung disease

Antibiotics

- Mild to moderate disease severity in the nodular bronchiectasis pattern**



- Severe bronchiectasis or presence of one or more cavities**



Azithromycin or clarithromycin



Rifampin



Ethambutol



Intravenous amikacin

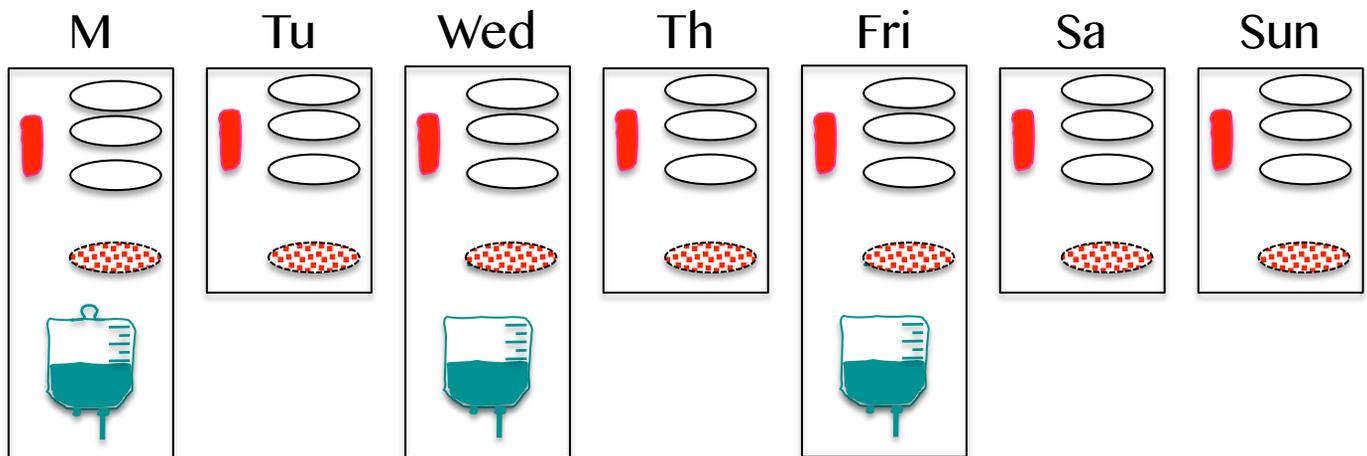
Number of pills depicted may not represent actual dosing.

Treatment of MAC lung disease

Macrolide Resistance
 "A Big Deal" (Dr. David Griffith)

*due to mutation of the 23S rRNA gene

- Every effort should be to prevent development of macrolide resistance as the macrolides (azithromycin, clarithromycin) are the most important drugs against most NTM.
- **Macrolide resistance** (MIC ≥ 32 $\mu\text{g/mL}$) may be already present when the diagnosis is first made or it may be acquired* due to inappropriate treatment with macrolide monotherapy or macrolide + an ineffective agent (e.g., fluoroquinolone).
- Ethambutol is the most important companion drug to prevent macrolide resistance; thus, ethambutol should be used with macrolide whether or not the NTM is resistant to ethambutol. As a corollary, MAC should not be treated with macrolide + rifampin only as this dual regimen can breed resistant strains.



Rifampin Ethambutol

Intravenous amikacin

or or

Other options

Clofazimine

Bedaquiline

Oxazolidone (e.g., linezolid)

Once IV amikacin stopped

Inhaled liposomal Amikacin (Arikayce®)

Treatment outcome for MAC lung disease

	Culture conversion (%)	Treatment failure (%)
<u>Macrolide sensitive</u>		
Non-cavitary	80%	20%
Cavitary	50-80%	20-50%
<u>Macrolide resistant</u>		
No surgery or AG*	5%	95%
Some surgery/AG*	15%	85%
Surgery + prolonged AG*	80%	20%

*AG = aminoglycoside such as amikacin

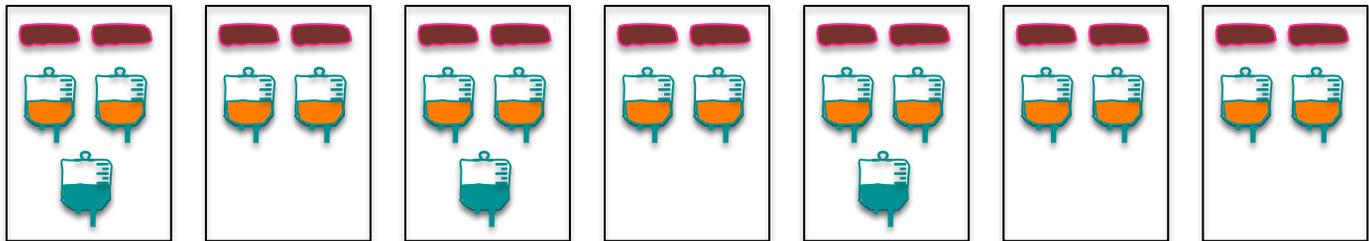
Treatment of *M. abscessus* complex lung disease

Antibiotics

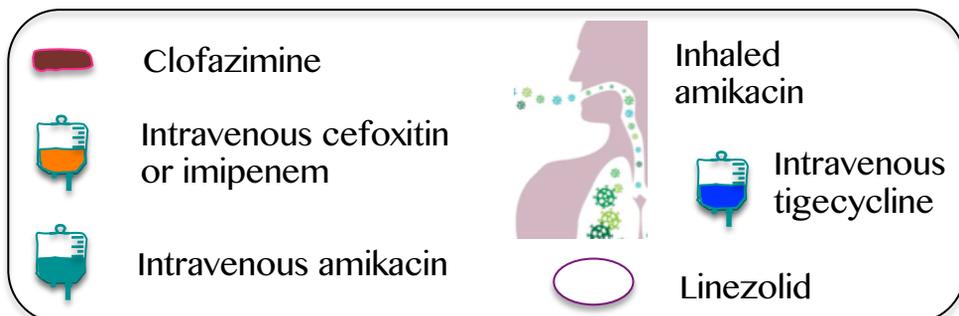
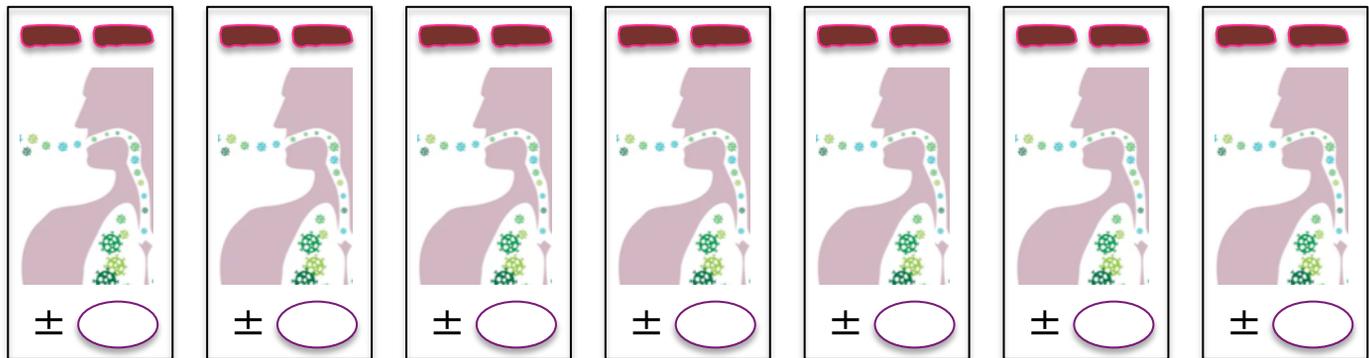
- M. abscessus abscessus* or *M. bolletii* with a functional *erm41* gene (macrolides not used because *erm41* causes macrolide resistance to develop).

M Tu Wed Th Fri Sa Sun

Induction



Maintenance



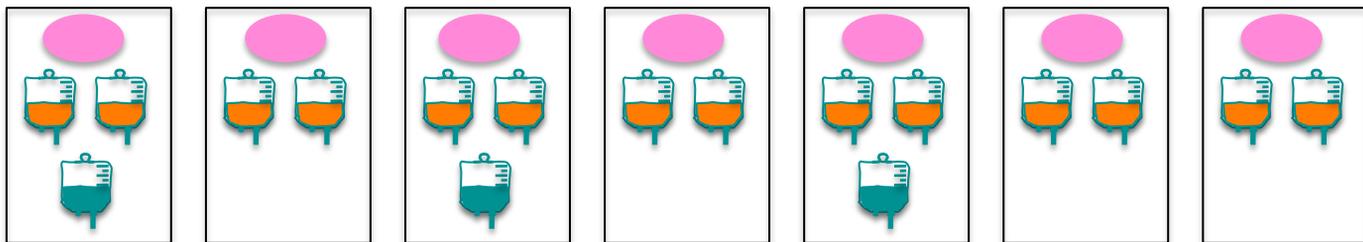
Treatment of *M. abscessus* complex lung disease

Antibiotics

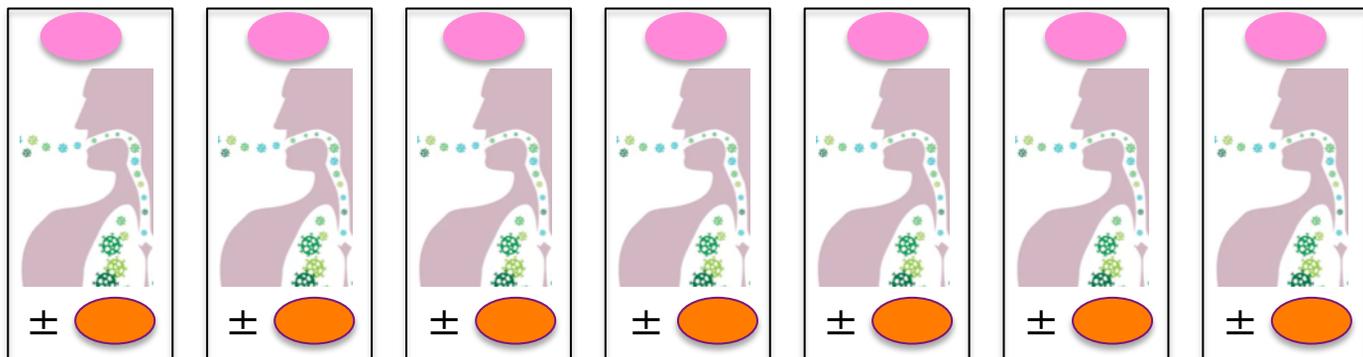
- M. abscessus abscessus*, *M. bolletii*, or *M. massiliense* **without** a functional *erm41* gene.

M Tu Wed Th Fri Sa Sun

Induction



Maintenance



	Azithromycin or clarithromycin		Inhaled amikacin
	Intravenous ceftioxin or imipenem		Moxifloxacin
	Intravenous amikacin		

Treatment of NTM lung disease

Antibiotic drug toxicity and measures to minimize toxicity and increase efficacy

Drug	Toxicity	Ways to minimize toxicity and/or increase efficacy
Macrolides	Diarrhea, hearing loss, tinnitus, metallic taste, prolonged QTc	Either with or without food, but with food tolerability may improve. Clarithromycin may reduce metabolism of other drugs and raise their levels; e.g., colchicine, statins, warfarin, etc).
Rifampin	Increases metabolism of other drugs	Take on empty stomach as food decreases absorption by ~30%. Pills can be modified into a liquid suspension.
Ethambutol	Optic neuritis (color blindness, scotoma, decreased visual acuity), hepatitis	With or without food.
IV amikacin	Kidney toxicity, ear toxicity (hearing loss, tinnitus, imbalance)	Monitor drug levels. Avoid other kidney-toxic drugs; e.g., NSAIDs.
Inhaled liposomal amikacin suspension (Arikayce®)	Dysphonia, cough, dyspnea; may still cause kidney and ear toxicities but less likely than IV amikacin.	Arikayce® is normally given once daily but may be given 3X/week if not well tolerated.

Treatment of NTM lung disease

Antibiotic drug toxicity and measures to minimize toxicity and increase efficacy

Drug	Toxicity	Ways to minimize toxicity and/or increase efficacy
Clofazimine	GI intolerance (nausea, vomiting, diarrhea, abdominal pain), skin discoloration, prolonged QTc	Take with food (unofficial recommendation).
Fluoro-quinolone	Tendonitis	Take at least 2 hrs before or 6 hrs after dairy products, antacids, iron, calcium, or zinc
Imipenem	Seizures, bone marrow suppression, increased liver function tests	Dose of both drugs should be adjusted for renal function. Imipenem should not be administered when renal function is severely reduced unless hemodialysis instituted in 48 hrs.
Cefoxitin	Thrombophlebitis, hypotension, rash	
Linezolid	Nausea, vomiting, diarrhea; low platelet count, bone marrow suppression; acidosis, serotonin syndrome	Serotonin syndrome more likely to occur with use of other drugs that can increase serotonin levels
Tigecycline	Nausea, vomiting, diarrhea; acute pancreatitis, low blood sugar, anaphylaxis	

Treatment of NTM lung disease

Mucus clearance mechanisms: the best method is the one you do regularly!

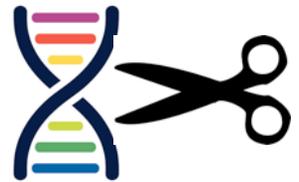
- Pharmacologic



Expectorant
(e.g., guaifenesin)



Inhaled mannitol powder
(a sugar to help liquify sputum)



Pulmozyme®
("chews up" the sticky DNA – indicated for CF patients only)

- Non-pharmacologic

Aerobika®



Acapella Valve®



High-frequency oscillatory vest



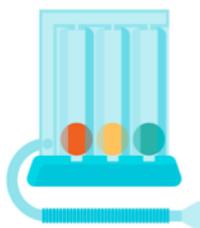
Chest physiotherapy & postural positioning



Hydration



Incentive spirometry



Exercise



Huff cough



Foods that may affect mucus production

Foods that may increase mucus

- Red meat
- Milk
- Cheese
- Yogurt
- Ice Cream
- Butter
- Eggs
- Bread
- Pasta
- Cereal
- Bananas
- Cabbage
- Potatoes
- Corn and corn products
- Soy products
- Sweet desserts
- Candy
- Coffee
- Tea
- Soda
- Alcoholic beverages

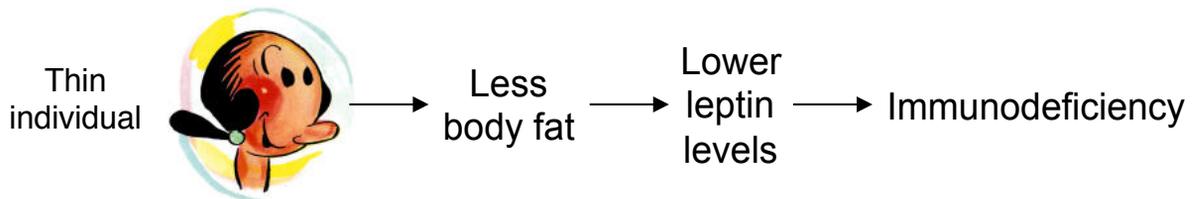
Foods that may decrease mucus

- Salmon
- Tuna
- Sardines
- Flounder
- Pumpkin
- Pumpkin seeds
- Grapefruit
- Pineapple
- Watercress
- Celery
- Pickles
- Onion
- Garlic
- Honey or agar
- Ginger
- Lemon
- Cayenne pepper
- Chamomile
- Olive oil
- Broth
- Decaf tea

Treatment of NTM lung disease

Nutrition and important role of fat, and other basic health-promoting measures

- Thin individuals appear to be more susceptible to NTM lung disease. One possibility is due to a deficiency of the fat-derived hormone leptin, which is important in increasing host immunity against NTM. **Thus, maintain ideal or closer to ideal body weight.**



- Eat healthy fats / eggs.
- Mirtazepine is a sleep aid that also increases appetite.
- Pneumococcal and influenza vaccines (see *Appendix 9*).
- Make sure 25-OH vitamin D₃ level is between 30 and 60 ng/mL.
- See Website on Nutrition from NTMir® www.NTMinfo.org

Treatment of NTM lung disease

Role of surgery

- **Clinical indications for surgery include:**
 - Severe localized disease *and*
 - Deemed able to tolerate surgery *and*
 - Poor response to drug therapy, the development of drug resistance, and/or the presence of disease-related complications (recurrent and severe hemoptysis).
- Surgery does not obviate need for antibiotics; *i.e.*, antibiotics are still required to treat NTM.
- Surgical resection for severe localized disease has been shown to increase the chance that sputum cultures for NTM will become negative.

2006 – pre-op



2010 – post-op



Right middle lobe NTM disease in the pre-op CT scans (arrows)

What can you do to reduce exposure to NTM?

Changes to your activities

- Avoid aerosols of soil and water (see Appendices 8 & 9).

Water aerosols



Soil aerosols



- Avoid water where there is a lot of bubble generation (hot tub, jacuzzi, indoor swimming pools).



- **Avoid cigarette smoke exposure**

- **Self-education**

- View NTM Info & Research® (NTMir®) website (www.NTMinfo.org, Webinar, “Insight” pamphlet, contacts).
- Join local NTM support group.
- NTMir®-sponsored Physician-Patient Conference at yearly American Thoracic Society Scientific Conference, typically May of each year.

What can you do to reduce exposure to NTM?

Proactive measures to prevent or treat NTM lung disease

- Do airway clearance regularly.
- Take antibiotics appropriately.
- **Prevent reflux of stomach contents into esophagus**
 - Foam wedge / adjustable bed to elevate head-of-bed at least 30° (see left diagram below).
 - Avoid body positions that promote reflux (see right diagram below).
 - Avoid food or drink 2-3 hrs before lying down.
 - If not needed, avoid drugs that may promote reflux (e.g., albuterol inhalers).
 - Avoid prone sleeping position as head of bed elevation not feasible.

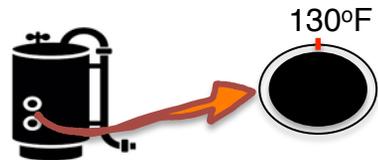


- Find **medical professionals with expertise, enthusiasm, and patience** to treat NTM lung disease.

What can you do to reduce exposure to NTM?

Changes to the environment

- Increase **hot water heater temperature to 130°F** (be careful of scalding)



- **Flush out hot water heater yearly.**
- For bronchodilators (e.g., albuterol), meter dose inhaler preferred over nebulizer (latter more likely to form biofilms). If nebulizer needed, clean meticulously / replace the apparatus to prevent biofilm formation.
- Make sure water reservoir for humidification of supplemental O₂ and CPAP or bi-level apparatus are cleaned thoroughly at least weekly to prevent biofilm formation.
- Showerheads
 - Replace if there is excess buildup of grime.
 - Avoid showerheads with fine mist

preferred



**NOT
recommended**

- Choose homes with copper over galvanized or plastic pipes.
- Avoid humidifiers but if needed, evaporative humidifiers are preferred over ultrasonic ones.

Skin and soft tissue infections

How do we acquire them?

- **Contaminated water, medications, or instrument** in medical and surgical procedures



- **Trauma** – resulting in skin break and contamination with NTM-containing material



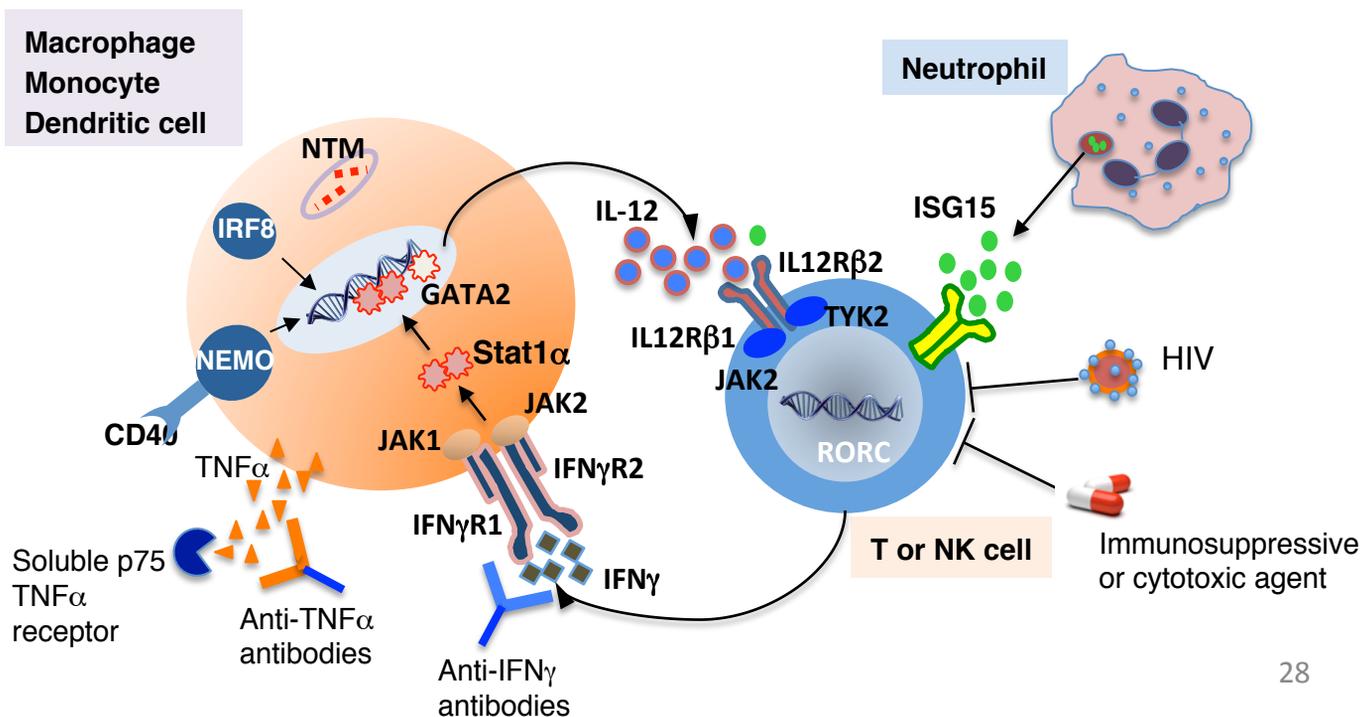
- **Nail salons** – with exposure to NTM-contaminated water and biofilm; e.g., pedicure salons.



NTM infection of internal organs other than the lungs

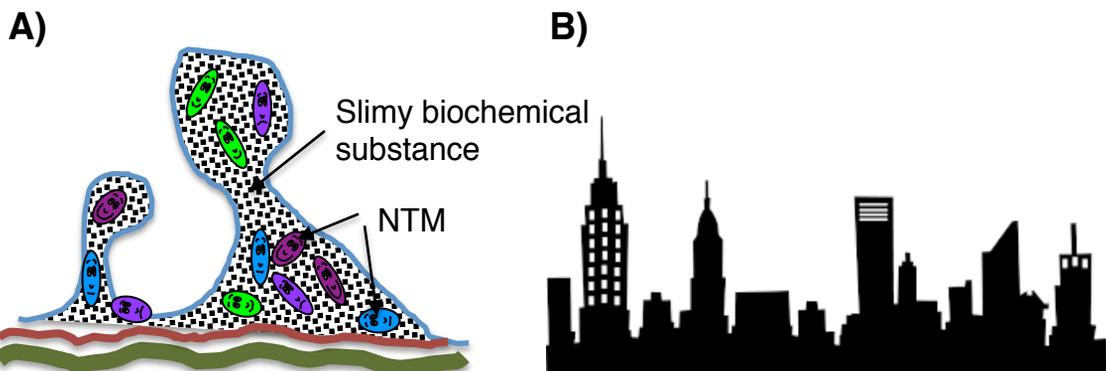
Who are at risks?

- Untreated AIDS virus infection.
- Immunosuppressive drugs / transplant recipients.
- An autoimmune disorder due to the presence of an antibody against interferon-gamma ($\text{IFN}\gamma$).
- Contaminated heater-cooler units used in open-chest heart surgery may result in aerosol of NTM (*M. chimaera*) that has been shown to cause infections of heart valves, aortic grafts, left ventricular-assisted devices, sternal wounds, vertebra, liver, and widespread infection including the blood.
- Inherited disorders of the immune system (see diagram below).



Appendix 1 – glossary of terms

- **Biofilms:** are like cities for microbes, consisting of microbes (people) living in 3-D structures of extracellular polymeric substances (buildings), the latter comprised of polysaccharides, proteins, lipids, and DNA (brick & mortar). Examples of biofilms:
 - Plaque / slimy film that forms on teeth surfaces.
 - Slimy material on sides of pools, inside pipes, and any solid-water interfaces.



Analogy of a biofilm to a city dwelling. (A) Side view of a thin biofilm in which there is a slimy biochemical substance in which bacteria and other microorganisms reside. (B) Conceptually, a biofilm is analogous to a city scape in which the skyscrapers (slimy biochemical substance) house people (NTM).

- **Bronchiectasis:** Permanent dilatation of the airways due to genetic condition and/or repeated airway infections.
- **Bronchoalveolar lavage (BAL):** performed by bronchoscopy (see below) in which sterile saline is instilled into the lungs and suctioned back out. A common indication for BAL is to obtain respiratory samples for culture in those unable to cough up sputum.

Appendix 1 – glossary of terms (continued)

- **Bronchoscopy:** a procedure performed under conscious sedation in which a flexible optic fiber tube is inserted into the nose or mouth and into the airways to inspect the airways, suction out secretions, perform biopsy, and perform BAL.
- **Cavity:** a relative large hole in the lung tissue due to necrosis from prolonged infection.
- **DNase (Pulmozyme®):** an enzyme that breaks down DNA in sputum. DNA from inflammatory cells contributes greatly to the thick, sticky sputum. Given as a nebulizer.
- **Expectorant:** a medicine that helps one to expel sputum.

Appendix 1 – glossary of terms (continued)

- **Huff cough:** increases movement of secretions from the smaller to the larger airways, increasing the chance that the sputum is coughed out. To perform a huff cough, breathe in $\frac{3}{4}$ full, hold for 2-3 seconds, and blow out but make a “ha” sound (as if fogging a mirror), repeat twice, and followed by a regular cough to bring out the sputum.
- **Pulmonary rehabilitation:** a series of sessions that includes education about your lung condition, proper medication use (e.g., inhaler use), proper use of various respiratory devices (e.g., supplemental oxygen, airway clearance devices, CPAP or bi-level, etc) as well as exercise programs geared for individuals with breathing problems.
- **Tree-in-bud opacities:** a CT scan description of inflammation in the small airways (bronchiolitis) seen as lines and small nodules that resemble small branches on a tree with spring buds sprouting off.
- **Video-assisted thoracoscopic surgery (VATS):** a “less invasive” surgery in which smaller incisions are made in the chest to allow insertion of instruments that can visualize and resect a segment or lobe of a lung.

Appendix 2 – oxygen (O₂) delivery systems

- **Compressed O₂** – comes in many different size aluminum cylinders.
- **Liquid O₂** – comes with large free-standing tank from which the portable liquid O₂ tank may be filled.
- **O₂ concentrator** – concentrates air into O₂ (maximum delivery of O₂ is 6 liter per minute, LPM) and comes with free-standing device (electrical powered) and a portable device (battery powered).

Home units and portable compressed O₂ cylinders



Home units and portable liquid O₂



Home units and portable O₂ concentrators

Appendix 3 – pulse oximeter

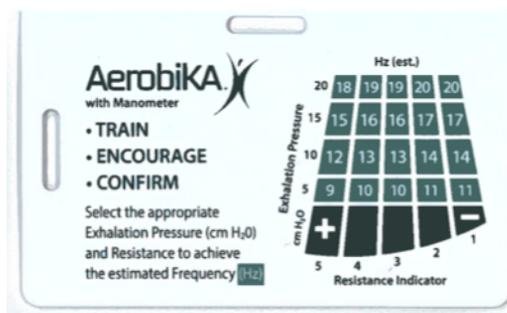
- Measures the amount of oxygen (O_2) in the blood as % of the hemoglobin that are bound to O_2 (SpO_2).
- Indispensable if prescribed supplemental O_2 , air travel, or traveling to higher elevations.
- Testing should be done at rest, physical activity, and during sleep (with special nocturnal oximeter that records continuously) to determine need for supplemental O_2 and dose.
- Keep SpO_2 ~90 to 92% by adjusting the O_2 flow.
- **Use**
 - Insert finger into pulse oximeter probe.
 - The pulse rate and SpO_2 reading will appear in ~5-10 seconds.
 - Keep finger-pulse oximeter still as much as possible for accurate reading.
 - Fingernail polish has minimal effects on reading although black and blue color polishes may decrease the SpO_2 by a few % points; one solution is to rotate the probe 90° from usual placement.

Appendix 4 – use of Aerobika®

- Best to be trained by a Respiratory Therapist before use.
- **Use:**
 - Place mouthpiece in mouth.
 - Inhale bigger than normal breath and hold 2-3 sec.
 - Exhale for 3-4X longer than inspiration, if able.
 - Do 10-20 breaths as tolerated.
 - Perform 2-3 huff coughs, followed by a deep cough.
 - Repeat for 10-15 min total at each session 2-4X per day or as tolerated.
- Aerobika® may come with a **manometer**, which gauges whether the expiratory blow is adequate. The manometer contains a **green zone** (5-20 cm H₂O), **yellow zone** (20-40 cm), and **red zone** (40-60 cm). It is recommended to stay within the **GREEN ZONE**; e.g., 10-15 cm H₂O pressure.
- Based on the chart below, at a resistance setting of “3”, if one exhales to 10-15 cm H₂O pressure, this results in an airway beating frequency of 13-16 Hz.
- Aerobika® may be used in-line with a nebulizer that contains a bronchodilator or hypertonic saline.



Aerobika with manometer



Aerobika with in-line nebulizer 34

Appendix 5 – use of Acapella®



- Best to be trained by a Respiratory Therapist before use.
- Acapella® combines both positive expiratory pressure therapy and airway vibrations to mobilize secretions and can be used in virtually any postural positions; *i.e.*, sitting, standing or reclining.
- Acapella® is color-coded (DH green for high-flow and DM blue for low-flow; most adults should use the green one).
- **Use of the Acapella® valve**
 - Assure proper setting of the resistance dial on the end of the Acapella® valve. Start at the mid-resistance point and rotate toward + or - to increase or decrease resistance as tolerated. Adjust resistance so that you can exhale for at least 3 sec.
 - Sit up with good posture to use the Acapella although various positions may be required for optimal drainage of secretions.
 - Place the Acapella® mouthpiece in the mouth. Seal lips tightly around the mouthpiece.
 - Take in a bigger than normal breath and hold for 2-3 sec.
 - Exhale actively (NOT forcefully) until the flutter sound ceases.
 - Repeat 10 times, then perform 3 huff coughs, followed by a big cough to bring out the sputum.
 - Repeat above for 10-15 min 2-4X per day.
- Clean the Acapella® at the end of the day in liquid dish detergent and rinse and dry thoroughly overnight.
- Disinfect Acapella® weekly by removing the mouthpiece from the body and soak in 70% rubbing (isopropyl) alcohol for 5 min or 3% hydrogen peroxide for 30 min. Rinse thoroughly with water and drain/dry in a vertical position.

Appendix 6 – high frequency chest wall oscillation - vest

- A HFCWO-vest is comprised of two main parts: a wearable vest that is connected to an air-pulse generator.
- The high frequency inflation-deflation cycle (felt as vibrations) of the vest loosens airway secretions and move them up into the large airways so that they are easier to cough up.
- **Several manufacturers:** The Vest[®], InCourage[®], Smart Vest[®], Hill-Rom[®], Monarch[®], and AffloVest[®] (portable vest) with differences in how the vest is secured.
- Considered to be more useful for patients with bronchiectasis in the lower lobes.
- Frequency and duration time of each use: typically, HFCWO-vest is used for 5 min → huff cough → repeat for 20-30 minutes for each session, performed twice daily.

Appendix 7 – cleaning respiratory devices

- **Aerobika**

- If there is a manometer, it should NOT get wet.
- **Cleaning after last use of the day:** (i) soak all disassembled parts EXCEPT the manometer in liquid dish detergent & water for 15 minutes, rinse, shake off excess water and allow to air dry or (ii) dishwasher (top rack in basket) with sterilization cycle and dishwasher detergent.
- **Disinfecting weekly:** remove manometer first, and disinfect all disassembled parts EXCEPT the manometer by one of 4 methods: (i) boil by placing the disassembled parts in a colander for 5 minutes, (ii) soaked in 70% isopropyl alcohol for 5 minutes → rinse well, (iii) soaked in 3% hydrogen peroxide for 30 minutes, and (iv) Quick Clean Micro-Steam bags (Medela®) where the device is placed into bag with 2 ounces of water, and then heat with 800-1100 watt microwave for 3 min daily (the Micro-Steam bags should NOT be used for the Acapella® device). Each bag can be used 20 times.

- **Reusable nebulizer (AeroEclipse® XL)**



- **Cleaning after each use:** (i) Rotate the mode selector to the dotted arrow, the breath activated position (green button up), take apart nebulizer, wash in liquid dish detergent and water, and rinse well, (ii) dishwasher. Dry completely before reassembling.
- **Disinfecting (every other day):** take apart nebulizer, boil all parts except tubing and mask for 5 minutes, shake off excess water, cool, connect to air compressor and turn it on to facilitate drying. Replace tubing every 2 weeks.

Appendix 8 – if you must garden...

- Dampen the soil first to lessen aerosolization of particulate matter.
- Wear a N-95 mask and garden in the morning or evening as the mask can be stifling.
- Avoid gardening on windy days.
- Avoid mowing lawns and avoid exposure when others are mowing.
- Potting soil may also contain NTM so do the potting outside to increase air exchange and wear a N-95 mask.
- **N-95 masks** – make sure they fit properly. Below are three types of N-95 masks.



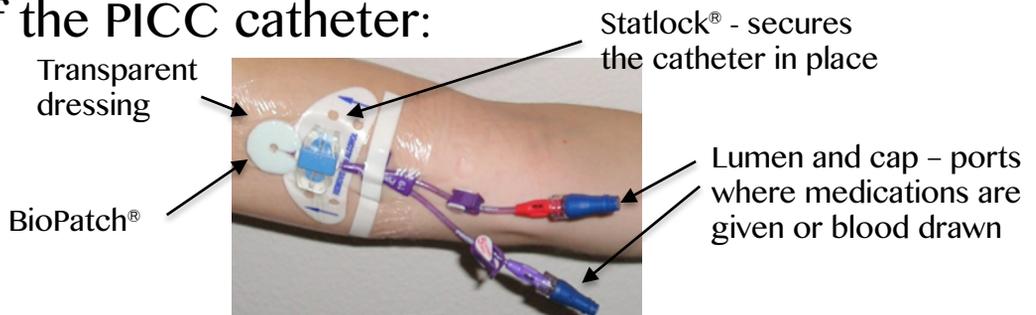
Appendix 9 – hints to prevent superimposed respiratory infections...

- Avoid crowds / carry and use hand sanitizers
- Use your elbow / arm to greet people (“elbow shake”) and to open doors, press elevator buttons, etc. Justify this by smiling and saying *“I am not ill but I just don’t want to pass any germs to you.”*
- Do not to touch your eyes or nose after being in public places without first sanitizing hands.
- **Influenza vaccine:** obtain yearly
 - High dose for ≥ 65 years old.
 - For those with egg allergy, vaccine available grown in cell culture.
 - Quadrivalent vaccine provide coverage for an extra viral strain.
- **Pertussis:** Tdap[®] one time dose in adulthood for the pertussis part.
- **Pneumococcal vaccine** schedule:
 - Both PCV13 (Pevnar[®]) and PPSV23 (Pneumovax[®]) are recommended for those ≥ 65 yrs old, with cardiopulmonary disorders of any age, and their contacts.
 - **Pneumococcal vaccine-naïve** : PCV13 \rightarrow wait ≥ 1 year \rightarrow PPSV23
 - **Previous PPSV23:** if ≥ 1 yr since PPSV23, then give PCV13
 - **Previous PPSV23 at < 65 yrs but now ≥ 65 yrs:** if ≥ 1 yr since PPSV23, then give PCV13, wait ≥ 1 yr, then give PPSV23.

Appendix 10 – peripherally-inserted central catheter (PICC)

- A long intravenous catheter intended for use for weeks to few months to administer IV medications.

- Parts of the PICC catheter:



- It is typically inserted into the larger vein near the elbow. The PICC is significantly longer than the standard IV catheter, with the tip ending just above the right heart.
- **Do's of PICC care**
 - Everyone must wash hands and wear mask before servicing PICC.
 - Antiseptic soaked BioPatch® around catheter at site of entry.
 - Change dressing at least once weekly. Use a special dressing for showering.
 - Seek medical attention ASAP for fever, bleeding around PICC site that does not stop with pressure, increasing redness at site of entry, intractable pain, or catheter that has partially or fully pulled out.
- **Don'ts of PICC care**
 - Do not push catheter back in if it partially or wholly comes out.
 - Do not submerge arm with PICC in water.
 - Avoid strenuous activity with the arms in the first 2 wks of insertion.
 - No blood pressure or needle stick on PICC arm.

Appendix 11 – port-catheter

- A **port-catheter (aka Port-a-cath)** is a long-term intravenous device that in principle is similar to the PICC but can remain in place much longer (months to years).
- A **port** is a small medical appliance is that placed by a surgeon beneath the skin on the chest wall.
- A **long catheter** connects the port to a large vein in the chest.
- Brief overview of accessing and caring the port-catheter:
 - Clean hands, use sterile gloves, clean skin over port site, and \pm topical anesthetic.
 - Stretch skin over port with one hand and insert non-coring needle into the dome of the port with the other.
 - Secure and cover the non-coring needle.

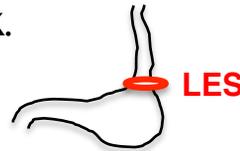


Appendix 12 – proper order of multiple inhaled therapies

1. **Nasal wash**
2. **Albuterol or levalbuterol (Xopenex[®]) ± ipratropium (Atrovent[®]).**
3. **Hypertonic saline (3 to 10%) – may be used in-line with Aerobika[®]**
4. **HFCWO-vest – can be used with saline & airway clearance devices.**
5. **DNase (Pulmozyme[®]), if ordered.**
6. **Inhaled steroids (Flovent[®], Pulmicort[®], Q-var[®]) or combined inhaled steroids + long-acting bronchodilator (Symbicort[®], Advair[®], Dulera[®]).**
7. **Long-acting bronchodilators (Serevent[®], Foradil[®], Spiriva[®]).**
8. **Inhaled antibiotics:**
 - Amikacin liposomal (Arikayce[®])
 - Tobramycin (TOBI[®])
 - Aztreonam (Cayston[®])
 - Colistimethate sodium (Coly-Mycin[®]) or Colistin

Appendix 13 – Gastro-esophageal reflux disease (GERD)

- **Definition:** reflux of stomach contents into the esophagus and possibly higher.
- **Significance:** reflux can damage the esophagus as well as cause aspiration of stomach contents into the lungs.
- Normally, the lower esophageal sphincter (LES) closes off the lower esophagus when one is not swallowing. In GERD, the LES is weak and allows reflux.



- Proton pump inhibitors only decrease acid production by the stomach but does not prevent GER.
- Because GERD is more likely to occur in the supine or head/torso down positions, sleep at $\geq 30^\circ$ head-of-bed elevation and avoid positions where the head is below the mid chest.
- **Drugs that can worsen GERD:** albuterol, oxybutynin, diphenhydramine (Benadryl[®]), tricyclic antidepressant, calcium channel blockers, nitrates, opioids, progesterone, quinidine, benzodiazepines, and theophylline.
- **Foods that can worsen GERD:** coffee, chocolate, caffeine, alcohol, peppermint, garlic, onions, fatty-spicy foods, alcohol (especially red wine), citrus fruits, tomatoes.

Appendix 13 – GERD (continued)

- **Risks of PPI** (proton pump inhibitor; e.g., Aciphex[®], Nexium[®], Prevacid[®], Prilosec[®], Protonix[®])
 - **Association likely causative:** hypomagnesemia, vitamin B12 deficiency, and small intestine overgrowth.
 - **Possible association:** osteoporosis-related bone fractures, pseudomembranous colitis, acute and chronic kidney disease, and dementia.
 - **Speculative but plausible:** Potentially increase growth or survival of swallowed NTM, which may then be refluxed and aspirated.
- **Surgery for severe GERD:** the two following websites will provide an introduction to the available procedures. Patients are advised to get at least two expert opinions on their pros and cons as well as talking to patients who have undergone such procedures.
 - **Linx Reflux Management** – <https://www.massgeneral.org/digestive/services/procedure.aspx?id=2305> (must highlight, copy, & paste onto Search Browser)
 - **Nissen fundoplication** – https://en.wikipedia.org/wiki/Nissen_fundoplication (must highlight, copy, & paste onto Search Browser)

Appendix 14 – Medicare

- **Medicare Part A** – hospital insurance
 - Inpatient care.
 - Short-term Medicare-approved skilled nursing care (not custodial or long-term care).
 - Home Health Care, Hospice.
- **Medicare Part B** – durable medical equipment, preventive and diagnostic services
 - Durable medical equipment (O₂).
 - Many preventative services (e.g., vaccines and prescription drugs like transplantation anti-rejection medications).
- **Medicare Part C** – aka Medicare Advantage
 - Are managed care plans typically administered by HMO or PPO, allowing them to deliver Medicare benefits under their umbrella and contracting network.
 - This can result in cost savings, but generally restricts patients to in-network services and providers (*i.e.*, HMO is usually strictest and PPO a bit more choice).
 - Combines Medicare A, B and D into a managed care plan.
- **Medicare Part D** – prescription drug coverage
 - Without a Part D plan, patients are responsible for the total cost of all drugs.
 - Plans vary greatly with different co-pays and deductibles to be met.
 - Sometimes covers vaccines.
 - Part D covers infusion drug costs, while Part B covers infusion services.

Appendix 15 – Top Ten Recommendations to prevent or treat NTM lung infection

1. Avoid aerosols of soil and water.
2. Raise hot water heater temperature to 130°F and flush yearly.
3. Do airway clearance religiously.
4. Take measures to prevent GERD.
5. If underweight, eat healthy fatty foods.
6. Avoid cigarette smoke exposures.
7. Keep vitamin D levels at good levels & keep active.
8. Take antibiotics as directed.
9. Join NTM support group to get advice and emotional support. Educate yourself as much as possible about NTM infection from providers, other NTM patients, support group leaders, your own readings, and from on-line information provided by NTMir®.
10. Find **medical professionals with expertise, enthusiasm, and patience** to treat NTM lung disease.

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