How and when to treat patients with infections due to *Mycobacterium abscessus* and other nontuberculous mycobacteria (NTM)

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Nontuberculous mycobacteria

- NTM are environmental, opportunistic pathogens, found in soil and water
- The number of recognised new species† is increasing rapidly
- The incidence of NTM as human pathogens is rising*
- Of the >150 NTM species reported and isolated from humans, some 25 species are strongly associated with a variety of human diseases
- NTM pulmonary disease (NTM-PD) is the most frequent disease manifestation
- Different NTM species cultured from clinical specimen differ in their clinical relevance but also differ strongly by region#

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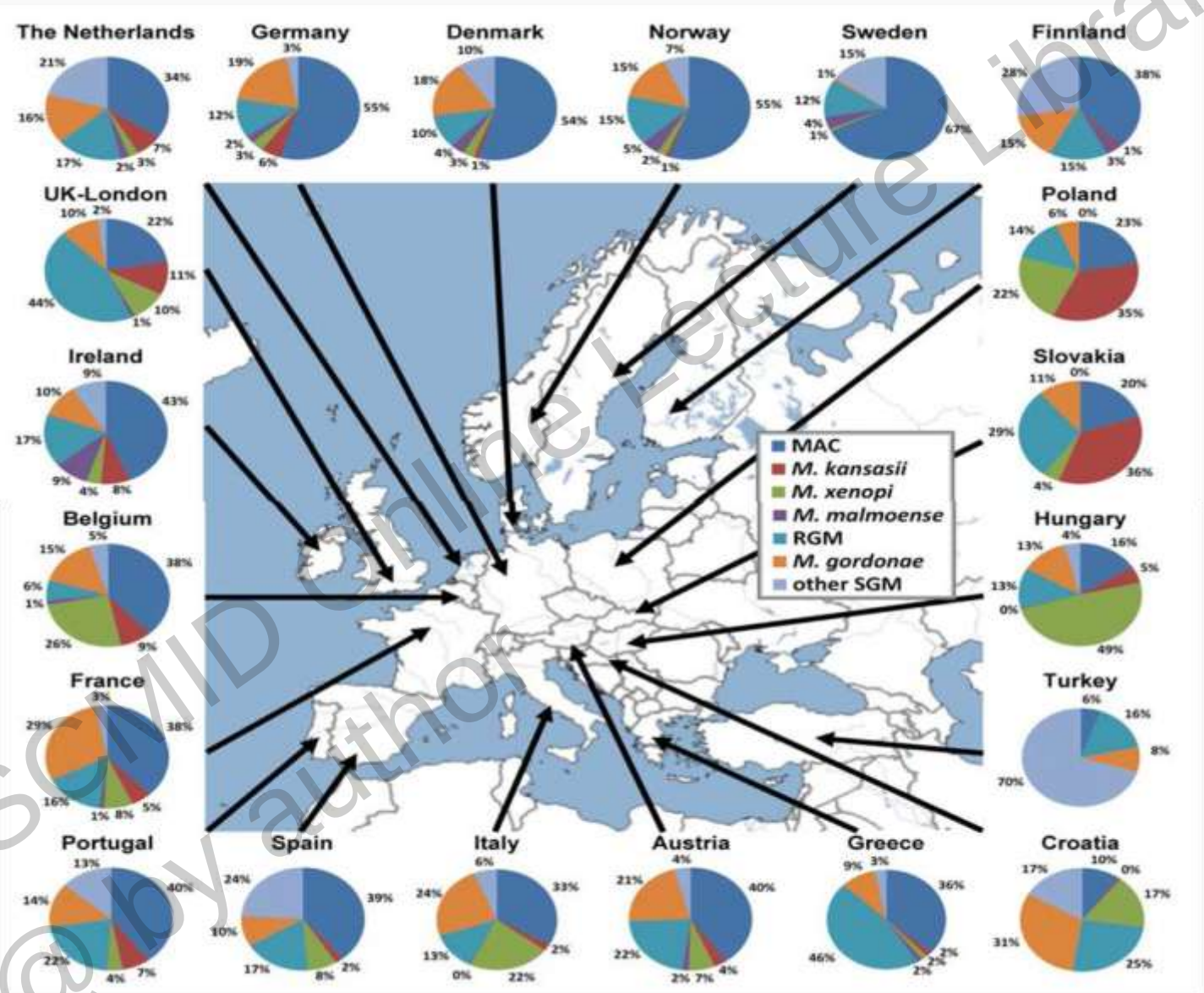
NTM species distribution differs by region



NTM species cultured from respiratory samples

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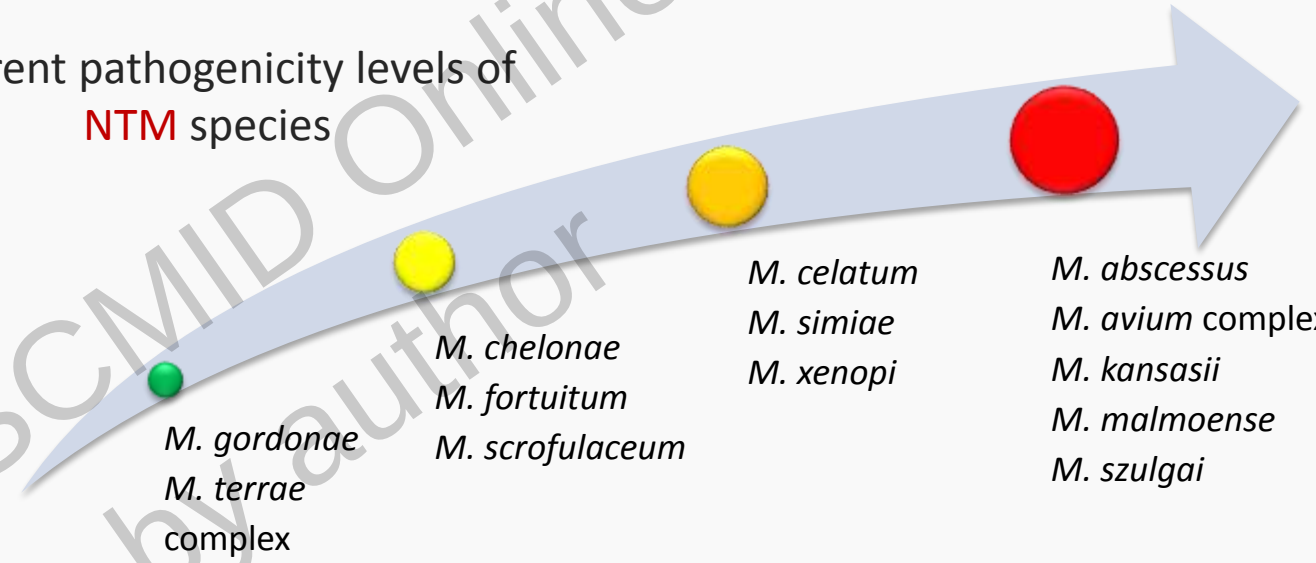
Is identification at the level of species useful for a clinician?

- NTM differ in their growth rate, temperature tolerance, and drug susceptibility
- NTM species differ in their clinical relevance[##] (especially important for interpretation of the relevance of NTM species recovered from a respiratory sample
- Some NTM are preferentially involved in specific pathologies

different pathogenicity levels of NTM species



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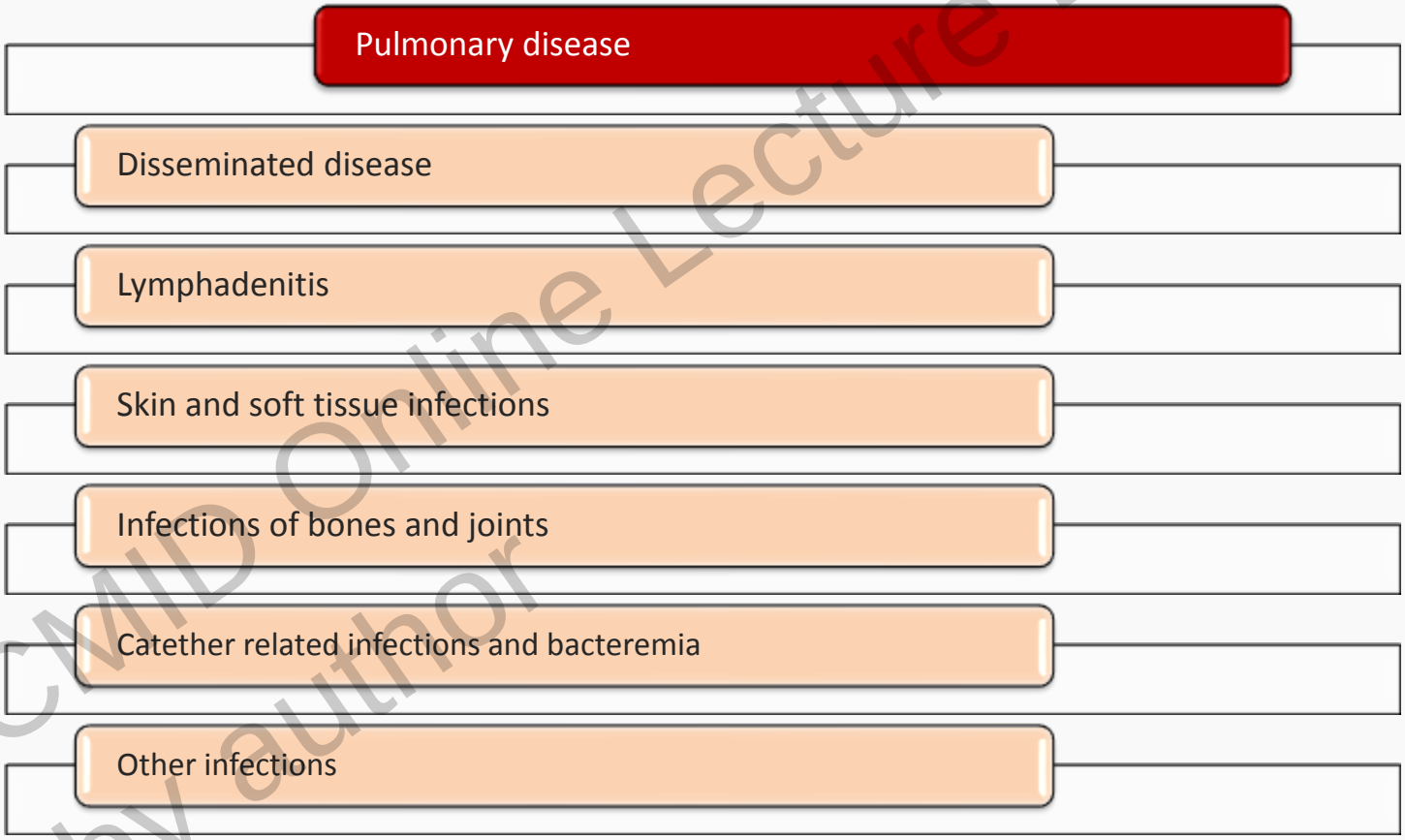
Disease manifestations of NTM infections

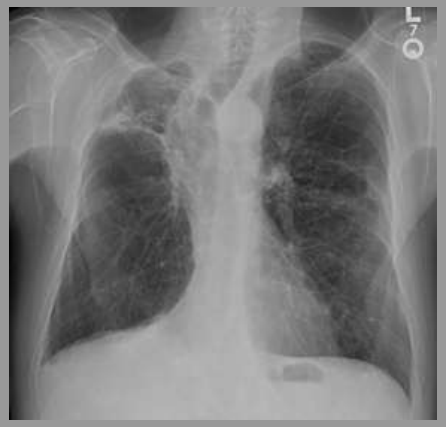


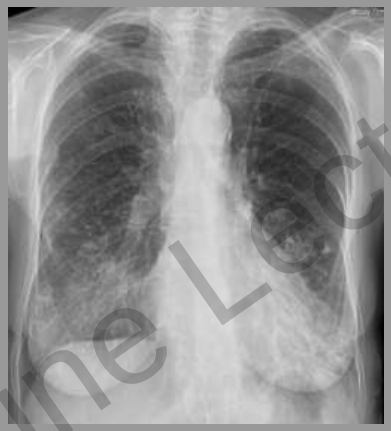
NTM-PD

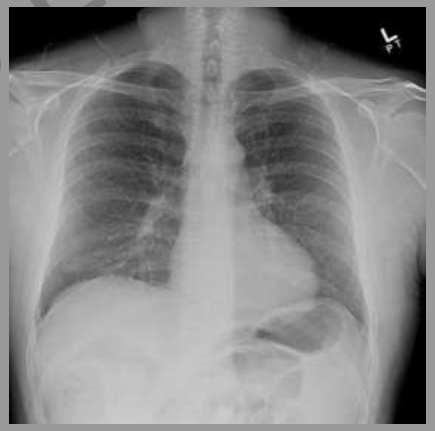
Fibrocavitary NTM-PD

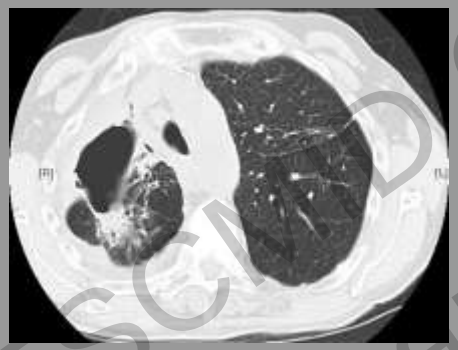
nodular/bronhiectatic NTM-PD

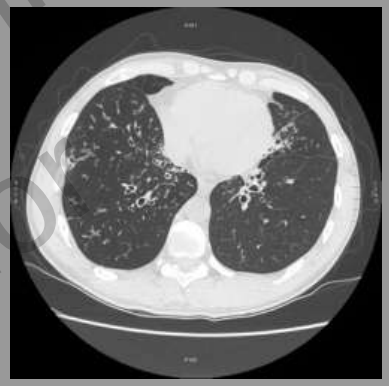
Hypersensitivity pneumonitis (Hot tub lung)

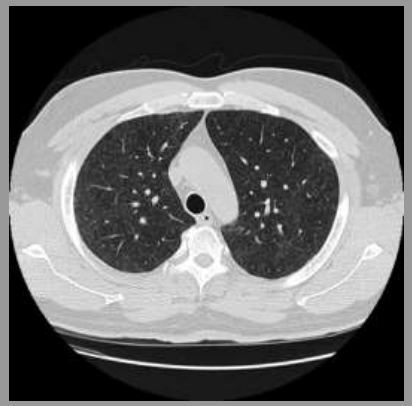












Most common causative agents: *M. avium* complex (MAC), followed by *M. kansasii, M. xenopi,* and *M. abscessus,* in area-specific order

Diagnostic criteria for NTM-PD

- American Thoracic Society (ATS) - originally published in 1997; revised in 2007.
- General guidelines mainly based on the most common NTMs (MAC, *M. abscessus*)
- Critical issue: since the NTM are widespread in the environment, a single isolation is usually NOT sufficient for diagnosis/initiation of therapy

ATS/IDSA (2007) diagnostic criteria :

clinical (presence of respiratory symptoms and exclusion of other diagnoses) **AND**

radiological (cavitations and/or nodules with/withouth bronchiectasies) **AND**

microbiological (2 or more (+) sputum cultures or a (+) culture from at least one bronchial wash or lavage or (+) sputum culture and biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB)

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Diagnostic dilemmas

- Over-rigorous criteria might delay or prevent the diagnosis
- Too lenient criteria could result in often unnecessarilly long, potentially toxic and expensive therapy

- Possible solution - use separate, more stringent criteria for NTM species of low relevance, and less stringent criteria for species considered to be of high clinical relevance in the local setting
- This approach requires complete and up to date insight in locally prevalent NTM and their clinical relevance

Treatment guidelines

- Basic principle - use multiple drugs to increase efficacy and to prevent acquired resistance
- Guidelines* suggest standard regimens based on accurate identification of species, but
- Treatment of NTM-PD still has a very limited evidence base, and the efficacy of currently recomended treatment regimens differ strongly between studies which may be related to the relative frequency of cavitary disease and/or duration of the follow-up
- Duration:
  - according to the guidelines*: at least 12 months from sputum conversion
  - varies widely by patient, disease severity and tolerance to medications
  - average duration is 12-24 months
  - RGM infections (especially due to *M. abscessus*) may require intermittent treatment across lifetime
- Surgery has limited role in specific circumstances

*Griffith DE et al. Am J Respir Crit Care Med 2007; 175:367-416.

Treatment recommendations

American Thoracic Society

- *M. avium* complex — RIF-EMB-macrolide (+/- aminoglycoside) >12 mo
- *M. kansasii* — INH-RIF-EMB 12 mo
- *M. xenopi* — RIF-EMB-macrolide-moxifloxacin?
- *M. simiae* — Macrolide-moxifloxacin-cotrimoxazole-…?
- *M. abscessus* — 3-4 of amikacin, cefoxitin/imipenem, macrolide*, linezolid, tigecycline
- With **surgical debulking** whenever feasible

Treatment duration

- Pulmonary disease: 12 months after culture conversion

Griffith DE, et al., *Am J Respir Crit Care Med* 2007

Treatment dilemmas

- Even with the firm diagnosis of NTM-PD, the question remains:

to treat or not to treat?

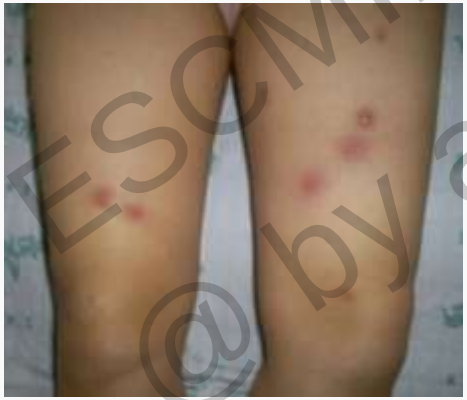
- Generally slowly progressive disease
- Most of the patients are elderly and have several co-morbidities
- Therapy is complex, of long duration and often expensive and toxic
- Compliance is often poor
- Different NTM species have different level of pathogenicity

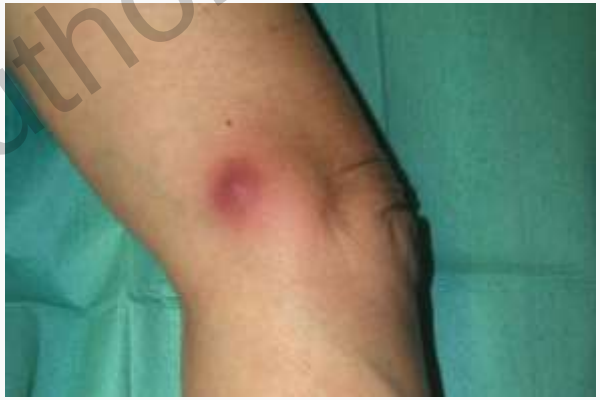
The decision should me made with taking into account the severity and the type of the disease (cavitary/fibronodular?), level of immuno-supression, NTM species identified, and cost/ benefit ratio for an individual patient

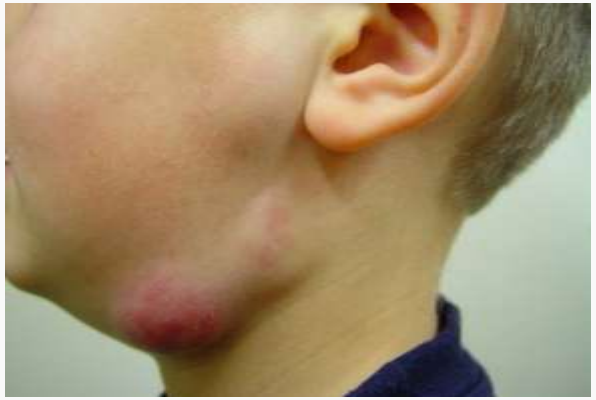
Other NTM disease manifestations

- Disseminated disease
- Lymphadenitis
- Skin and soft tissue infections
- Infections of bones and joints
- Catether related infections
- Other infections

- Establishing diagnosis is usually more straightforward compared to NTM-PD
- Treatment: according to the guidelines for a specific disease form and identified NTM species
- Surgery has a role in the treatment of certain disease manifestations







Key points

- The incidence of NTM isolation and NTM diseases is rising
- NTM species differ in their clinical relevance and geographical distribution, and identification at species level is of a great importance for a clinician
- NTM-PD is the most frequent disease manifestation
- The outcomes of treatment differ between species, and NTM-PD caused by *M. abscessus, M. xenopi* and *M. simiae* have particulary poor outcomes.
- The management strategy of NTM-PD is faced with several diagnostic and/or treatment dilemmas
- Available treatment recommendations have limited evidence base, and the efficacy of currently recomended treatment regimens differs strongly between studies
- We need high-quallity clinical trials to progress in treating these infections

Q & A

- .....

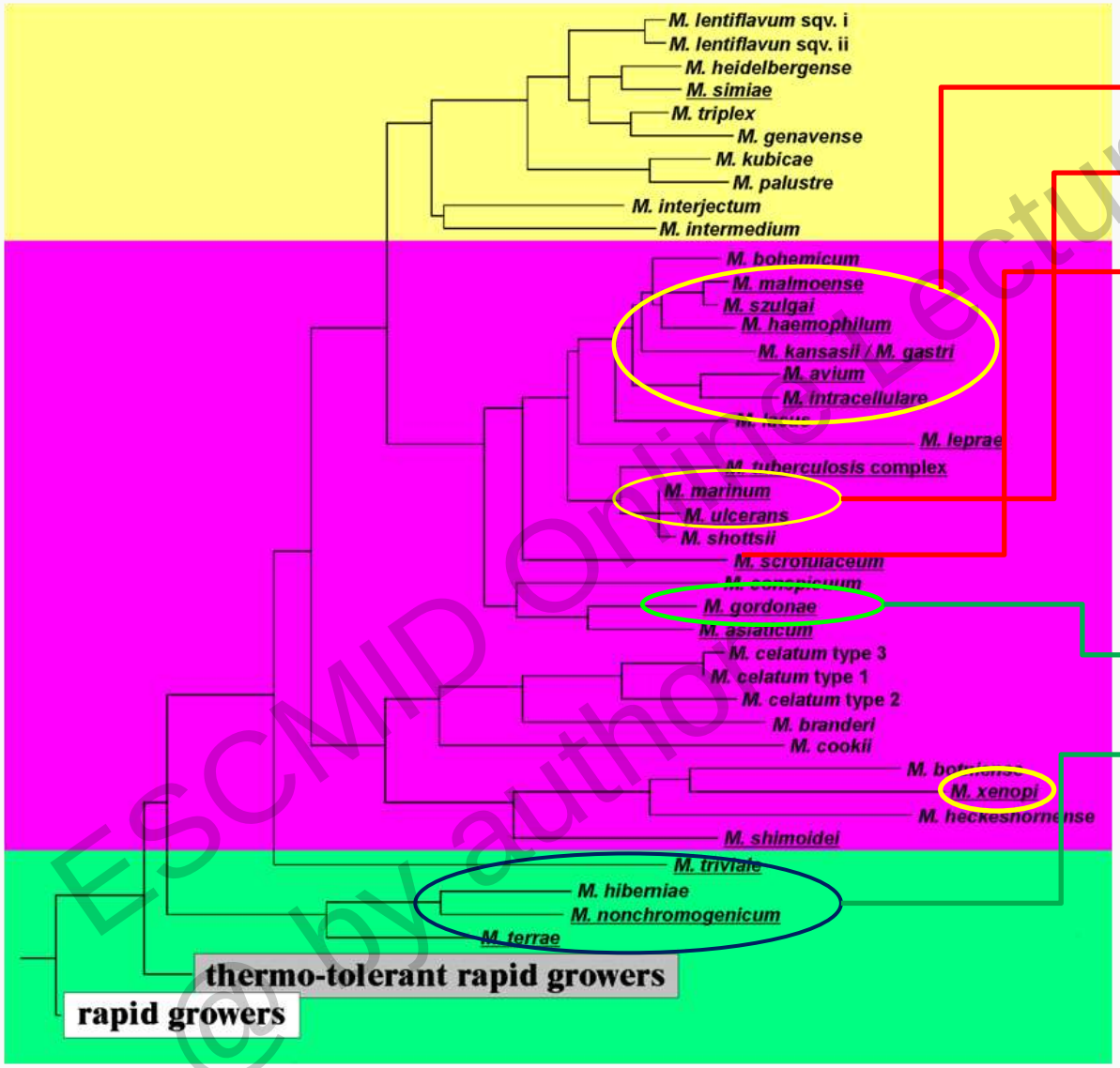
Nontuberculous mycobacteria

- Nontuberculous mycobacteria (NTM) – encompass all mycobacteria except *M. tuberculosis* complex (MTC) and *M. leprae*
- NTM synonyms – environmental mycobacteria, atypical mycobacteria, mycobacteria other than tuberculosis
- NTM are environmental, opportunistic pathogens, found in soil and water
- NTM are adapted for residence in drinking water distribution systems as they are disinfectant-resistant, surface adherent, and able to grow on low concentrations of organic matter

Nontuberculous mycobacteria

- NTM differ in their growth rate, temperature tolerance, and drug susceptibility, making the correct species identification important
- NTM are not susceptible to isoniazid and pyrazinamide
- Different species present variable susceptibility to macrolides, quinolones, aminoglycosides, rifamycins
- The distinction between rapidly growing mycobacteria (RGM) and slowly growing mycobacteria (SGM) is clinically relevant since they have different susceptibility patterns
- the distinction between chromogenic and nonchromogenic species is not clinically relevant “per se”

Slowly growing mycobacteria (SGM)



Most commonly encountered SGM species that are usually clinically relevant

Most commonly encountered SGM species that are usually NOT clinically relevant

Rapidly growing mycobacteria (RGM)

Most commonly encountered RGM species that usually are clinically relevant

Nontuberculous mycobacteria

- The incidence of NTM as human pathogens is rising*
- The number of recognised new species† is increasing rapidly - on average 3 new species/year described in the last two decades
- Of the >150 NTM species reported and isolated from humans, some 25 species are strongly associated with a variety of human diseases
- No (or rare**) inter-human transmission
- Different NTM species cultured from clinical specimen, but also a clinical relevance of a particular NTM species, differ strongly by region#

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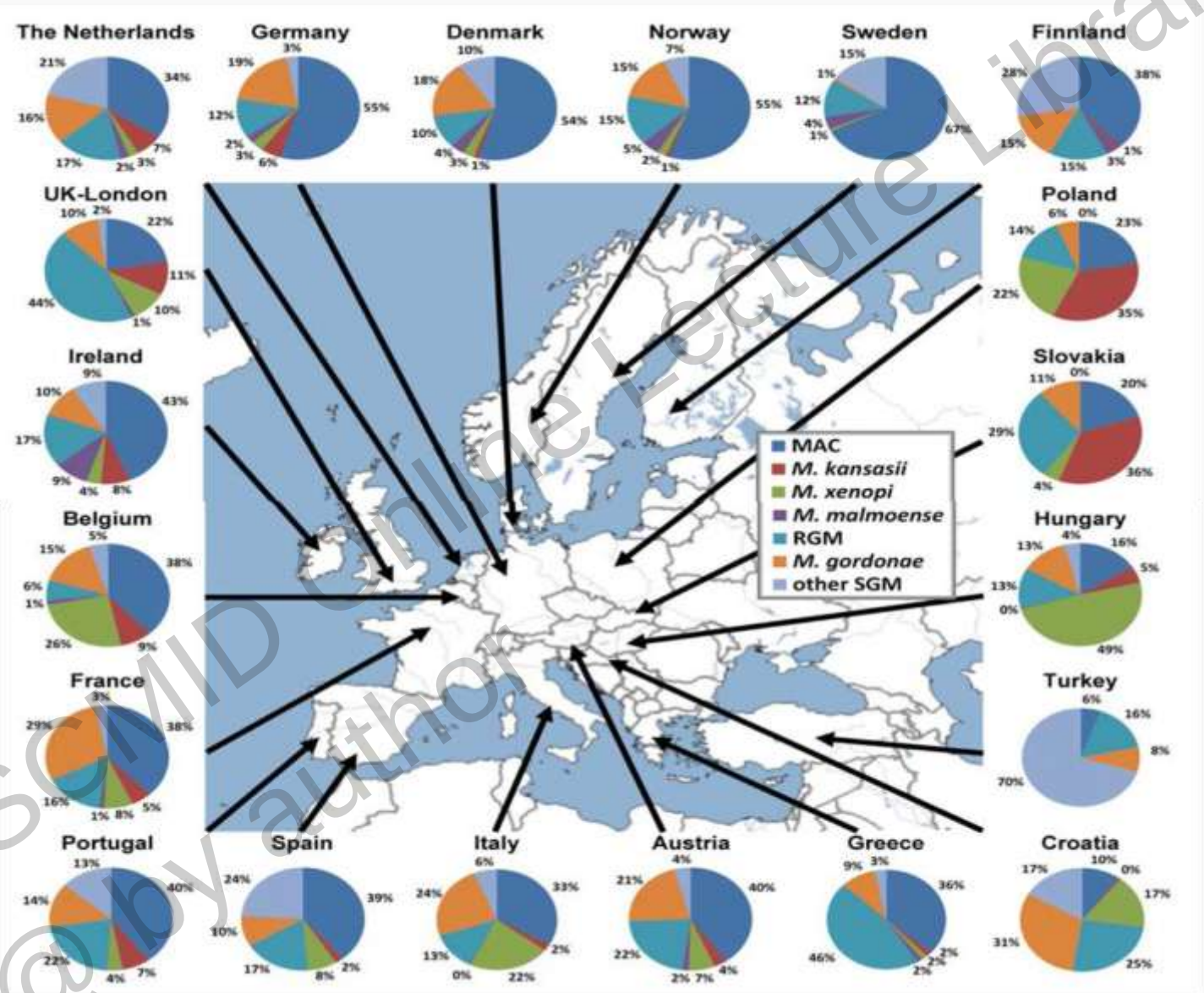

NTM species cultured from respiratory samples

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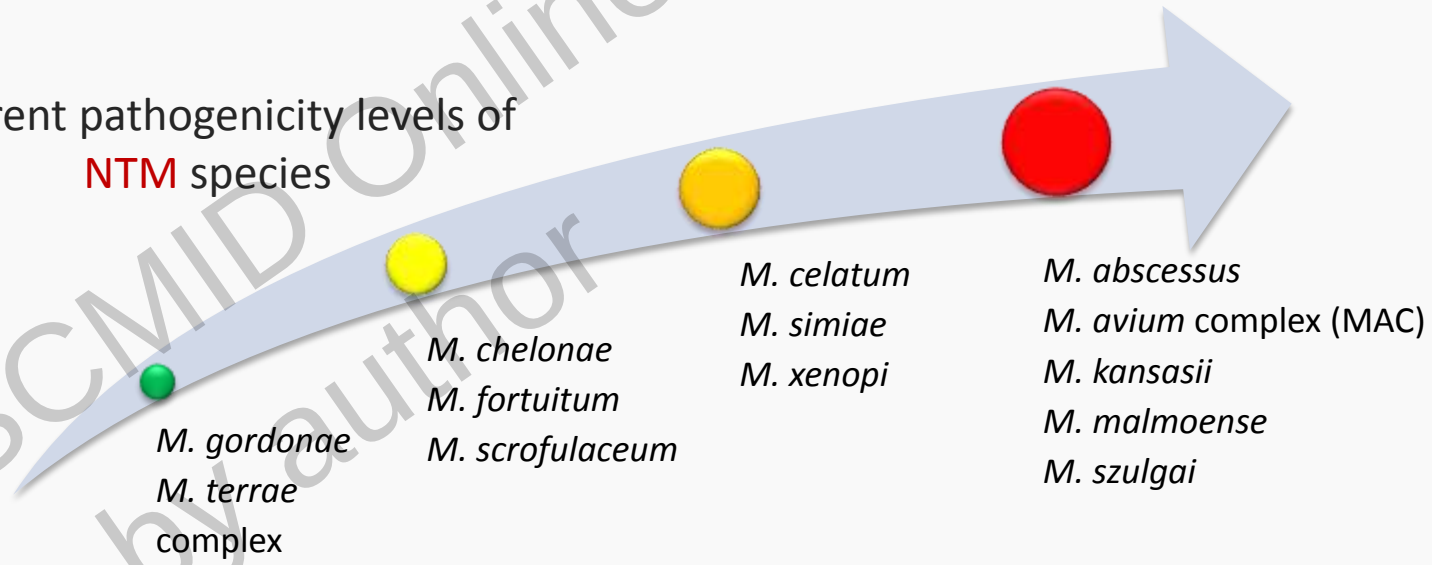
Is identification at the level of species useful for a clinician?

- NTM species differ in their clinical relevance[##]
- This is especially important when interpreting the relevance of NTM species recovered from a respiratory sample
- Some NTM are preferentially involved in specific pathologies
- Various NTM are characterized by different susceptibility pattern

different pathogenicity levels of NTM species



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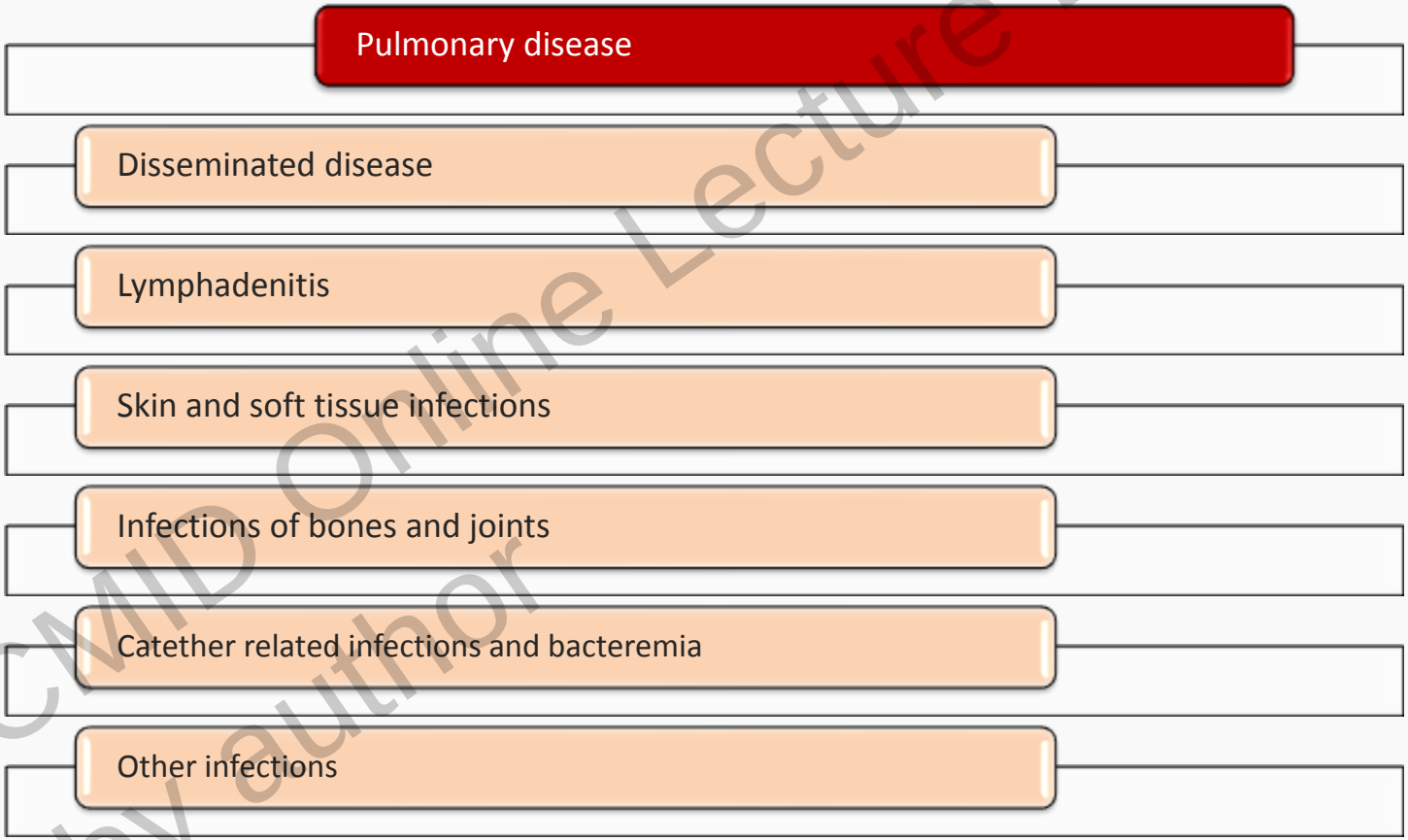
Clinical manifestations of NTM infections



NTM pulmonary disease (NTM-PD)

- most frequent manifestation of NTM infection
- occurs commonly in structural lung disease (COPD, bronchiectasis, CF, prior TB,...), but
- also occurs in women without clearly recognized pre-disposing factors (The "Lady Windermere" disease), and
- (less often) occurs in a form of interstitial lung disease ("Hot-tub lung")

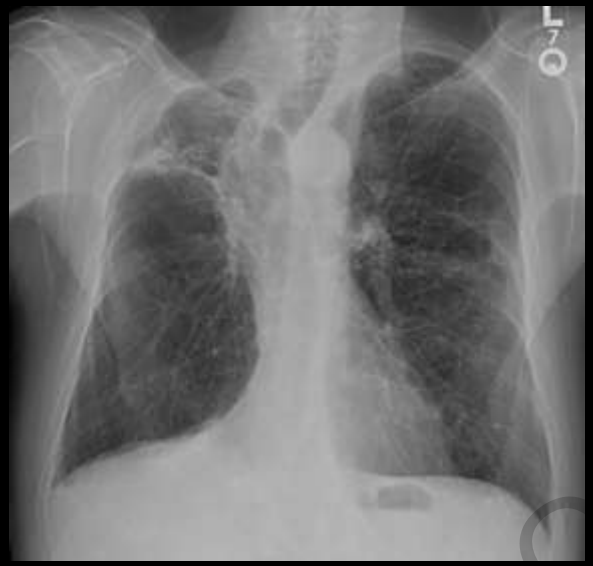
Symptoms – variable and nonspecific, but virtually all patients have chronic or recurring cough; evaluation is often complicated by symptoms caused by coexisting lung disease

Radiographic features – primarily fibrocavitary or nodular/bronhiectatic NTM-PD

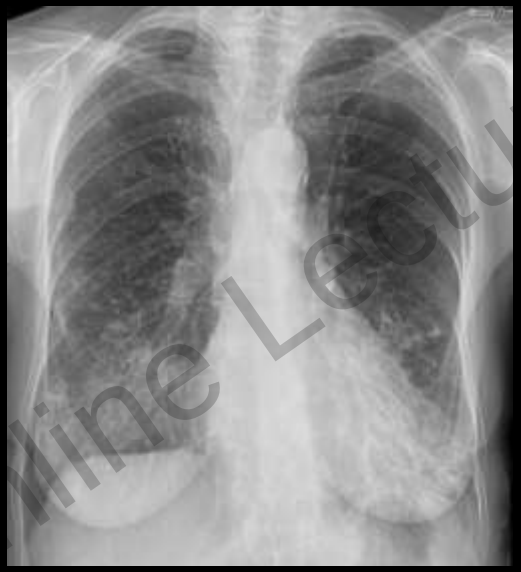
Mycobacterial cultures – Isolation of NTM in culture is essential for the diagnosis, BUT since NTM are ubiquitous enviromental pathogens, insignificant colonisation of respiratory tract and/or contamination of respiratory specimens occurs

Radiographic features

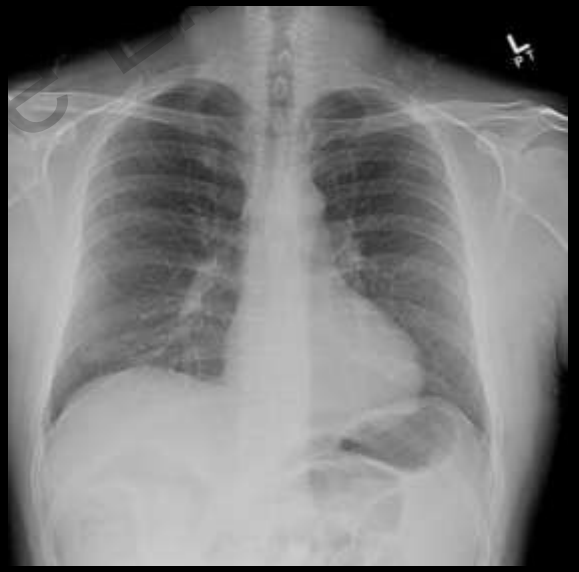
Fibrocavitary NTM-PD

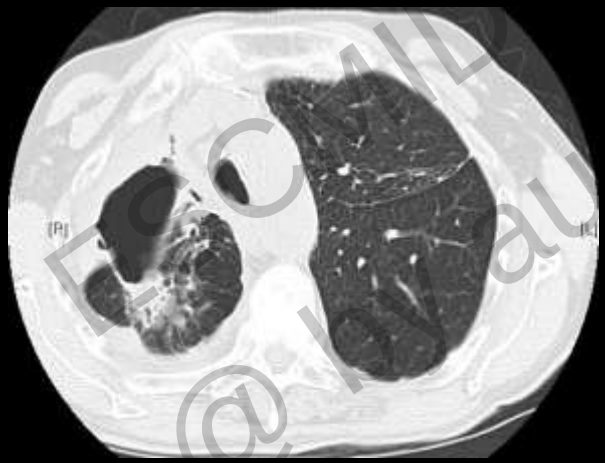


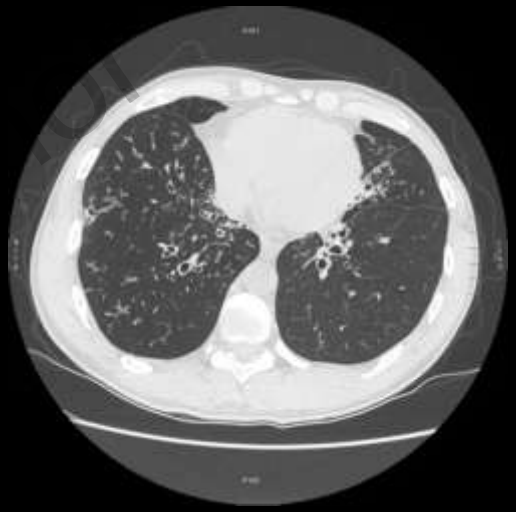
nodular/bronhiectatic NTM-PD

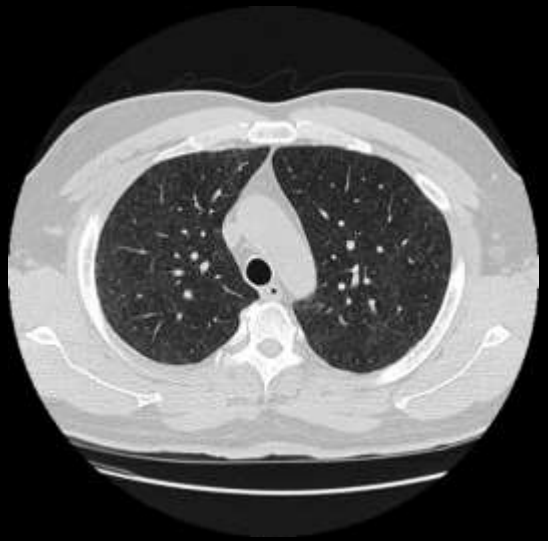


Hypersensitivity pneumonitis
(Hot tub lung)









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Diagnostic dilemmas

- Over-rigorous criteria might delay or prevent the diagnosis
- too lenient criteria could result in often unnecessarilly long, potentially toxic and expensive therapy
- it could be helpful to use separate, more stringent criteria for NTM species of low relevance, and less stringent criteria for species considered to be of high clinical relevance in the local setting
- i.e., isolation of *M. kansasii* (worldwide) and *M. malmoense* (north-western Europe) from pulmonary specimens usually indicates disease, whereas *M. gordonae and M. simiae* typically represent contamination
- This approach requires complete and up to date insight in locally prevalent NTM and their clinical relevance

Treatment guidelines

- Basic principle - use multiple drugs to increase efficacy and to prevent acquired resistance
- Guidelines* suggest standard regimens based on accurate identification of species, e.g. regimen "X" for *M. abscessus or* "Y" *for* MAC
- Surgery has limited role in specific circumstances
- Role of in vitro susceptibility testing is debated
  - consistent agreement for in vitro testing for macrolides in MAC
  - standard panel for RGM, such as *M. abscessus* or *M. chelonae*
- Duration:
  - according to the guidelines*: at least 12 months from sputum conversion (negativisation)
  - varies widely by patient, disease severity and tolerance to medications
  - average duration is 12-24 months
  - RGM infections (especially due to *M. abscessus*) may require intermittent treatment across lifetime

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Treatment dilemmas

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- Generally slowly progressive disease
- Most of the patients are elderly and have several co-morbidities
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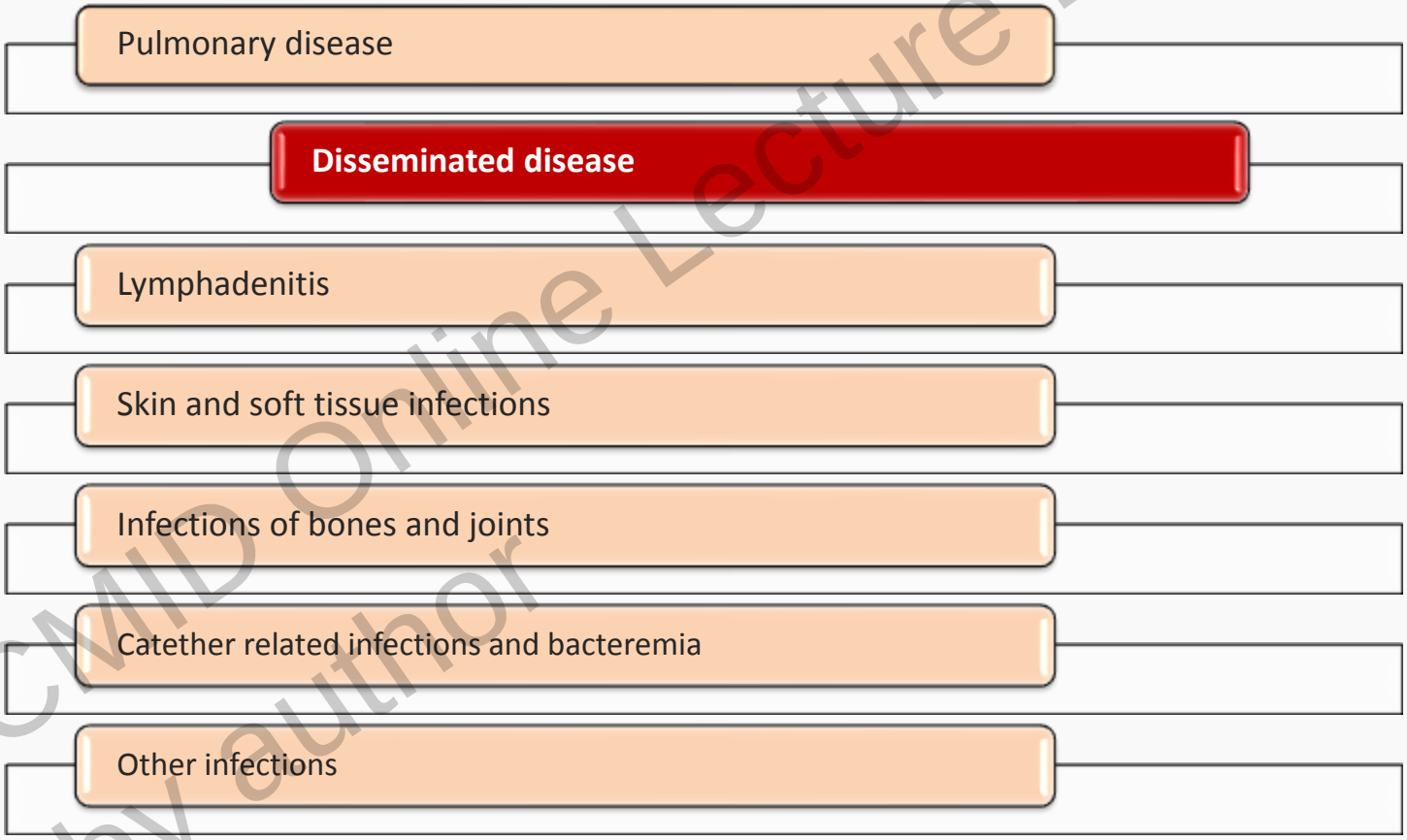
Clinical manifestations of NTM infections



Disseminated NTM disease (DNTM)

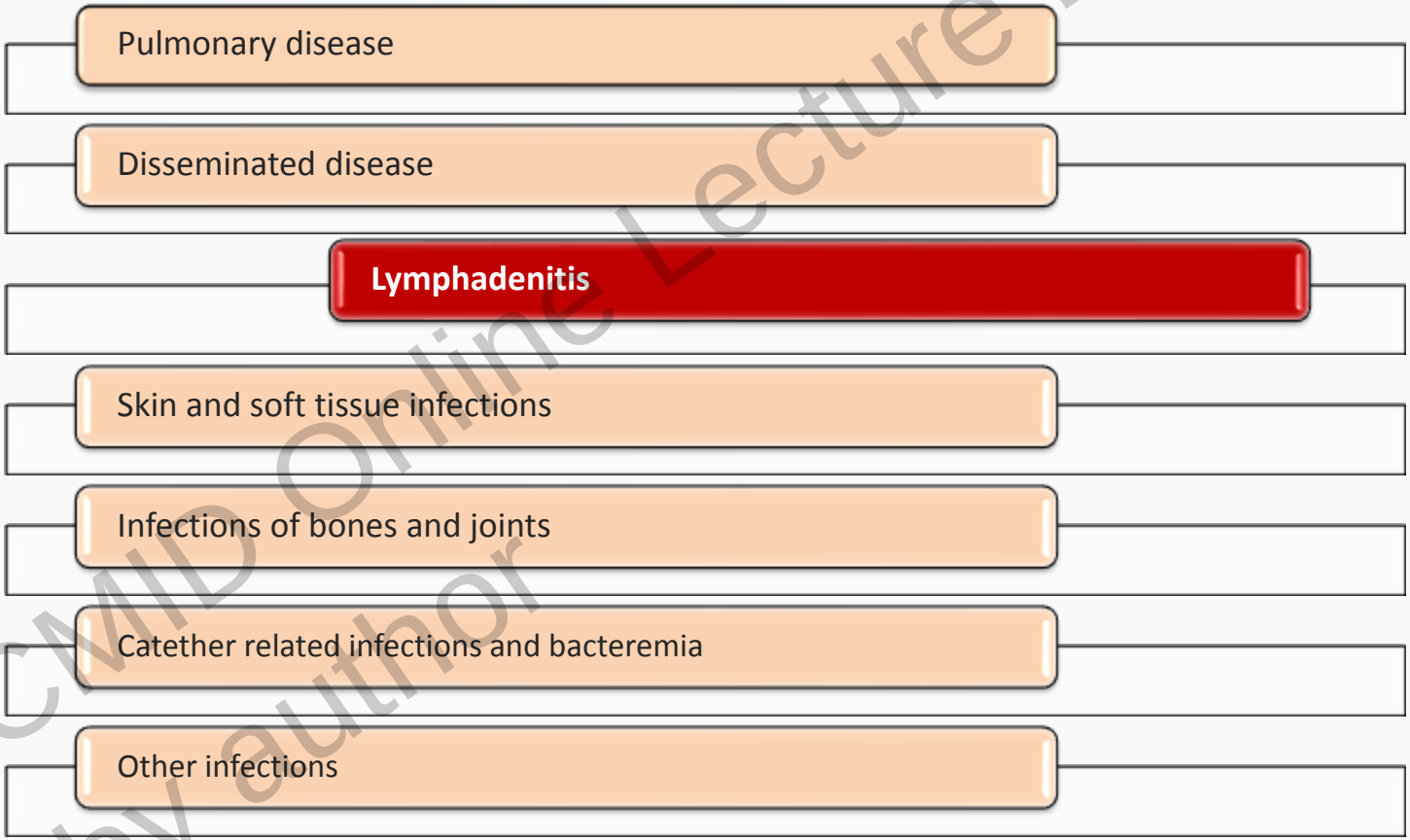
- Most commonly seen in immunocompromised patients
- At first – it was associated with MAC infection in patients with AIDS, but
- In immunocompromised patients any NTM infection can potentially be disseminated
- Most common NTM species causing DNTM: MAC, *M. chelonae*, *M. fortuitum*
- Diagnosis is based on identification of NTM (especially when it involves primary sterile sites) and treatment is mandatory

Regimen/duration of therapy depends on causative NTM species and disease severity

Treatment of disseminated MAC follows ATS guidelines for MAC-PD

Current recommendation for disseminated disease due to RGM:
in vitro susceptibility testing to determine the optimal drug treatment;
treatment with parenteral agents in combination with a macrolide in the initial phase (2 to 6 week course) followed by an additional 2 – 6 months regimen of one or two oral agents.

Clinical manifestations of NTM infections

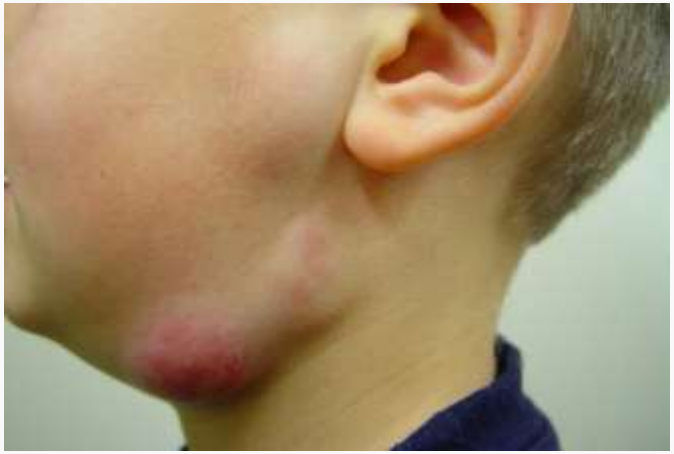


NTM lymphatic disease

- The most common form of NTM disease in childern
- In the absence of HIV infection, NTM lymphadenitis rarely affects adults
- Most common causative organisms: MAC, *M. scrofulaceum*, *M. malmoense*, and *M. haemophilum*
- Definite diagnosis: recovery of the causative organism from lymph node culture
- A large number of NTM lymph adenitis remain negative in culture; especially in the case of fastidious species like *M. haemophilum* and *M. malmoense*

Treatment:

for most cases of localised lymphadenitis (due to any NTM species) in immunocompetent patients – **complete surgical excision** of the involved lymph nodes



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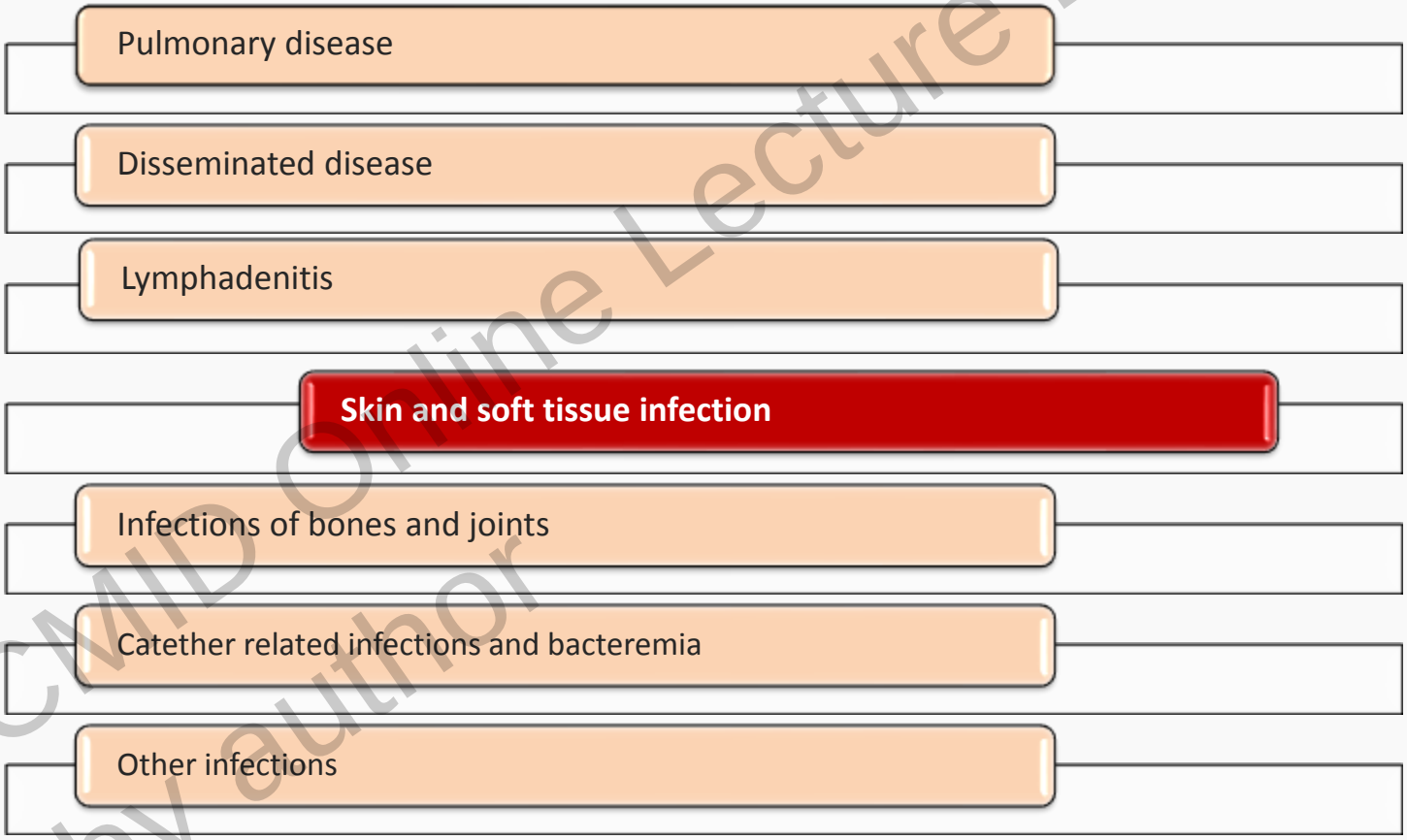
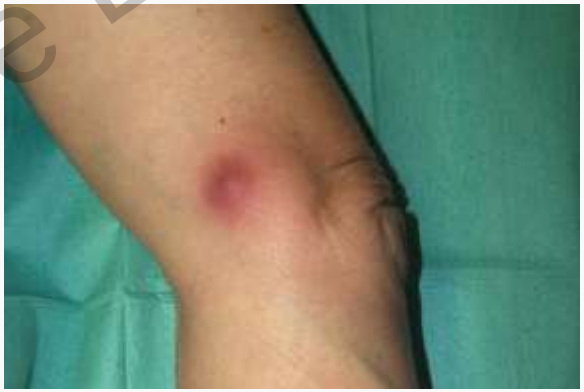


Skin and/or soft tissue disease

Most common causative species: *M. marinum* (causes "swimming pool" or "fish tank" granuloma), RGM *(M. abscessus, M. chelonae, M. fortuitum)*

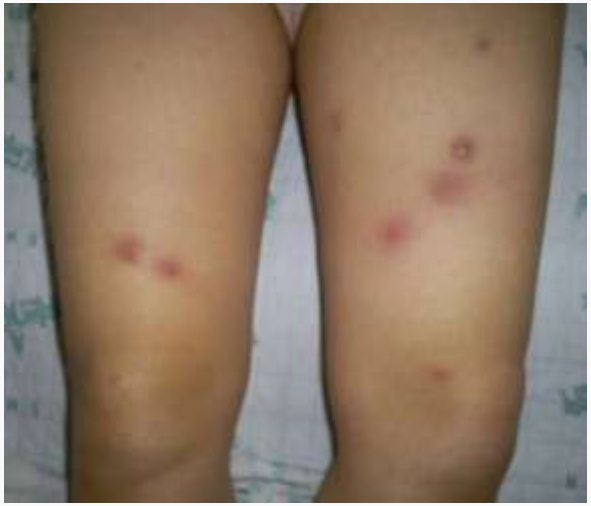
Diagnosis: recovery of the causative organism +/- typical histological features



Treatment
combination of two active agents up to 1 to 2 months after resolution of simptoms/lesions

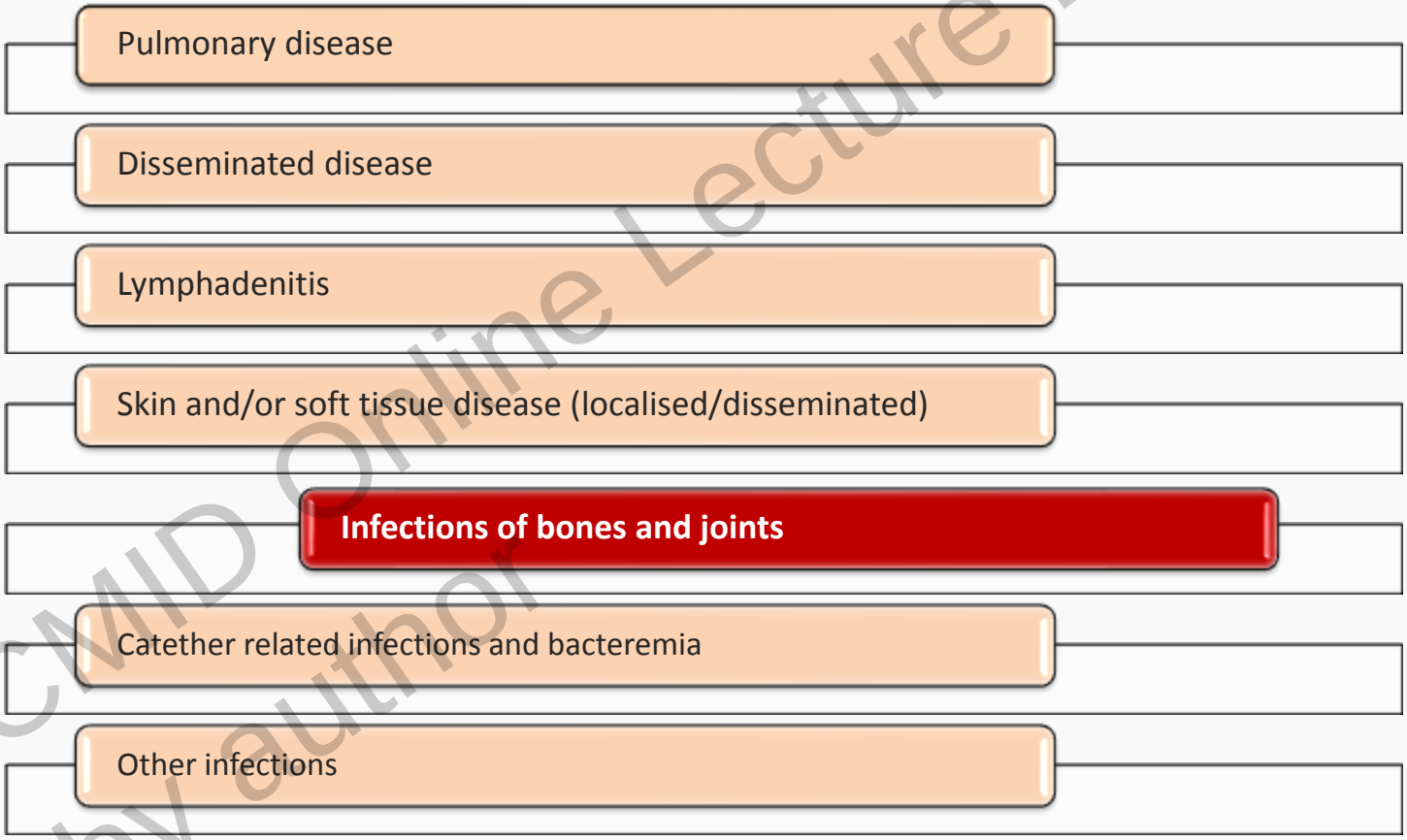
infections should be treated according to the guidelines for the specific species involved; in vitro susceptibility testing is often necessary (in the case of RGM, and especially *M. abscessus)*

surgical debridement may be important adjunctive therapy depending on the extent of the disease



Disseminated skin infection – usually part of the disseminated disease
Treatment - according to the guidelines for the disseminated dissease

Clinical manifestations of NTM infections



Infections of bones and joints

Synovia, tendon sheath, bones, inter-vertebral disks may be involved

Result from compound fractures, invasive traumas, surgical wounds (cardiac surgery in particular)

May involve almost any NTM species but *M. marinum*, *M. terrae* complex and RGM and are most commonly seen

M. marinum and *M. terrae* complex may cause chronic tenosynovitis, especially in the hand

Treatment - according to the NTM species involved

A minimum of 6 months of antimicrobial treatment is usually necessary

Surgical debridement – may be indicated in cases involving closed spaces of the hand or in cases of treatment failure

The optimal regimen for infections due to *M. terrae* complex is unknown; most experts agree that a macrolide-containing regimen similar to the MAC regimen is probably effective*; treatment often requires surgical debridement

*Smith DS et al. Clin Infect Dis 2000; 30:444-453.

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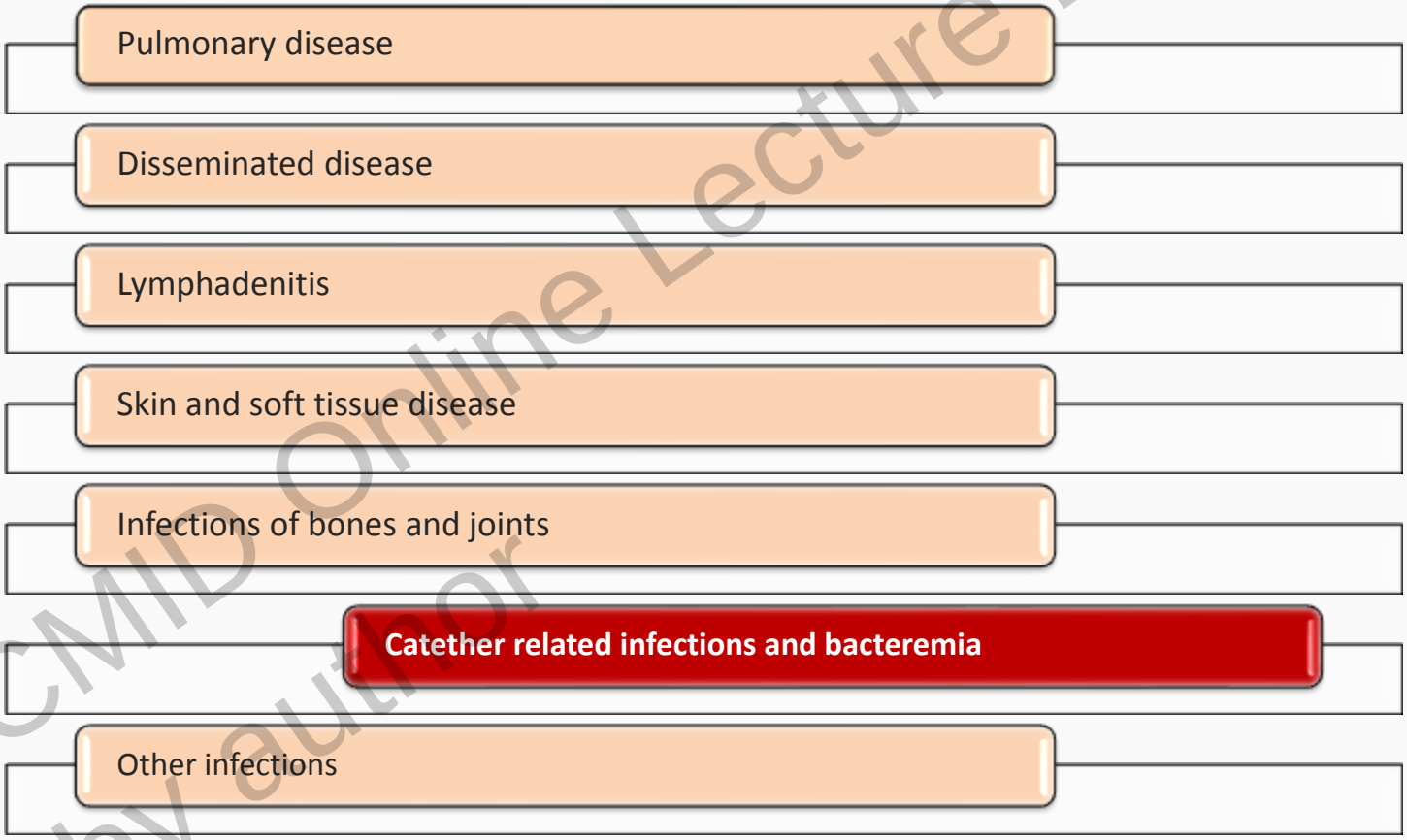

Catether related infections and bacteremia

- all **NTM** species can be associated with cathether infections and bacteremia
- typically associated with the use of long-term central venous catheters, hemodialysis shunts, peritoneal catheters, and ventriculoperitoneal shunts
- the most common health care-associated type of infection due to **RGM** in both immunocompetent and immunosuppressed patients*
- **RGM** are able to grow on blood cultures for common bacteria; with Gram staining, they may be confused with diphtheroid bacteria and considered cutis contaminants

Treatment

Removal of the infected catheter followed by antimicrobial treatment

Regimen and duration of antimicrobial treatment is based on guidelines**

for disseminated disease for individual **NTM** species

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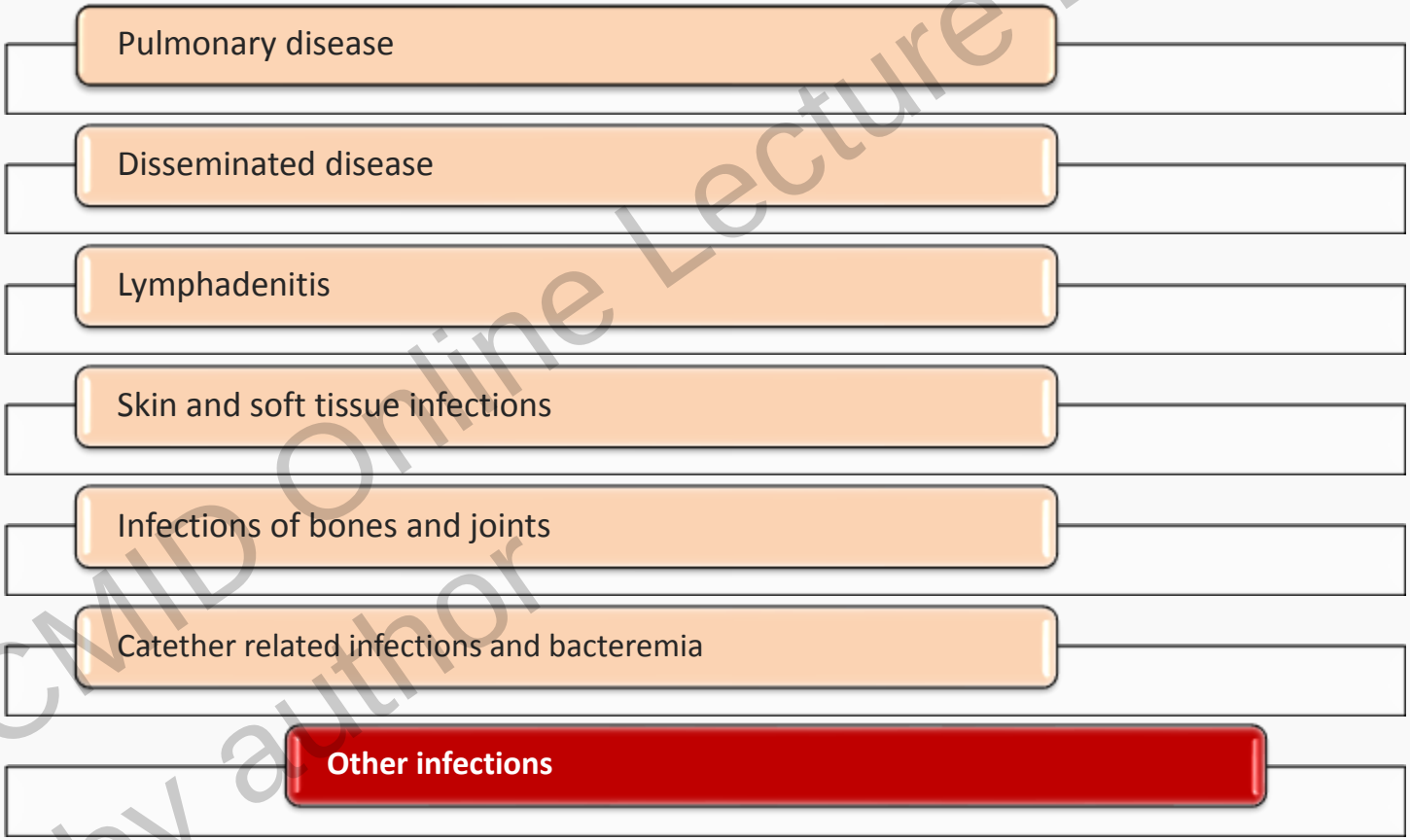

Other NTM infections

Otitis media

majority caused with *M. abscessus**;
risk factors include topical corticosteroid drops, placement of tympanostomy tubes and localised trauma

Treatment

antimicrobial treatment - three to four drugs (including parenteral drugs) in the initial 3 to 6 weeks phase followed by oral treatment for et least 6 months (based on in vitro susceptibility testing)

extensive debridement often required

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Ophtalmic infections

majority caused with RGMs**;
risk factors include the use of corticosteroids, immunosupression and LASIK and other ophtalmic procedures

Treatment

usually involves local instillation/topical treatment with antimicrobial agents according to recovered NTM species

infection is often refractory to treatment and lamelar keratectomy or penetraiting keratoplasty is often the last alternative

**Brown-Elliott BA et al. Cornea. 2012; 8:900-6.

Other NTM infections

CNS infection

majority of infections among both HIV and non-HIV infected patients is due to MAC;

Other species include *M. kansasii* and RGM

Overall high mortality

The most significant risk factors for RGM CNS infection – the presence of catheters and local trauma (including prior surgery)

Treatment

MAC CNS infection - clarithromycin, rimfapin and ethambutol penetrate the CNS well; recomended duration of therapy – at least 6 months; intrathecal therapy with aminoglycoside has been proposed, but no clinical studies have been performed

RGM CNS infection - most experts reccomend aggressive surgical debridement and treatment with antimicrobials (three to four drugs) based on species identification and in vitro susceptibility testing – duration of at least 6 months

Conclusions

- NTM are environmental, opportunistic pathogens that can cause a wide variety of human diseases
- The incidence of NTM isolation and NTM diseases is rising
- Identification at species level is of a great importance for a clinician
- In vitro susceptibility testing is generally not performed except in special, well defined cases
- The management strategy of pulmonary NTM disease is faced with several diagnostic and/or treatment dilemmas
- Diagnosis of other disease forms is simpler, but therapy is also prolonged, complex and of uncertain outcome
- Increasing the awareness and knowledge about these pathogens and diseases is essential for improving the care for patients

How and when to treat patients with infections due to *Mycobacterium abscessus* and other nontuberculous mycobacteria (NTM)

Mateja Jankovic Makek, MD, PhD

University Hospital Centre
Department for Respiratory Diseases
University of Zagreb, Croatia

ECCMID meeting, Copenhagen, April 25th – April 28th 2015

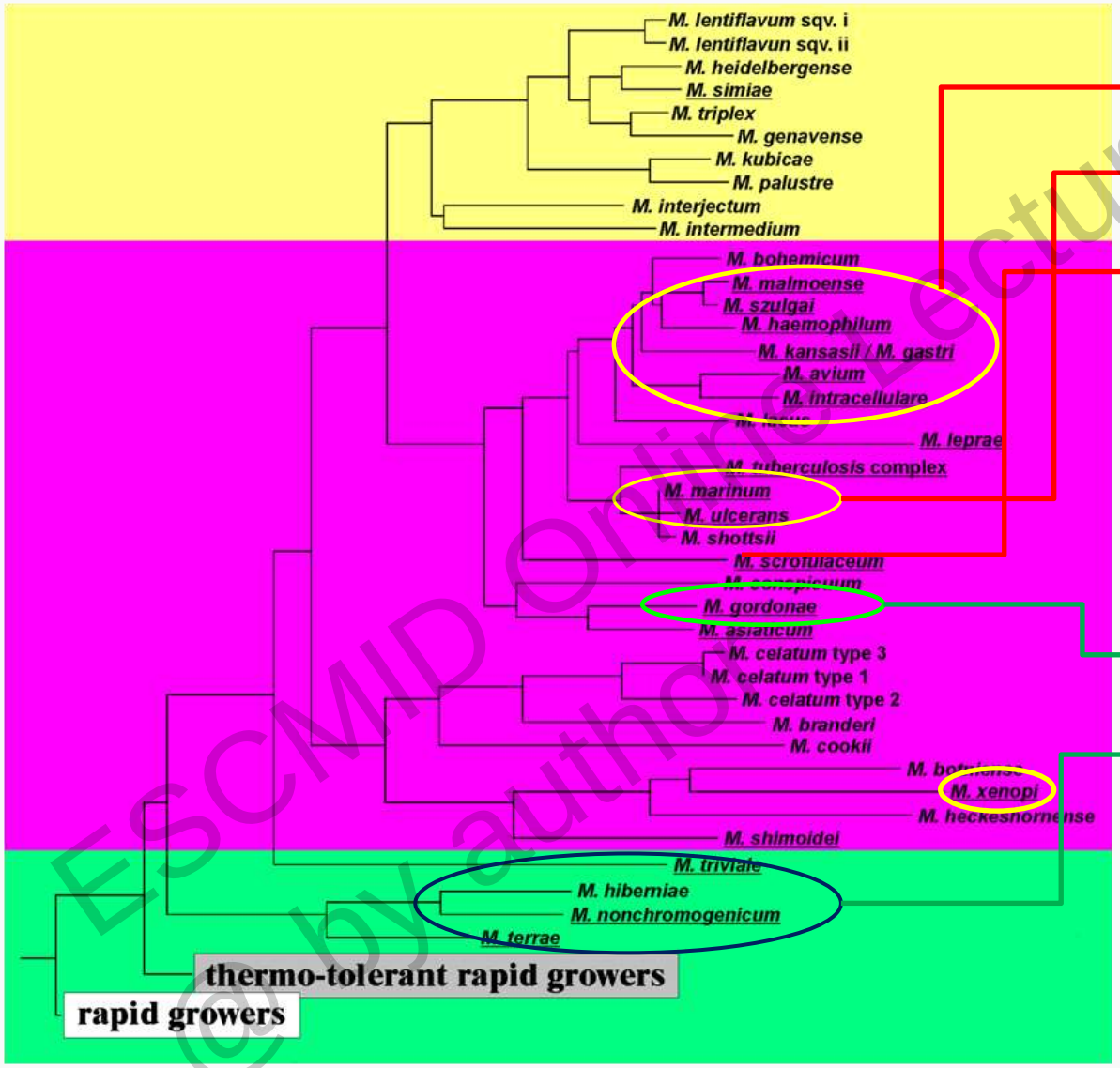
Nontuberculous mycobacteria

- Nontuberculous mycobacteria (NTM) – encompass all mycobacteria except *M. tuberculosis* complex (MTC) and *M. leprae*
- NTM synonyms – environmental mycobacteria, atypical mycobacteria, mycobacteria other than tuberculosis
- NTM are environmental, opportunistic pathogens, found in soil and water
- NTM are adapted for residence in drinking water distribution systems as they are disinfectant-resistant, surface adherent, and able to grow on low concentrations of organic matter

Nontuberculous mycobacteria

- NTM differ in their growth rate, temperature tolerance, and drug susceptibility, making the correct species identification important
- NTM are not susceptible to isoniazid and pyrazinamide
- Different species present variable susceptibility to macrolides, quinolones, aminoglycosides, rifamycins
- The distinction between rapidly growing mycobacteria (RGM) and slowly growing mycobacteria (SGM) is clinically relevant since they have different susceptibility patterns
- the distinction between chromogenic and nonchromogenic species is not clinically relevant “per se”

Slowly growing mycobacteria (SGM)



Most commonly encountered SGM species that are usually clinically relevant

Most commonly encountered SGM species that are usually NOT clinically relevant

Rapidly growing mycobacteria (RGM)

Most commonly encountered RGM species that usually are clinically relevant

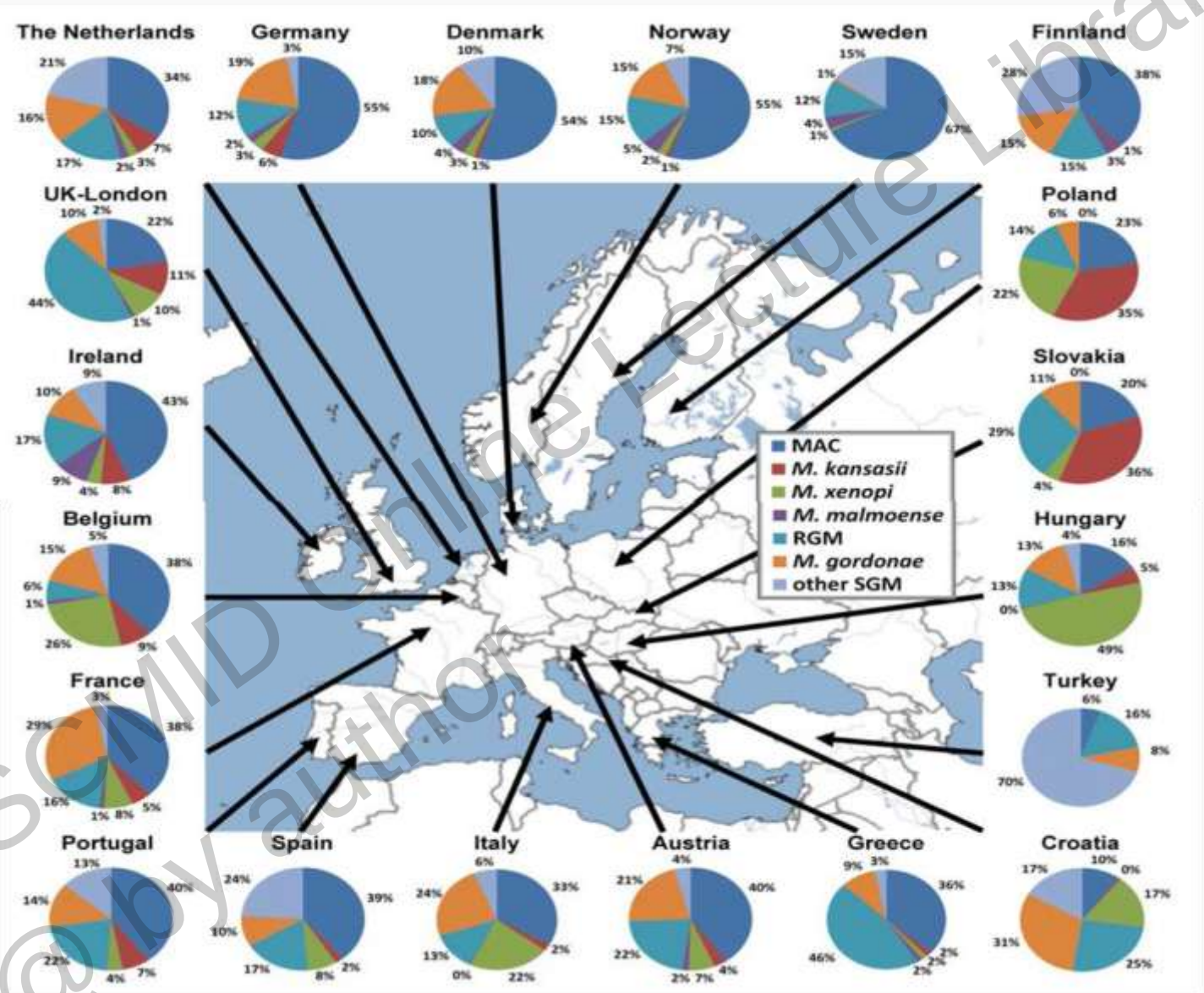
Nontuberculous mycobacteria

- The incidence of NTM as human pathogens is rising*
- The number of recognised new species† is increasing rapidly - on average 3 new species/year described in the last two decades
- Of the >150 NTM species reported and isolated from humans, some 25 species are strongly associated with a variety of human diseases
- No (or rare**) inter-human transmission
- Different NTM species cultured from clinical specimen, but also a clinical relevance of a particular NTM species, differ strongly by region#

*Behr MA et al. Future Microbiol 2009; 4:1009-20.
Griffith DE et al. Am J Respir Crit Care Med 2007; 175:367-416.
Hernandez-Garduno et al. Emerg Infec Dis 2010; 16:1047.
Maras TK et al. Thorax 2007; 8:661-6.
Van Ingen J et al. Int J Tuberc Lung Dis 2010; 14:1176-80.
Andrejak C et al. Am J Respir Crit Care Med 2010; 181:514-21.

†Tortoli E. Clin Microb Rev. 27(4):727-752.
**Aitken ML et al. Am J Respir Crit Care Med 2012; 185(2):231-2.
#Hoefsloot W et al. ERJ 2013; 42:1604-13.
Houben D et al. Cell Microbiol 2012;14(8):1287-98.
Grifith DE et al. Am J Respir Crit Care Med 2007;175:367-416.
Martin-Casabona N et al. 2004;8:1186-93.
Marras TK et al. Clin Chest Med 2002;23:553-67.

NTM species distribution differs by region



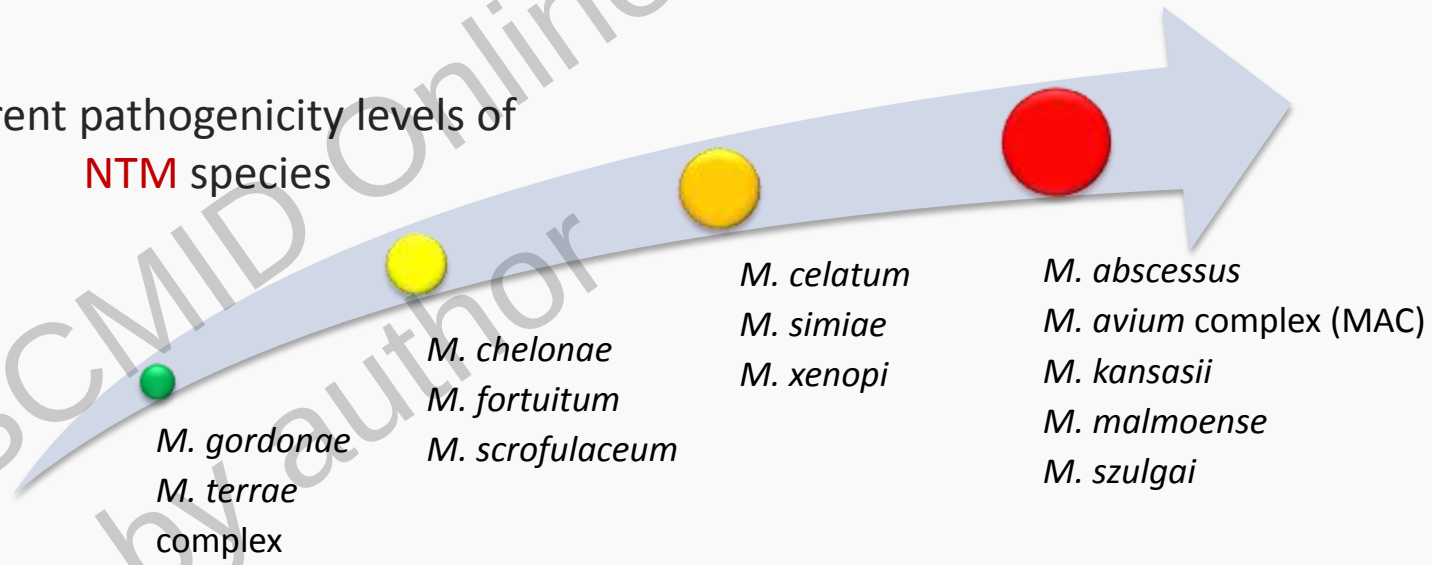
NTM species cultured from respiratory samples

Hoefsloot W et al. ERJ 2013; 42:1604-13.

Is identification at the level of species useful for a clinician?

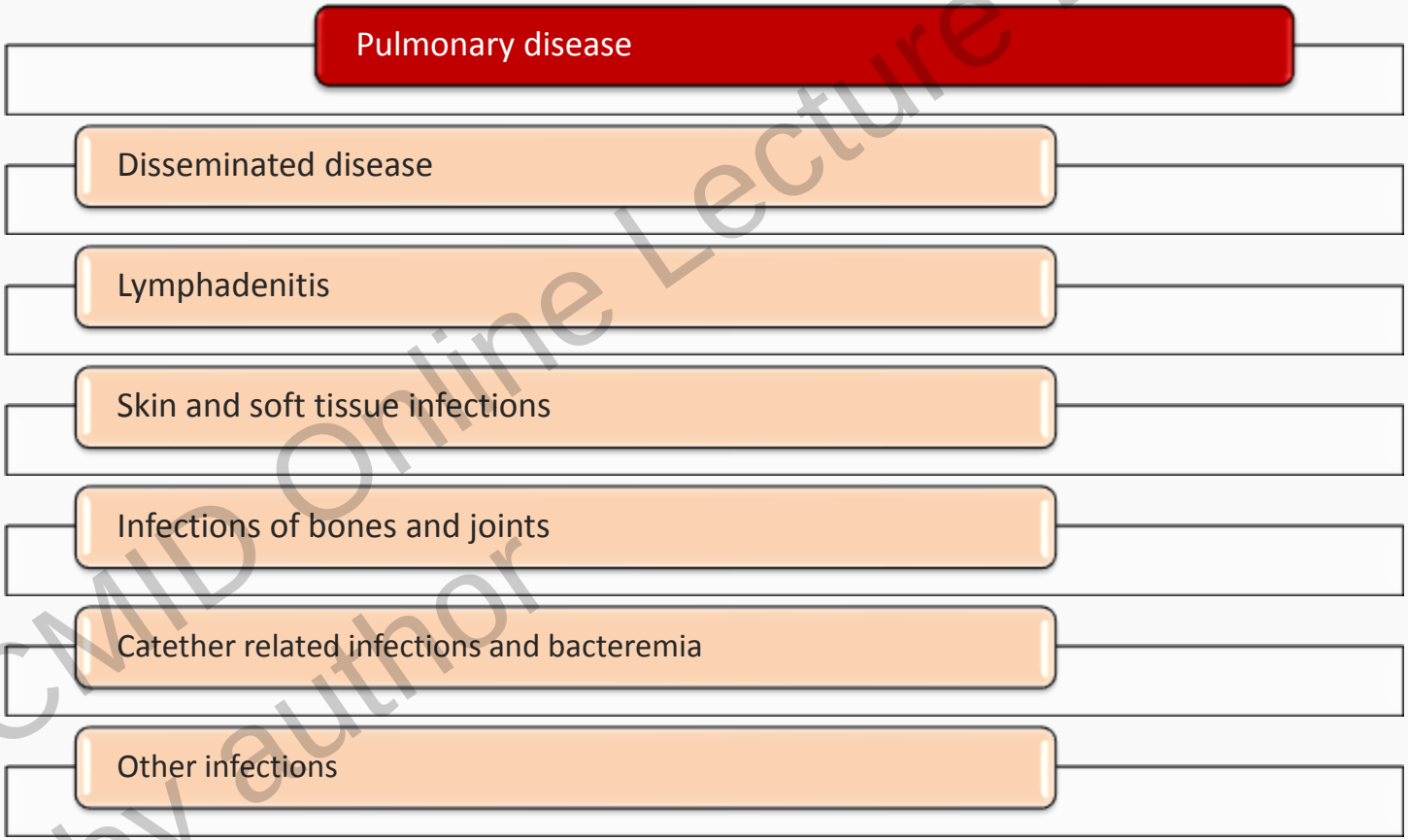
- NTM species differ in their clinical relevance[##]
- This is especially important when interpreting the relevance of NTM species recovered from a respiratory sample
- Some NTM are preferentially involved in specific pathologies
- Various NTM are characterized by different susceptibility pattern

different pathogenicity levels of NTM species



[##]Grifith DE et al. Am J Respir Crit Care Med 2007;175:367-416.
van Ingen J et al. Thorax 2009; 64:502-6.
Jankovic M et al. Int J Tuberc Lung Dis 2013; 17(6):836-841.

Clinical manifestations of NTM infections



NTM pulmonary disease (NTM-PD)

- most frequent manifestation of NTM infection
- occurs commonly in structural lung disease (COPD, bronchiectasis, CF, prior TB,...), but
- also occurs in women without clearly recognized pre-disposing factors (The "Lady Windermere" disease), and
- (less often) occurs in a form of interstitial lung disease ("Hot-tub lung")

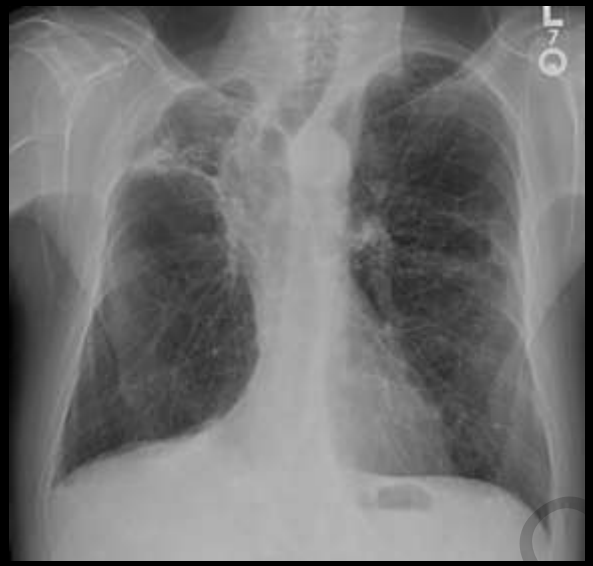
Symptoms – variable and nonspecific, but virtually all patients have chronic or recurring cough; evaluation is often complicated by symptoms caused by coexisting lung disease

Radiographic features – primarily fibrocavitary or nodular/bronhiectatic NTM-PD

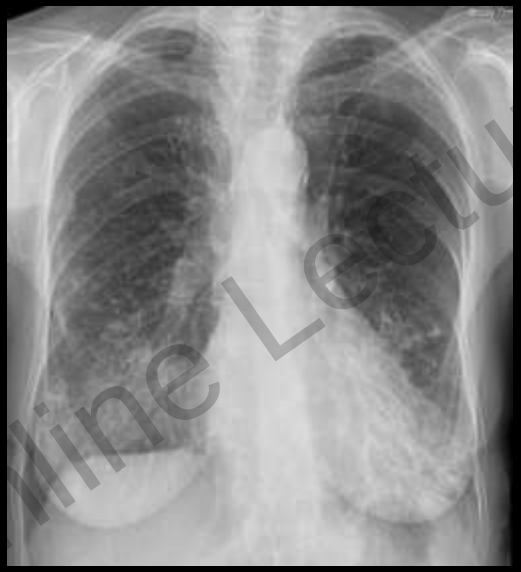
Mycobacterial cultures – Isolation of NTM in culture is essential for the diagnosis, BUT since NTM are ubiquitous enviromental pathogens, insignificant colonisation of respiratory tract and/or contamination of respiratory specimens occurs

Radiographic features

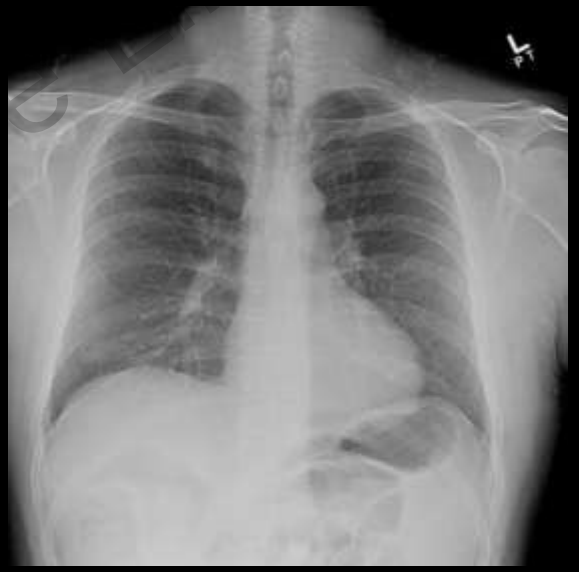
Fibrocavitary NTM-PD

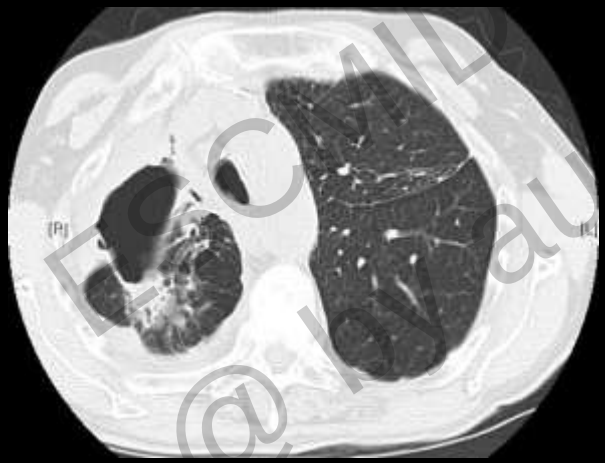


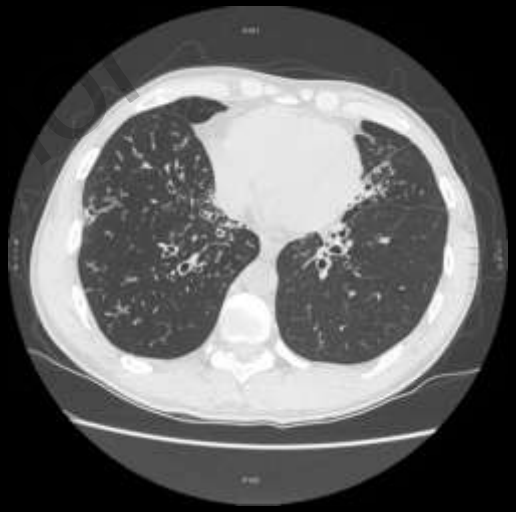
nodular/bronhiectatic NTM-PD

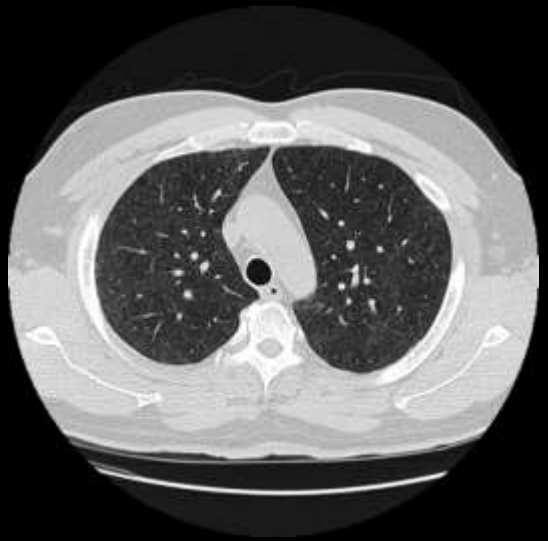


Hypersensitivity pneumonitis
(Hot tub lung)









Diagnostic criteria for NTM-PD

- American Thoracic Society (ATS) - originally published in 1997; revised in 2007.
- General guidelines mainly based on the most common NTMs (MAC, *M. abscessus*)
- Critical issue: since the NTM are widespread in the environment, a single isolation is usually NOT sufficient for diagnosis/initiation of therapy

ATS/IDSA (2007) diagnostic criteria :

clinical (presence of respiratory symptoms and exclusion of other diagnoses) **AND**

radiological (cavitations and/or nodules with/withouth bronchiectasies) **AND**

microbiological (2 or more (+) sputum cultures or a (+) culture from at least one bronchial wash or lavage or (+) sputum culture and biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB)

Griffith DE et al. Am J Respir Crit Care Med 2007; 175:367-416.

Diagnostic dilemmas

- Over-rigorous criteria might delay or prevent the diagnosis
- too lenient criteria could result in often unnecessarilly long, potentially toxic and expensive therapy
- it could be helpful to use separate, more stringent criteria for NTM species of low relevance, and less stringent criteria for species considered to be of high clinical relevance in the local setting
- i.e., isolation of *M. kansasii* (worldwide) and *M. malmoense* (north-western Europe) from pulmonary specimens usually indicates disease, whereas *M. gordonae and M. simiae* typically represent contamination
- This approach requires complete and up to date insight in locally prevalent NTM and their clinical relevance

Treatment guidelines

- Basic principle - use multiple drugs to increase efficacy and to prevent acquired resistance
- Guidelines* suggest standard regimens based on accurate identification of species, e.g. regimen "X" for *M. abscessus or* "Y" *for* MAC
- Surgery has limited role in specific circumstances
- Role of in vitro susceptibility testing is debated
  - consistent agreement for in vitro testing for macrolides in MAC
  - standard panel for RGM, such as *M. abscessus* or *M. chelonae*
- Duration:
  - according to the guidelines*: at least 12 months from sputum conversion (negativisation)
  - varies widely by patient, disease severity and tolerance to medications
  - average duration is 12-24 months
  - RGM infections (especially due to *M. abscessus*) may require intermittent treatment across lifetime

*Griffith DE et al. Am J Respir Crit Care Med 2007; 175:367-416.

Treatment dilemmas

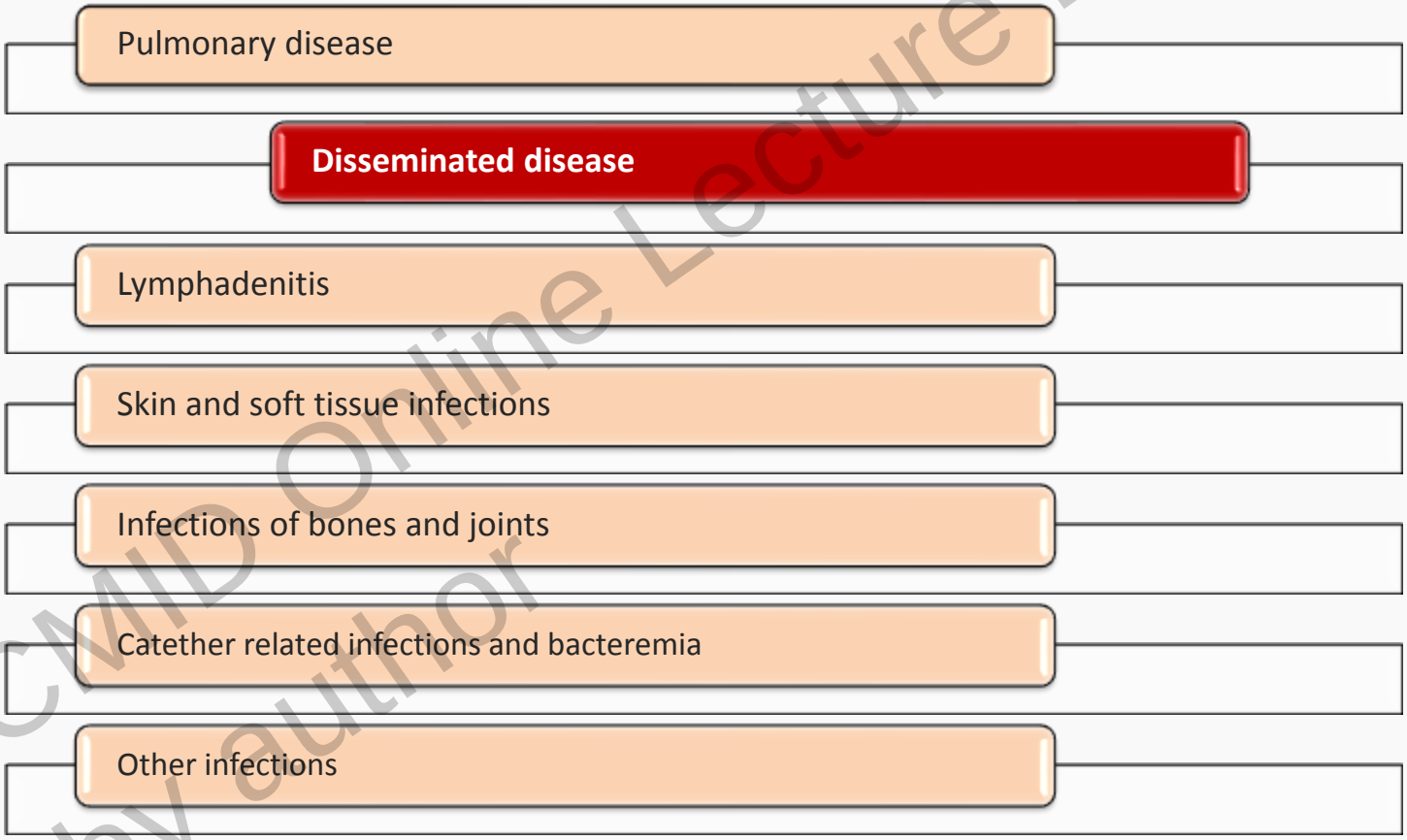
- Even with the firm diagnosis of NTM-PD, the question remains:

to treat or not to treat?

- Generally slowly progressive disease
- Most of the patients are elderly and have several co-morbidities
- Therapy is complex, of long duration and often expensive and toxic
- Compliance is often poor
- Different NTM species have different level of pathogenicity

The decision should me made with taking into account the severity and the type of the disease (cavitary/fibronodular?), level of immuno-supression, NTM species identified, and cost/ benefit ratio for an individual patient

Clinical manifestations of NTM infections



Disseminated NTM disease (DNTM)

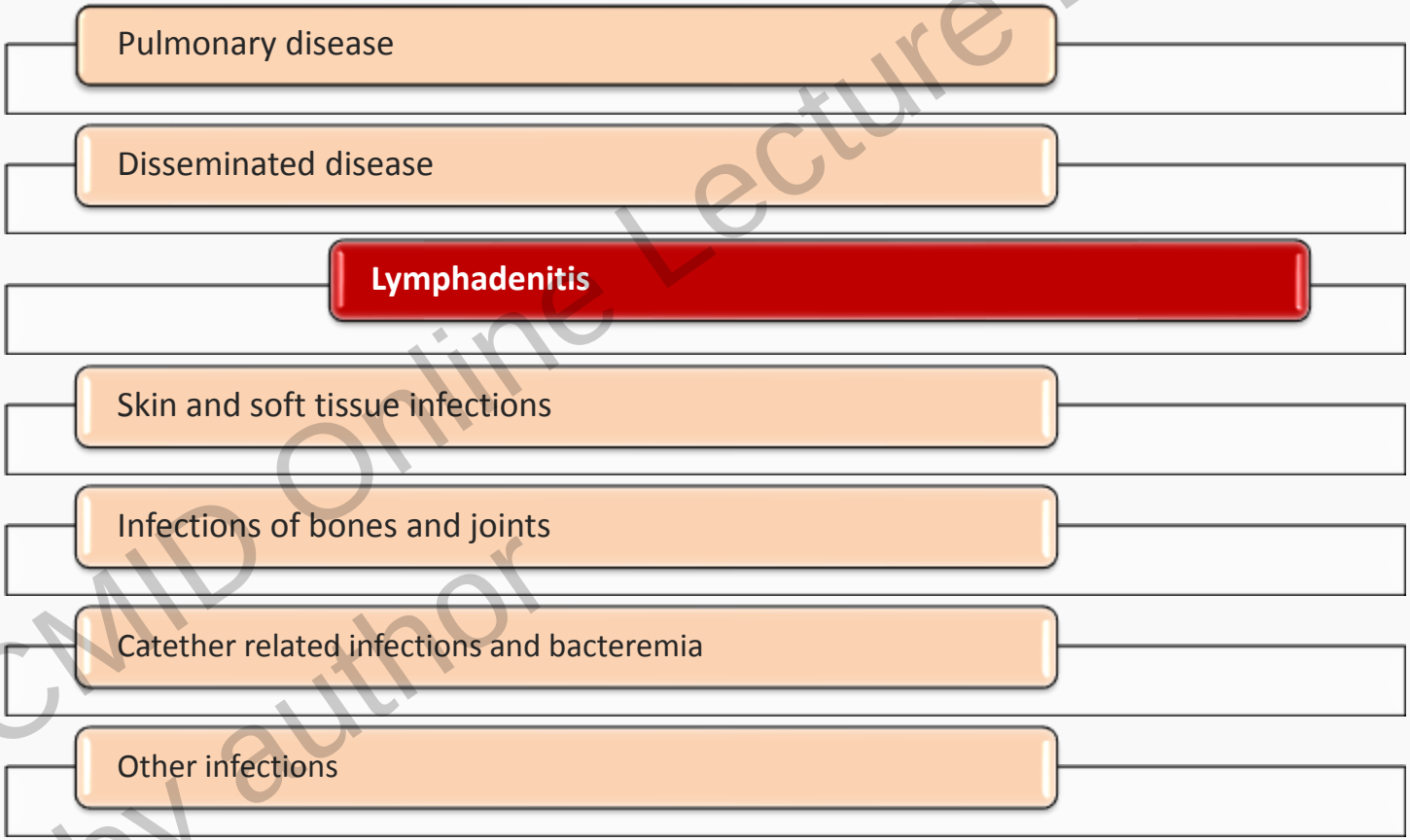
- Most commonly seen in immunocompromised patients
- At first – it was associated with MAC infection in patients with AIDS, but
- In immunocompromised patients any NTM infection can potentially be disseminated
- Most common NTM species causing DNTM: MAC, *M. chelonae*, *M. fortuitum*
- Diagnosis is based on identification of NTM (especially when it involves primary sterile sites) and treatment is mandatory

Regimen/duration of therapy depends on causative NTM species and disease severity

Treatment of disseminated MAC follows ATS guidelines for MAC-PD

Current recommendation for disseminated disease due to RGM:
in vitro susceptibility testing to determine the optimal drug treatment;
treatment with parenteral agents in combination with a macrolide in the initial phase (2 to 6 week course) followed by an additional 2 – 6 months regimen of one or two oral agents.

Clinical manifestations of NTM infections

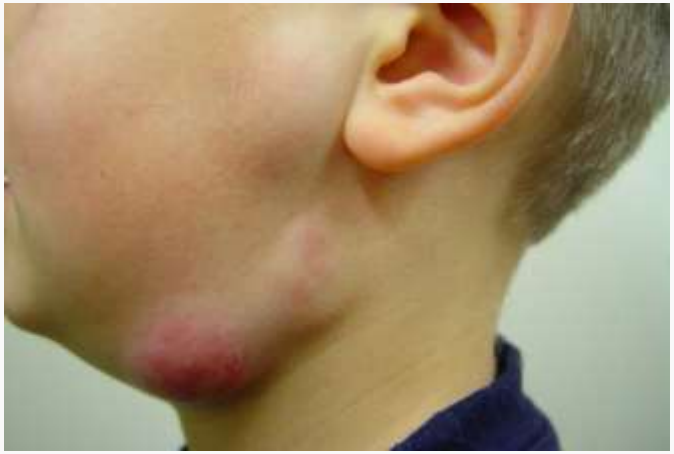


NTM lymphatic disease

- The most common form of NTM disease in childern
- In the absence of HIV infection, NTM lymphadenitis rarely affects adults
- Most common causative organisms: MAC, *M. scrofulaceum*, *M. malmoense*, and *M. haemophilum*
- Definite diagnosis: recovery of the causative organism from lymph node culture
- A large number of NTM lymph adenitis remain negative in culture; especially in the case of fastidious species like *M. haemophilum* and *M. malmoense*

Treatment:

for most cases of localised lymphadenitis (due to any NTM species) in immunocompetent patients – **complete surgical excision** of the involved lymph nodes



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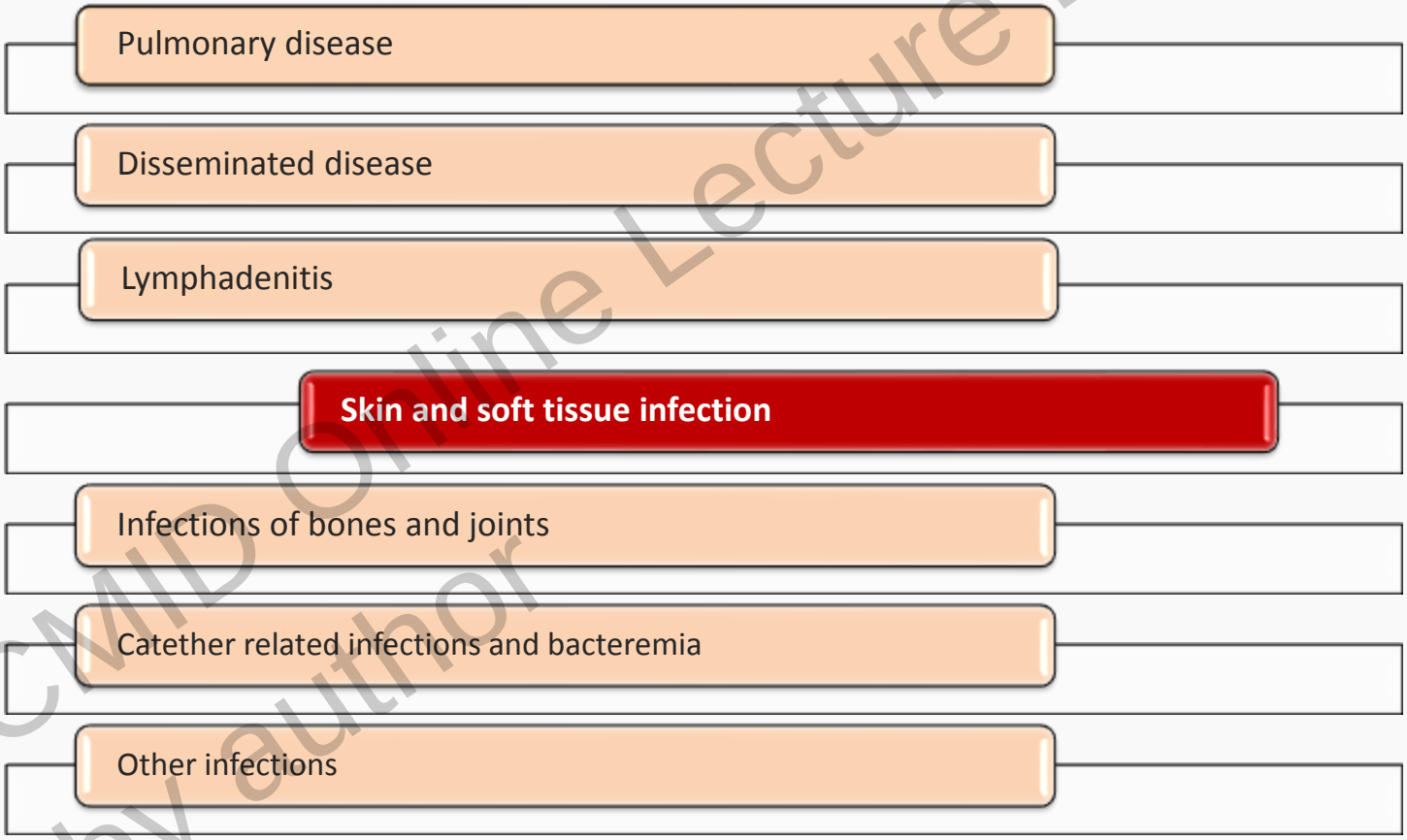
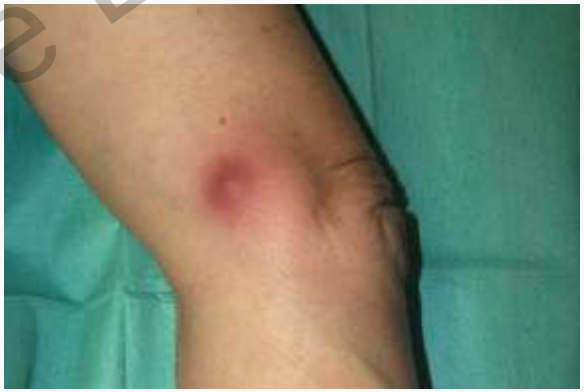


Skin and/or soft tissue disease

Most common causative species: *M. marinum* (causes "swimming pool" or "fish tank" granuloma), RGM (*M. abscessus, M. chelonae, M. fortuitum*)

Diagnosis: recovery of the causative organism +/- typical histological features

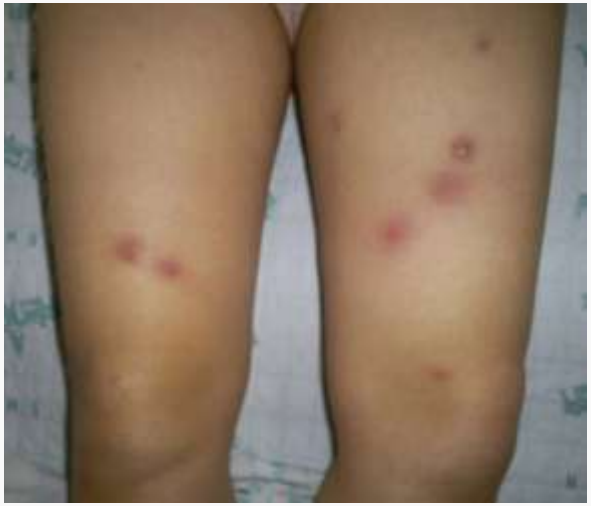


Treatment

combination of two active agents up to 1 to 2 months after resolution of simptoms/lesions

infections should be treated according to the guidelines for the specific species involved; in vitro susceptibility testing is often necessary (in the case of RGM, and especially *M. abscessus)*

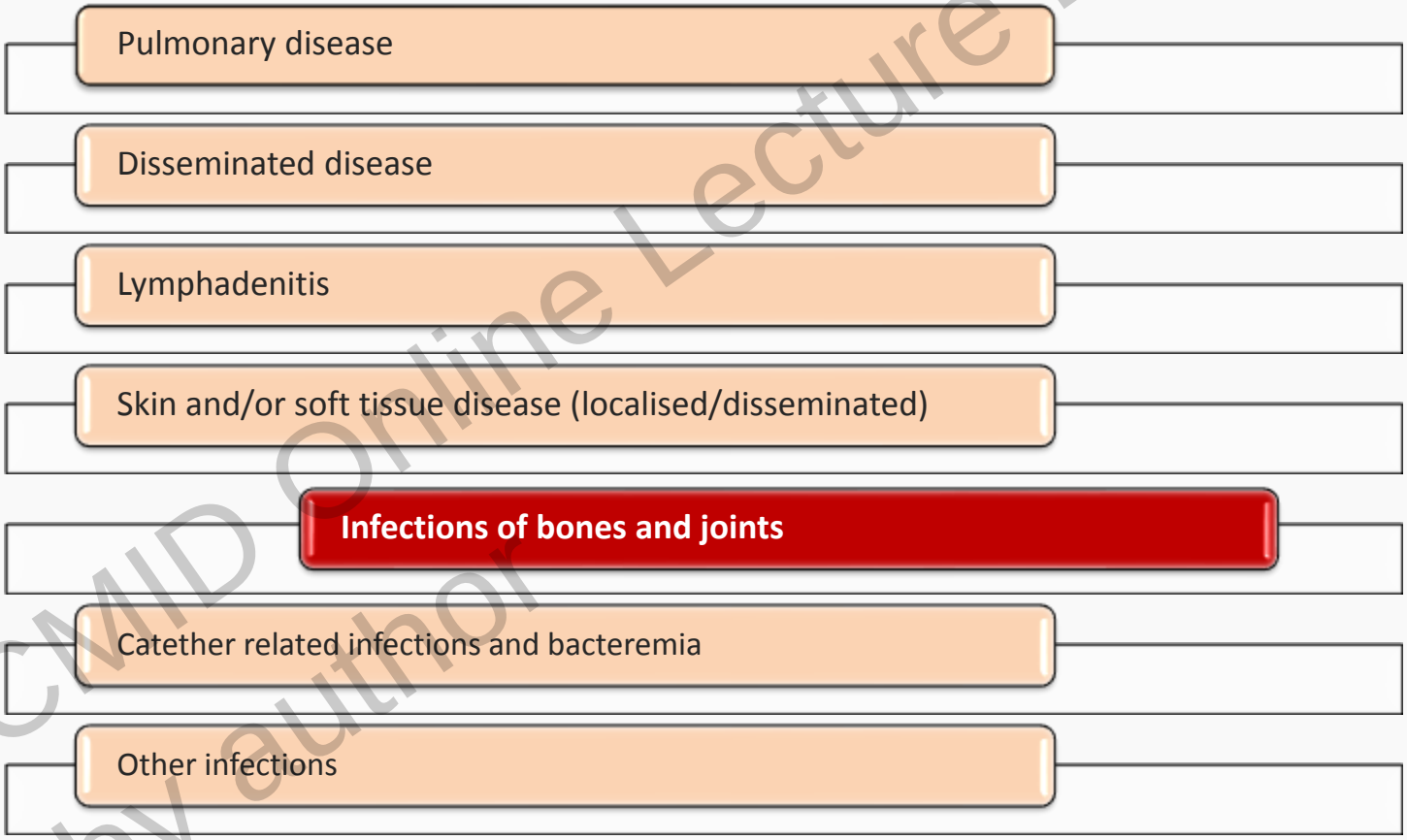
surgical debridement may be important adjunctive therapy depending on the extent of the disease



Disseminated skin infection – usually part of the disseminated disease

Treatment - according to the guidelines for the disseminated dissease

Clinical manifestations of NTM infections



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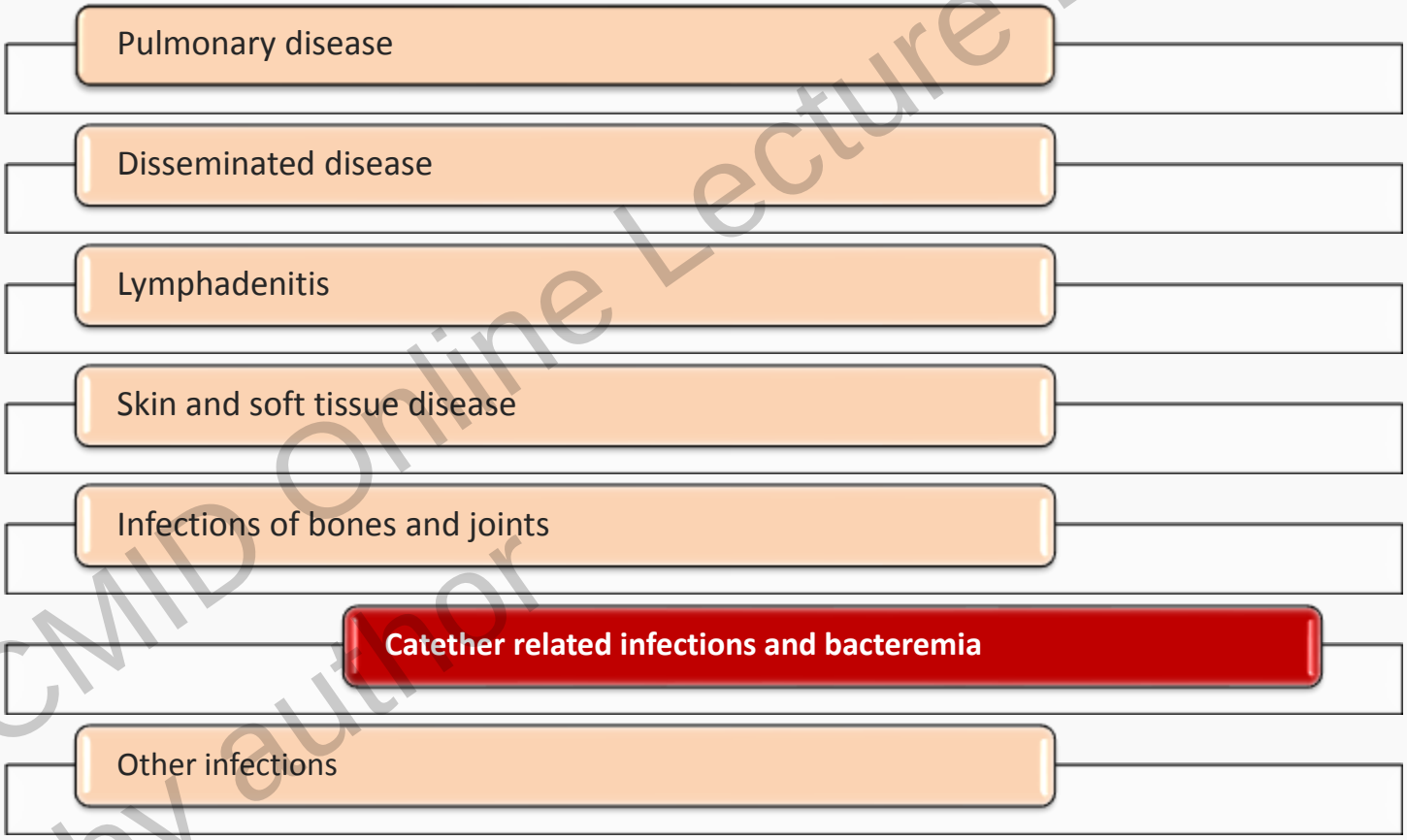

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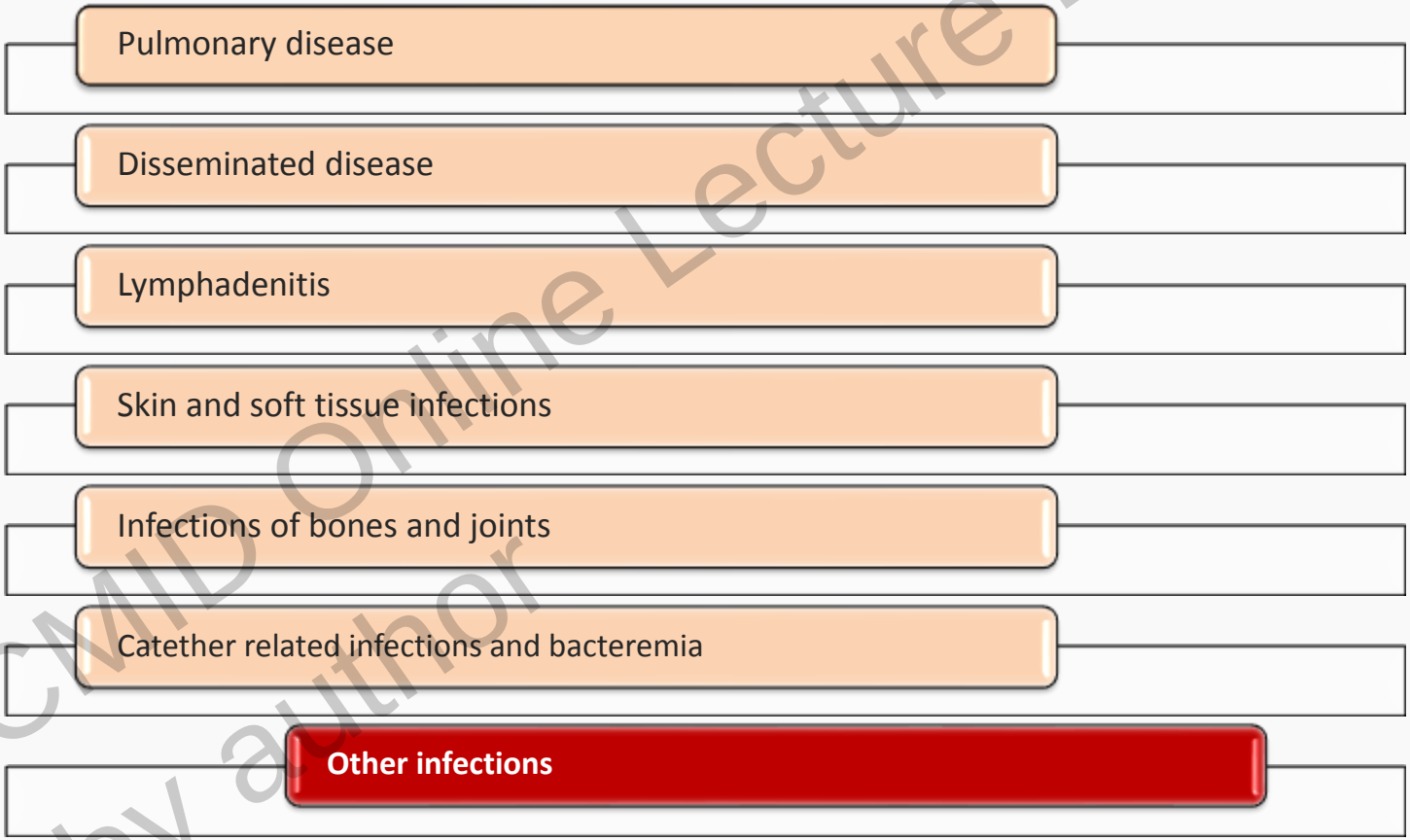

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