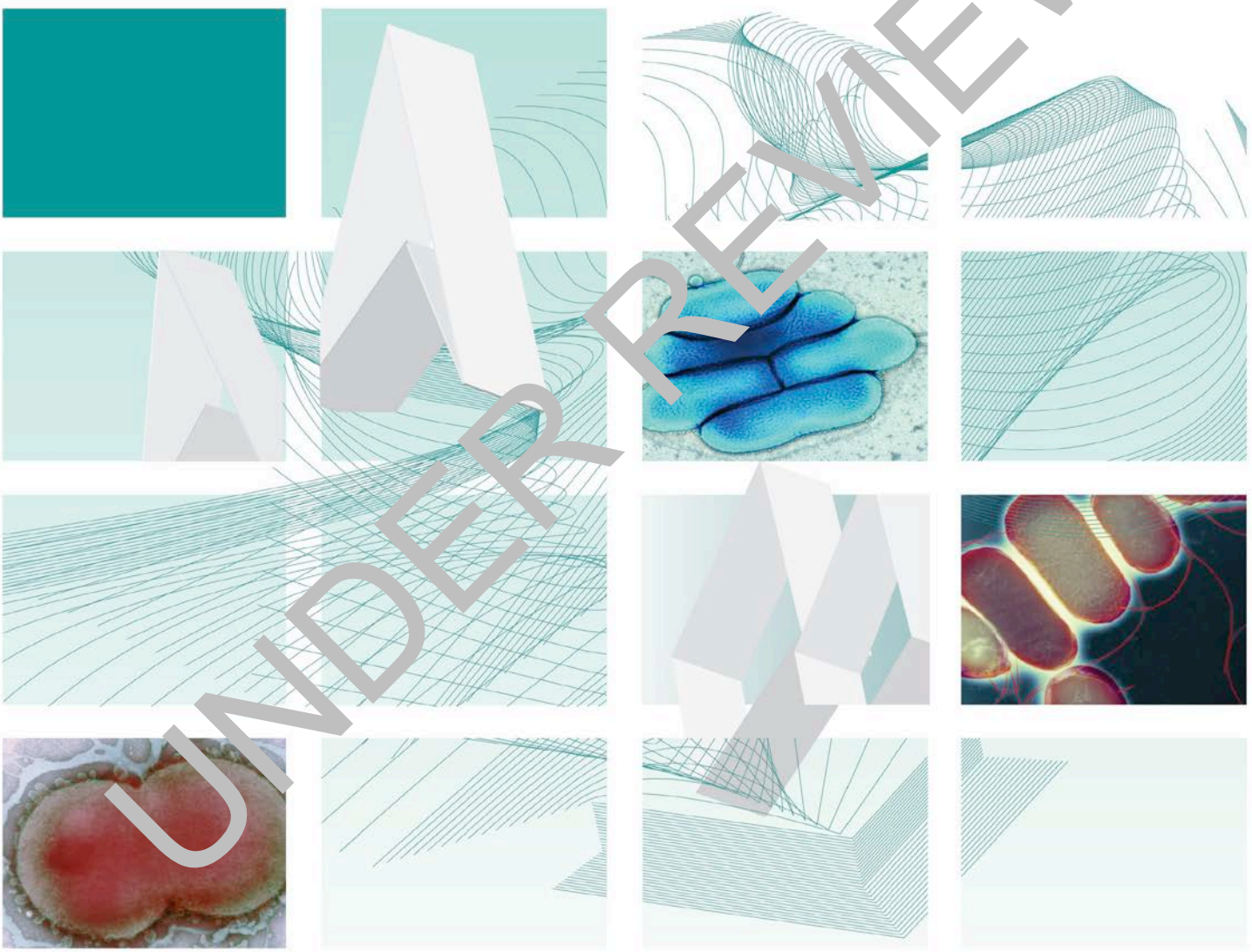
Public Health England

NHS

UK Standards for Microbiology Investigations

Identification of Aerobic Actinomycetes



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Issued by the Standards Unit, Microbiology Services, PHE

Acknowledgments

UK Standards for Microbiology Investigations (SMIs) are developed under the auspices of Public Health England (PHE) working in partnership with the National Health Service (NHS), Public Health Wales and with the professional organisations whose logos are displayed below and listed on the website http://www.hpa.org.uk/SMI/Partnerships. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see http://www.hpa.org.uk/SMI/WorkingGroups).

The contributions of many individuals in clinical, specialist and reference laboratories who have provided information and comments during the development of this document are acknowledged. We are grateful to the Medical Editors for editing the medical content.

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UK Standards for Microbiology Investigations are produced in association with:

Contents

Amendment Table

Each SMI method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from standards@phe.gov.uk.

New or revised documents should be controlled within the laboratory in accordance with the local quality management system.

Amendment No/Date.	3/11.03.14
Issue no. discarded.	1.2
Insert Issue no.	1.3
Section(s) involved	**Amendment**
Whole document.	Document has been transferred to a new template to reflect the Health Protection Agency's transition to Public Health England. Front page has been redesigned. Status page has been renamed as Scope and Purpose and updated as appropriate. Professional body logos have been reviewed and updated. Standard safety and notification references have been reviewed and updated. Scientific content remains unchanged.

Amendment No/Date.	2/06.11.12
Issue no. discarded.	1.1
Insert Issue no.	1.2
Section(s) involved	**Amendment**
Referrals.	Reference laboratory changed.

UK Standards for Microbiology Investigations[#]: Scope and Purpose

Users of SMIs

- SMIs are primarily intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK.
- SMIs provide clinicians with information about the available test repertoire and the standard of laboratory services they should expect for the investigation of infection in their patients, as well as providing information that aids the electronic ordering of appropriate tests.
- SMIs provide commissioners of healthcare services with the appropriateness and standard of microbiology investigations they should be seeking as part of the clinical and public health care package for their population.

Background to SMIs

SMIs comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages.

Syndromic algorithms are supported by more detailed documents containing advice on the investigation of specific diseases and infections. Guidance notes cover the clinical background, differential diagnosis, and appropriate investigation of particular clinical conditions. Quality guidance notes describe laboratory processes which underpin quality, for example assay validation.

Standardisation of the diagnostic process through the application of SMIs helps to assure the equivalence of investigation strategies in different laboratories across the UK and is essential for public health surveillance, research and development activities.

Equal Partnership Working

SMIs are developed in equal partnership with PHE, NHS, Royal College of Pathologists and professional societies.

The list of participating societies may be found at http://www.hpa.org.uk/SMI/Partnerships. Inclusion of a logo in an SMI indicates participation of the society in equal partnership and support for the objectives and process of preparing SMIs. Nominees of professional societies are members of the Steering Committee and Working Groups which develop SMIs. The views of nominees cannot be rigorously representative of the members of their nominating organisations nor the corporate views of their organisations. Nominees act as a conduit for two way reporting and dialogue. Representative views are sought through the consultation process.

SMIs are developed, reviewed and updated through a wide consultation process.

[#]Microbiology is used as a generic term to include the two GMC-recognised specialties of Medical Microbiology (which includes Bacteriology, Mycology and Parasitology) and Medical Virology.

Quality Assurance

NICE has accredited the process used by the SMI Working Groups to produce SMIs. The accreditation is applicable to all guidance produced since October 2009. The process for the development of SMIs is certified to ISO 9001:2008.

SMIs represent a good standard of practice to which all clinical and public health microbiology laboratories in the UK are expected to work. SMIs are NICE accredited and represent neither minimum standards of practice nor the highest level of complex laboratory investigation possible. In using SMIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. SMIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. SMIs also provide a reference point for method development.

The performance of SMIs depends on competent staff and appropriate quality reagents and equipment. Laboratories should ensure that all commercial and in-house tests have been validated and shown to be fit for purpose. Laboratories should participate in external quality assessment schemes and undertake relevant internal quality control procedures.

Patient and Public Involvement

The SMI Working Groups are committed to patient and public involvement in the development of SMIs. By involving the public, health professionals, scientists and voluntary organisations the resulting SMI will be robust and meet the needs of the user. An opportunity is given to members of the public to contribute to consultations through our open access website.

Information Governance and Equality

PHE is a Caldicott compliant organisation. It seeks to take every possible precaution to prevent unauthorised disclosure of patient details and to ensure that patient-related records are kept under secure conditions.

The development of SMIs are subject to PHE Equality objectives http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317133470313. The SMI Working Groups are committed to achieving the equality objectives by effective consultation with members of the public, partners, stakeholders and specialist interest groups.

Legal Statement

Whilst every care has been taken in the preparation of SMIs, PHE and any supporting organisation, shall, to the greatest extent possible under any applicable law, exclude liability for all losses, costs, claims, damages or expenses arising out of or connected with the use of an SMI or any information contained therein. If alterations are made to an SMI, it must be made clear where and by whom such changes have been made.

The evidence base and microbial taxonomy for the SMI is as complete as possible at the time of issue. Any omissions and new material will be considered at the next review. These standards can only be superseded by revisions of the standard, legislative action, or by NICE accredited guidance.

SMIs are Crown copyright which should be acknowledged where appropriate.

Suggested Citation for this Document

Public Health England. (2014). Identification of Aerobic Actinomycetes. UK Standards for Microbiology Investigations. ID 10 Issue 1.3. http://www.hpa.org.uk/SMI/pdf.

Scope of Document

This SMI describes the identification of branching Gram positive bacilli isolated from clinical specimens. Colonies may be isolated on blood agar or egg containing media.

This SMI should be used in conjunction with other SMIs.

Introduction

Taxonomy

The nomenclature of the group comprising the branching Gram positive rods is complicated. Considerable morphological diversity is not only seen among genera, but also among strains of the same taxon.

Characteristics[1]

Nocardia species

Nocardia species produce rudimentary to extensively branched vegetative hyphae, 0.5-1.2μm in diameter, which grow on the surface and penetrate agar media. The hyphae often fragment into rod-shaped or coccoid elements. Aerial hyphae are almost always produced. Short to long chains of conidia may be found on the aerial hyphae and occasionally on substrate hyphae. Cells stain Gram positive to Gram variable and are usually acid-fast. Growth is aerobic, producing chalky, matt or velvety colonies. Colonial morphology will vary according to the medium or incubation temperature used. The colonies may be brown, tan, pink, orange, red, purple, grey or white. Colonies on solid media may be smooth and moist or granular, irregular, wrinkled or heaped with a velvety surface due to aerial filamentation. Soluble brown or yellow pigments may be produced. *Nocardia* are catalase positive and grow on Sabouraud glucose agar, blood agar, brain heart infusion agar and Lowenstein-Jensen medium. Added carbon dioxide (5-10%) promotes more rapid growth. On Sabouraud dextrose agar, colonies of *N. asteroides* complex vary from salmon pink to orange. *N. brasiliensis* colonies are usually orange-tan. *N. otitidiscavarum* colonies are pale tan whereas *N. transvalensis* may vary in colour from pale tan to violet. Colonies in pure culture can grow after only 48hr incubation. In mixed cultures other rapidly growing bacteria may obscure small *Nocardia* species colonies, which may take several weeks to develop. Modified Thayer-Martin medium or buffered charcoal-yeast extract agar may enhance recovery of *Nocardia* species[2].

Microscopic examination of Gram-stained clinical specimens may give a rapid and specific diagnosis. Thin, delicate, weakly to strongly Gram positive, irregularly stained or beaded branching filaments are characteristic of *Nocardia* species. Multiple clinical specimens should be submitted for culture. *Nocardia* species may not be detected unless pus from a discharging fistula or abscess is examined. Smears and cultures of specimens are often negative unless specimens are obtained by biopsy. Routine blood cultures are not usually positive. Many *Nocardia* species from clinical material are variably acid-fast on primary isolation. This is rapidly lost in subcultured colonies. Modified Kinyoun stain decolourised with a weak acid (1-2% sulphuric acid instead of acid-alcohol) should be used. A single *Nocardia* colony isolated from CSF or a normally sterile site such as soft tissue abscess, pleural space or joint fluid from a patient with an appropriate clinical presentation should never be ignored. These

organisms are seldom laboratory contaminants and are not part of the body's normal flora. Sputum digestion procedures (eg N-acetyl-L-cysteine or sodium hydroxide) may produce negative *Nocardia* species cultures. There are currently no serodiagnostic tests available[3].

Since *Nocardia* species are ubiquitous in nature, the isolation of these microorganisms from specimens may not be significant clinically. The presence of *Nocardia* in sputum culture may not always indicate invasive infection, but may reflect laboratory contamination or respiratory colonisation. The clinical and microbiological difficulties include the non-specific presentation of the infection, a frequent requirement for invasive diagnostic biopsy procedures, difficulty in isolating the *Nocardia* and problems in identification and taxonomic classification. *N. farcinica* is commonly misidentified as *N. asteroides, Rhodococcus* or *Gordona* species.

Streptomyces species

Streptomyces species produce vegetative hyphae 0.5-2.0μm in diameter, which form an extensively branched mycelium that rarely fragments. This matures to form chains of three to many non-motile spores. A few species produce spores on the substrate mycelium. Cells are Gram positive but not acid-alcohol fast. Growth is obligately aerobic and the optimum growth temperature is 25°C–35°C. Initially the colonies produced are relatively smooth surfaced, but later they develop aerial mycelium which may appear floccose, granular, powdery or velvety. Colonies are discrete, lichenoid, leathery or butyrous. The vegetative and aerial mycelia may be pigmented and diffusible pigments may also be produced. Metabolism is oxidative and the catalase test is positive. Nitrates are reduced to nitrites and aesculin is degraded.

Rhodococcus species

Rhodococcus species produce cocci which may germinate into short rods, form filaments with side projections, branching or extensively branched hyphae. The next generation of cocci, or short rods, is produced by fragmentation of the rods, filaments or hyphae. Microscopic aerial hyphae and spores are not usually produced, and spores are not produced. Cells stain Gram positive and are usually partially acid-fast. Growth occurs aerobically.

There are three main colony types of *R. equi*. The classic colony type is pale pink and slimy. The second is colonet and non-slimy, and the third is pale yellow, non-slimy, and more opaque. Colonies of other rhodococci may be rough, smooth or mucoid and pigmented cream, buff, yellow, coral, orange or red. Colourless variants may occur particularly of *R. equi*. *R. equi* has a variable microscopic morphology (bacillary to coccoid forms) and may be discarded as a contaminiant[4]. The cyclic variation in morphology of *R. equi* and some non-equi rhodococci depends upon incubation time and growth conditions. All rhodococci from clinical specimens are weakly acid-fast. Colonial and cell morphology cannot be used distinguish among *Rhodococcus*, *Gordonia* and *Tsukamurella* species. Commercial identification systems do not provide reliable identification of *Rhodococcus* species and clinically important isolates should be referred to the Reference Laboratory[5].

Oerskovia species

Oerskovia species produce extensively branching vegetative hyphae approximately 0.5μm in diameter which grow on the surface and penetrate into agar. The hyphae break up into rod-shaped, motile, flagellate rods. Non-motile strains may also occur.

An aerial mycelium is not formed. Cells stain Gram positive, although part of the thallus may become Gram negative with age and coryneforms may be seen. Growth is facultatively anaerobic and the catalase test is positive when grown aerobically and negative when grown anaerobically. The species may be pigmented yellow. Glucose is metabolised both oxidatively and fermentatively.

Morphologically similar organisms

Actinomadura species

Actinomadura species produce extensively branching vegetative hyphae which form a dense non-fragmenting substrate mycelium. The aerial mycelium may be absent or moderately developed to form short or occasionally long chains of arthrospores when mature. The spore chains are straight, hooked or irregular spirals. The aerial mycelium may be blue, brown, cream, grey, green, pink, red, white or yellow. The colonies have a leathery or cartilaginous appearance when the aerial mycelium is absent. Colonies are usually mucoid and have a molar tooth appearance after two days incubation at 35°C. Growth is aerobic and occurs within the temperature range 10°C–60°C. Cells stain Gram positive and are non-acid-fast.

Amycolata species

Amycolata species produce branching vegetative hyphae 0.5-2.0μm in diameter, which tend to fragment into squarish elements. Aerial mycelium may be produced which may remain stable, or differentiate into long chains of smooth-walled ellipsoidal to cylindrical spores. Chains of spores are also produced on vegetative hyphae.

Amycolata autotrophica is a rare human pathogen. It is Gram positive with branched filaments, which are not acid-fast by the Kinyoun method. Aerial hyphae are abundant and aesculin is hydrolysed.

Amycolatopsis species

Amycolatopsis species produce branching substrate hyphae 0.5 -2.0μm in diameter which fragments into squarish elements. Aerial mycelium may be produced and the aerial hyphae may be sterile or differentiate into long chains of smooth-walled, squarish to ellipsoidal spore-like structures. Spores may be produced on vegetative hyphae.

Dermatophilus congolensis

Dermatophilus congolensis grows only on complex media, and the aerial mycelium will grow only in atmospheres containing added carbon dioxide. The substrate mycelium consists of long tapering filaments which branch laterally at right angles. *D. congolensis* may be easily recognised microscopically. Septa are formed in transverse, horizontal and vertical longitudinal planes to produce up to eight parallel rows of motile spores. Cells stain Gram positive but are not acid-fast.

Isolation of *D. congolensis* may be difficult. Clinical material, preferably the underside of scabs, should be streaked on a blood plate and incubated aerobically or with added carbon dioxide at 35°C–37°C. Growth is aerobic, facultatively anaerobic and catalase positive. The metabolism is non-fermentative but acid is produced from some carbohydrates. The optimum growth temperature is 37°C.

Gordonia species

Cells are short rods or cocci which resemble thin beaded coccobacilli. They stain Gram positive or Gram variable and are usually partially acid-fast. Colonies on blood agar are dry, wrinkled, raised and beige, brownish, pink, or orange and red after three to seven days incubation. Growth is aerobic. Colonial and cell morphology cannot distinguish among *Rhodococcus, Gordonia* and *Tsukamurella*.

Nocardiopsis species

Nocardiopsis species produce a well developed substrate mycelium. The hyphae are long, densely branched and may fragment into coccoid and bacillary forms. The aerial mycelium is also well developed and abundant, and the aerial hyphae fragment completely into spores of various lengths. The growth temperature range is 10°C-45°C.

Rothia species

Rothia contains five species including *Rothia mucilaginosa* (previously named *Stomatococcus mucilaginosus)*. In Gram stains a mixture of cocci, rods and filaments are seen. It is catalase positive, and optimum growth temperature is 35°C-37°C. *R. dentocariosa* is a facultative anaerobe: it produces spider-like, filamentous colonies when grown anaerobically. Under aerobic conditions colonies are convex or convoluted and glisten. *Rothia mucilaginosa* is a coccus 0.9–1.3mm in diameter, usually arranged in clusters.

Tsukamurella species

Tsukamurella species are straight to slightly curved rods 0.5-0.8 x 1.0–5.0μm. Very short rods may also be present. Cells are Gram positive and weakly to strongly acid-fast and occur singly, in pairs or in masses. They are non-motile, non-sporing and do not produce aerial hyphae. Growth is obligately aerobic, producing white/creamy to orange small, convex colonies 0.5-2.0mm in diameter; with entire, sometimes rhizoidal, edges which are dry but easily emulsified. The preferred growth temperature is below 37°C. Colonial and cell morphology cannot distinguish among *Rhodococcus Gordonia* and *Tsukamurella*.

Colonies of *Tsukamurella paurometabola,* the species associated with infection, grow on brain-heart infusion agar containing blood. They are 0.5-2.0mm in diameter, circular with an entire and occasionally a rhizoid edge; dry, easily emulsified and white to creamy to orange. Rough colonies are produced after prolonged incubation for up to seven days. These colonies are cerebreform and do not produce aerial hyphae but resemble rapidly growing mycobacteria. Most strains of *T. paurometabola* are acid-fast by the Kinyoun method.

Mycetoma

The important agents of actinomycetoma in humans are:

Actinomadura madurae

Actinomadura pelletieri

Nocardia brasiliensis

Streptomyces somaliensis

Less commonly involved are, *N. asteroides, N. otitidiscaviarum, N. dassonvillei* and *N. transvalensis. Aspergillus nidulans* and *Curvularia lunata* are also associated with mycetoma in the Sudan.

Principles of Identification

N/A

Technical Information/Limitations

Reliable identification of clinically significant actinomadurae, nocardiae, actinomycetes and streptomycetes is possible only by detecting key chemical markers. Identification should be confirmed by a Reference Laboratory. The standard phenotypic identification tests will give only a presumptive identification.

Method for demonstrating the micromorphology of cultures (for information)

Slide culture should be made of undisturbed colonies grown on minimal medium, such as tap water medium or cornmeal medium without dextrose. The culture preparations are incubated at 25°C and examined periodically for two to three weeks. Examine the slide cultures under a microscope in order to recognise the branched substrate mycelium, aerial mycelium and sporulation. The substrate hyphae of *Nocardia* species appear as very fine, dichotomously branched filaments. Movement of the objective up and down through several planes will reveal aerial hyphae. The presence of aerial hyphae differentiates the genus *Nocardia* from other related genera (*Rhodococcus, Gordona, Tsukamurella, Corynebacterium* and *Mycobacterium*). Only *Nocardia* species in this group of organisms have aerial hyphae. The rapidly growing mycobacteria, which phenotypically resemble the nocardiae, have simple, relatively short substrate hyphae that branch at acute angles. In contrast, the complex substrate hyphae of the nocardiae branch at right angles and usually have secondary branches. Rhodococci grow as coccobacilli arranged in a zigzag pattern.

A. pelletieri differs from *A. madurae,* in that *A. madurae* hydrolyses aesculin and *A. pelletieri* does not.

The microscopic morphology of *D. congolensis* in cultures is similar to that in clinical specimens. The typical appearance of branched filaments divided in their transverse and longitudinal planes is diagnostic. Wet mounts of colonies, smears of colonies or clinical material should be stained with methylene blue or by Giemsa stain. A Gram-stained preparation is not helpful in visualising this organism because it is too dark, and obscures crucial morphologic details. Completely coccal elements may be seen, many with flagellae or irregularly arranged cells in packets. Germinating spores and branched segmented or non-segmented filaments may be seen. Motility is usually seen in isolates from fresh cultures. If only cocci are seen and *D. congolensis* is suspected, prepare a younger culture to examine for hyphae. Very small (0.5-1.0mm) round colonies may be seen on brain-heart infusion agar containing blood which is incubated for 24hr. The colonies are usually grey-white, adherent and pit the medium. After two to five days an orange pigment develops. β-haemolysis is frequently present and is more prominent on areas of the medium where the colonies are crowded. There is no growth on Sabouraud dextrose agar. *D. congolensis* is catalse positive and urea is hydrolysed in 24hr. Nitrate is not reduced and acid, but no gas, is produced from glucose in 48hr.

Rhodococci can be easily distinguished from most *Corynebacterium* species which, except for *Corynebacterium aquaticum, Corynebacterium minutissimum* and the CDC group B-1, have a fermentative metabolism.

1 Safety Considerations[6-22]

Hazard Group 2 organisms.

Refer to current guidance on the safe handling of all Hazard group 2 organisms documented in this UK Standard for Microbiology Investigations[17,23,24].

The above guidance should be supplemented with local COSHH and risk assessments.

Compliance with postal and transport regulations is essential.

2 Target Organisms

Norcardia species which have been associated with infection:

N. asteroides sensu stricto

N. nova

N. farcinica

N. brasilinesis

N. otitidiscaviarum

N. transvalensis

N. brevicatena

N. carnea

N. pseudobrasiliensis

3 Identification

3.1 Microscopic Appearance

Gram stain (TP 39 – Staining Procedures)

Gram positive may be Gram variable depending on the age of the culture.

Norcardia species branching, fine, delicate filaments with fragmentation.

Rhodococcus, Gordona, Tsukamurella diphtheroid-like with minimal branching or coccobacillary.

Streptomyces species extensive branching with chains and spores; does not fragment easily.

Actinomadura species moderate, fine, intertwining branching with short chains of spores.

Dermatophilus species branched filaments divided into transverse and longitudinal planes; fine and tapered filaments.

Norcardiopsis species branching with internal spores.

Oerskovia species extensive branching; hyphae break up to motile, rod shaped elements.

Rothia species pleomorphic; predominately coccoid and bacillary (in broth) to branched filaments (solid media).

Modified ZN

If the stain is positive the isolate is probably a partially acid-fast aerobic actinomycete.

3.2 Primary Isolation Media

Chocolate agar incubated in 5-10% CO_2 at 35°C-37°C for 16-48hr.

Blood agar incubated in 5-10% CO_2 at 35°C-37°C for 16-48hr.

Fastidious anaerobe agar or equivalent, with or without neomycin (some aerobic organisms may be inhibited by neomycin) 40–48hr incubation anaerobically at 35°C-37°C.

Note: plates should be incubated for two to three weeks.

3.3 Colonial Appearance

Genus	Characteristics of growth on fastidious anaerobe agar after incubation
Nocardia species	Wrinkled often dry, chalky white appearance to orange-tan pigment, crumbly
Streptomyces species	Waxy heaped colonies with variable morphology
Oerskovia species	Yellow pigmented, extensive branching that grows on the surface and in to the agar
Gordonia, Rhodococcus, and *Tsukamurella* species	Non-haemolytic. Round, often mucoid with salmon-pink/red developing within 4 to seven days
Dermatophilus congolensis	Rough adherent grey-white colonies, that later develop orange pigments; often beta haemolytic
Actinomadura species	White to pink colour. Colonies are usually mucoid and have a molar tooth appearance
Rothia species	Small smooth to rough colonies dry appearance
Nocardiopsis species	Coarsely wrinkled and folded with well developed aerial mycelium

3.4 Test Procedures

Differentiation of branching Gram positive rods

Smears (in duplicate) from both colonies and clinical material should be stained with Gram stain and by the modified Kinyoun method. Isolates of *Streptomyces* species may show acid-fast coccoid forms and non-acid fast hyphae, but are considered non-acid fast. There must be a contrast between the carbol fuchsin and the counterstain. The demonstration of acid-fastness by isolates should be used only in conjunction with other tests as a supportive test and not as an absolute diagnostic test.

Nocardia species and *Streptomyces* species (β-galactosidase positive) may be differentiated from group IV mycobacteria (β-galactosidase negative) and rhodococci (β-galactosidase variable)[15].

3.5 Further Identification

Commercial identification kit or molecular techniques.

3.6 Storage and Referral

If required, subculture to blood agar and save the isolate on blood agar slopes for referral to the Reference Laboratory.

4 Identification of Aerobic Actinomycetes Flowchart

N/A

5 Reporting

5.1 Presumptive Identification

Presumptive identification may be made if appropriate growth characteristics, colonial appearance, Gram stain of the culture; and biochemical or molecular techniques.

5.2 Confirmation of Identification

Confirmation of identification can be made by the appropriate reference laboratory.

5.3 Medical Microbiologist

Inform the medical microbiologist when the request card bears relevant information.

5.4 CCDC

Refer to local Memorandum of Understanding.

5.5 Public Health England[25]

Refer to current guidelines on CDSC and COSURV reporting.

5.6 Infection Control Team

N/A

6 Referrals

6.1 Reference Laboratory

Contact appropriate devolved nation reference laboratory for information on the tests available, turn around times, transport procedure and any other requirements for sample submission:

Molecular Identification Service (MISU)
Microbiology Services Division

Public Health England
61 Colindale Avenue
London
NW9 5EQ
Contact PHE's main switchboard: Tel. +44 (0) 20 8200 4400

England and Wales
http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1158313434370?p=1158313434370

Scotland

http://www.hps.scot.nhs.uk/reflab/index.aspx

Northern Ireland

http://www.belfasttrust.hscni.net/Laboratory-MortuaryServices.htm

7 Notification to PHE[25,26] or Equivalent in the Devolved Administrations[27-30]

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify Public Health England (PHE) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days.

For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local PHE Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to PHE. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to PHE and many PHE Health protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

Note: The Health Protection Legislation Guidance (2010) includes reporting of Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCAIs) and Creutzfeldt–Jakob disease (CJD) under 'Notification Duties of Registered Medical Practitioners': it is not noted under 'Notification Duties of Diagnostic Laboratories'.

Other arrangements exist in Scotland[27,28], Wales[29] and Northern Ireland[30].

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