



Protecting and improving the nation's health

UK Standards for Microbiology Investigations

Investigation of Cerebrospinal Fluid Shunts



Issued by the Standards Unit, Microbiology Services, PHE

Bacteriology | B 22 | Issue no: 6.1 | Issue date: 12.06.15 | Page: 1 of 20

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 https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see https://www.gov.uk/government/groups/standards-for-microbiology-investigations-

https://www.gov.uk/government/groups/standards-for-microbiology-investigations-steering-committee).

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.

For further information please contact us at:

Standards Unit Microbiology Services Public Health England 61 Colindale Avenue London NW9 5EQ

Email: standards@phe.gov.uk

Website: https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories

PHE publications gateway number: 2015013

UK Standards for Microbiology Investigations are produced in association with:

































Logos correct at time of publishing.

Contents

AC	KNOWLEDGMENTS	2
ΑM	ENDMENT TABLE	4
UK	SMI: SCOPE AND PURPOSE	5
SC	OPE OF DOCUMENT	7
SC	OPE	7
INT	RODUCTION	7
TEC	CHNICAL INFORMATION/LIMITATIONS	9
1	SAFETY CONSIDERATIONS	11
2	SPECIMEN COLLECTION	11
3	SPECIMEN TRANSPORT AND STORAGE	12
4	SPECIMEN PROCESSING/PROCEDURE	12
5	REPORTING PROCEDURE	15
6	NOTIFICATION TO PHE OR EQUIVALENT IN THE DEVOLVED ADMINISTRATIONS	16
API	PENDIX: INVESTIGATION OF CEREBROSPINAL FLUID SHUNTS	17
RFI	FERENCES	18



NICE has accredited the process used by Public Health England to produce Standards for Microbiology Investigations. Accreditation is valid for 5 years from July 2011. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.

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.	9/12.06.15
Issue no. discarded.	6
Insert Issue no.	6.1
Section(s) involved	Amendment

Amendment No/Date.	8/18.05.15
Issue no. discarded.	5.2
Insert Issue no.	6
Section(s) involved	Amendment
Whole document.	Hyperlinks updated to gov.uk.
Page 2.	Updated logos added.
Types of specimen.	List of specimen types compressed.
Introduction.	Contents displayed in bullet points rearranged in to prevalence order.
Technical information/limitations.	Section expanded.
Section 2.5.3.	Tables amended to include specimen type.
Appendix.	Flowchart presentation amended to look more similar to the contents of the table.
References.	References reviewed and updated.

UK SMI#: scope and purpose

Users of SMIs

Primarily, SMIs are intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK. SMIs also 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. The documents also 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 https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. 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.

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

[#] 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.

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 https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity.

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

While 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. (2015). Investigation of Cerebrospinal Fluid Shunts. UK Standards for Microbiology Investigations. B 22 Issue 6. https://www.gov.uk/ukstandards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories

Scope of document

Type of specimen

Cerebrospinal fluid shunt, shunt tubing, pus

Scope

This SMI describes the processing and bacteriological investigation of cerebrospinal fluid shunts.

This SMI should be used in conjunction with other SMIs.

Introduction

Hydrocephalus

Hydrocephalus is a condition caused by the accumulation of excess cerebrospinal fluid (CSF) within the cerebral ventricular system¹. It occurs in both adults and children. If untreated, the prognosis is poor. It may be classified as²:

- communicating (no block between the ventricles and subarachnoid space)
- non-communicating (a block is present between the ventricles and subarachnoid space)

The common causes of hydrocephalus are an obstruction of the flow of CSF or a failure to absorb it, resulting from, in order of prevalence:

- major developmental abnormalities such as spina bifida
- meningitis
- perinatal haemorrhage
- trauma
- tumours, especially in the posterior fossa
- normal pressure hydrocephalus, a form of reversible dementia affecting the elderly
- overproduction of CSF

Treatment for hydrocephalus involves diverting CSF from the ventricular system to another compartment where it can be absorbed directly or indirectly into the bloodstream. This is done by means of a shunt. There is a risk of infection at the initial shunt insertion and at each subsequent insertion, and shunts may also be infected at other times.

Shunts

Shunts consist of drainage tubes incorporating one or more valves to control the direction and rate of CSF flow². The devices may also incorporate a reservoir. There are two main types of shunt²:

- ventriculo-atrial (VA) shunts are used to drain CSF from the ventricle to the right atrium
- ventriculo-peritoneal (VP) shunts are more commonly used in contemporary neurosurgical practice; in these, the route of drainage is from the ventricle to the peritoneal cavity

Shunt replacement is necessary from time to time due to growth of the recipient or to mechanical obstruction or infection of the device.

If a shunt has to be removed because of infection, CSF drainage has to be maintained. This can be achieved by means of an implanted reservoir (which can be tapped as required) or by an external ventricular drain (EVD). These systems allow instillation of intrathecal antibiotics to treat ventriculitis before implantation of a new shunt. They may themselves become secondarily infected. These systems are also used to relieve hydrocephalus in the short term in patients who may not require a permanent shunt.

CSF shunts become infected by the following routes, in order of significance:

- organisms directly colonise the shunt, usually at the time of surgery
- organisms travel along the shunt by retrograde spread
- organisms reach the CSF and the shunt via haematogenous spread

Indicators of infection differ according to the type of shunt. For instance:

- signs of VA and VP shunt malfunction (and/or meningitis) include symptoms such as headaches, vomiting, drowsiness and decreased level of consciousness, with or without fever
- infected VA shunts discharge organisms directly into the right cardiac atrium.
 This gives rise to intermittent fevers and signs of bacteraemia. Rarely, shunt nephritis may occur a long time (sometimes several years) after initial shunt surgery. It is a result of the formation and deposition of immune complexes on the glomeruli basement membranes, and is seen only in VA shunts
- infected VP shunts discharge organisms directly into the peritoneal cavity, or may become distally infected without causing meningitis. Abdominal pain as a result of local inflammation may occur, as may local erythema over the shunt track. Rarely, the distal portion of the shunt may perforate the bowel, leading to peritonitis and abscess formation. Sometimes in such cases, polymicrobial ventriculitis, including anaerobes, can be found

Peritoneal fluid may be sent for culture if there is evidence of peritoneal inflammation. Mixed infections, particularly if colonic anaerobic bacteria are present, suggest bowel perforation.

Shunts which are removed should be sent for culture. Shunt infections may be confirmed by recovering the organism from blood cultures (see <u>B 37- Investigation of blood cultures for organisms other than Mycobacterium species</u>), CSF (see <u>B 27-Investigation of cerebrospinal fluid</u>), shunt tubing, valves or a combination of these. It should be remembered that CSF microscopy may be unremarkable in shunt infection.

Intraventricular catheterisation (or external ventricular drainage) is used to monitor intracranial pressure in a variety of neurological and neurosurgical disorders, especially trauma³. Catheters used for this purpose may also be sent for culture (see

<u>B 20 - Investigation of intravascular cannulae and associated specimens</u>). Recently intracranial pressure 'bolts' have been introduced: this reduces the need for more invasive ventricular catheterisation in many patients.

Organisms isolated from CSF shunts and ventricular catheters include the following with coagulase negative staphylococci being the most common^{2,4}:

- coagulase negative staphylococci
- Staphylococcus aureus
- enterobacteriaceae
- coryneforms and *Propionibacterium* species
- enterococci
- pseudomonads
- streptococci
- yeasts
- Mycobacterium species

The staphylococci amount for 60-85% of infections. *P. acnes* has been found in about 10% of shunt infections but usually only after prolonged anaerobic incubation. External ventricular drainage infections are also caused mainly by staphylococci but there is often a larger proportion of Gram negative bacteria including *Acinetobacter* species.

Organisms which may be isolated but less frequently include anaerobes and fungi other than yeasts⁵⁻⁸.

The usual community-acquired bacteria (*Haemophilus influenza, Neisseria meningitidis* and *Streptococcus pneumoniae*, can cause meningitis in patients with shunts but they do not usually cause shunt infections, and the meningitis should be treated without removal of the shunt unless it is malfunctioning.

Biofilms have been shown to be a problem when dealing with shunt infections and can cause delays in the effect of treatment^{9,10}. CSF results are of questionable value when biofilm infections are involved. Some bacteria are more prone to form biofilms than others^{10,11}.

Technical information/limitations

Limitations of UK SMIs

The recommendations made in UK SMIs are based on evidence (eg sensitivity and specificity) where available, expert opinion and pragmatism, with consideration also being given to available resources. Laboratories should take account of local requirements and undertake additional investigations where appropriate. Prior to use, laboratories should ensure that all commercial and in-house tests have been validated and are fit for purpose.

Selective media in screening procedures

Selective media which does not support the growth of all circulating strains of organisms may be recommended based on the evidence available. A balance

Bacteriology | B 22 | Issue no: 6.1 | Issue date: 12.06.15 | Page: 9 of 20

therefore must be sought between available evidence, and available resources required if more than one media plate is used.

Specimen containers^{12,13}

SMIs use the term "CE marked leak proof container" to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: "The design must allow easy handling and, where necessary, reduce as far as possible contamination of, and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes".

1 Safety considerations¹²⁻²⁸

1.1 Specimen collection, transport and storage 12-17

Use aseptic technique.

Collect specimens in appropriate CE marked leak proof containers and transport in sealed plastic bags.

Compliance with postal, transport and storage regulations is essential.

1.2 Specimen processing¹²⁻²⁸

Containment Level 2 unless infection with a) *N. meningitidis*, b) a Hazard group 3 organism or c) TSE is suspected.

- a) Although *N. meningitidis* is in Hazard group 2, suspected and known isolates of *N. meningitidis* should always be handled in a microbiological safety cabinet. Sometimes the nature of the work may dictate that full containment level 3 conditions should be used eg for the propagation of *N. meningitidis* in order to comply with COSHH 2004 Schedule 3 (4e).
- b) Where Hazard Group 3 *Mycobacterium* species are suspected, all specimens must be processed in a microbiological safety cabinet under full containment level 3 conditions.
- c) If TSE is suspected, laboratory policies that take into account the local risk assessments may dictate that the use of a microbiological safety cabinet should be used when dispensing the specimen. Check recent ACDP guidelines on this area.

Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet²⁰.

Prior to staining, fix smeared material by placing the slide on an electric hotplate (65-75°C), under the hood, until dry. Then place in a rack or other suitable holder.

Note: Heat-fixing may not kill all *Mycobacterium* species²⁹. Slides should be handled carefully.

Centrifugation must be carried out in sealed buckets which are subsequently opened in a microbiological safety cabinet.

Specimen containers must also be placed in a suitable holder.

Refer to current guidance on the safe handling of all organisms documented in this SMI.

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

2 Specimen collection

2.1 Type of specimens

Cerebrospinal fluid shunt, shunt tubing, pus

2.2 Optimal time of specimen collection³⁰

For safety considerations refer to Section 1.1.

Bacteriology | B 22 | Issue no: 6.1 | Issue date: 12.06.15 | Page: 11 of 20

Collect specimens before antimicrobial therapy where possible³⁰.

Collect specimens other than swabs into appropriate CE marked leak proof containers and place in sealed plastic bags.

When a shunt is removed all three portions should be sent in separate microbiologically approved containers of the appropriate size¹³. This will include the proximal catheter, a valve or reservoir, and a distal catheter³¹. CSF is usually obtained from the shunt reservoir and sent concurrently for investigation (see <u>B 27 - Investigation of cerebrospinal fluid</u>).

2.3 Adequate quantity and appropriate number of specimens³⁰

Numbers and frequency of specimen collection are dependent on clinical condition of patient.

3 Specimen transport and storage^{12,13}

3.1 Optimal transport and storage conditions

For safety considerations refer to Section 1.1.

Specimens should be transported and processed as soon as possible³⁰.

If processing is delayed, refrigeration is preferable to storage at ambient temperature³⁰.

4 Specimen processing/procedure^{12,13}

4.1 Test selection

Microscopy and culture should be carried out as outlined below.

4.2 Appearance

Look for pus on external surface.

4.3 Sample preparation

For safety considerations refer to Section 1.2.

4.3.1 Pre-treatment

If the whole shunt is received intact, separate and process each portion separately.

If shunt tubing is received, cut a 5cm length aseptically from each end.

If CSF is visible in the shunt tubing or reservoir, aspirate it with a sterile pipette and process accordingly (see <u>B 27 - Investigation of cerebrospinal fluid</u>). It is important to record the section from which the CSF is withdrawn to assist in deciding the aetiology of the infection and significance of isolates obtained.

If no CSF in the reservoir flush the tubing with sterile saline and collect fluid in a CE Marked leak proof container in a sealed plastic bag. In the absence of CSF sample this can be used.

4.3.2 Specimen processing

Pus

Swab any visible pus on the surface of the tubing³¹.

(Process separately from the flushed tubing - see below).

Inoculate each agar plate with swab (see Q 5 - Inoculation of culture media for bacteriology).

For the isolation of individual colonies, spread inoculum with a sterile loop.

Tubing

Using a sterile pipette inoculate each agar plate with the uncentrifuged, flushed saline (see Q 5 - Inoculation of culture media for bacteriology).

Note: The use of broth medium for processing shunt tubing can lead to false positive results and is not recommended³¹.

For the isolation of individual colonies, spread inoculum with a sterile loop.

4.4 Microscopy

4.4.1 Standard

TP 39 - Staining procedures

Fluids

Any fluid aspirated from shunt tubing or other component is treated as CSF (see <u>B 27 - Investigation of cerebrospinal fluid</u>).

Pus (from external surfaces)

Prepare a thin smear on a clean microscope slide for Gram staining.

4.4.2 Supplementary

N/A

4.5 Culture and investigation

4.5.1 Culture media, conditions and organisms

Clinical details/	Specimen	Standard media	Incubation			Cultures read	Target organism(s)
conditions			Temp °C	Atmos	Time	reau	
Shunt infection	Cerebrospinal fluid shunt, shunt tubing,	Chocolate agar	35-37	5-10% CO ₂	40- 48hr	daily	Any organism
	pus	Blood agar	35-37	5-10% CO ₂	40- 48hr	daily	
		Fastidious anaerobe agar	35-37	anaerobic	10d ³²	≥40hr, 5d and at 10 days if you have an anaerobic cabinet otherwise at 10 days	Anaerobes

For these situations, add the following:

Clinical details/	Specimen	Optional media	Incubati	on		Cultures read	Target organism(s)
conditions		media	Temp °C	Atmos	Time	read	
If fungi are seen on microscopy	Cerebrospinal fluid shunt, shunt tubing, pus	Sabouraud agar	35-37	air	40- 48hr	≥40hr*	Yeasts Fungi

^{*}incubation may be extended to 10 days; in such cases plates should be read at ≥40hr and then left in the incubator/cabinet until day 10. If using jars then the first reading should be at 5 days. Certain opportunistic pathogens will require extended incubation. Laboratories should take precautions to stop plates drying out.

4.6 Identification

Refer to individual SMIs for organism identification.

4.6.1 Minimum level of identification in the laboratory

Anaerobes	species level
<u>β-haemolytic streptococci</u>	Lancefield group level
Coagulase negative staphylococci	"coagulase negative" level
All other organisms	species level if in pure culture or clinically indicated

Organisms may be further identified if this is clinically or epidemiologically indicated.

It may be useful to store coagulase negative staphylococci in case it is necessary to distinguish re-infections from relapsed infections.

4.7 Antimicrobial susceptibility testing

Refer to <u>British Society for Antimicrobial Chemotherapy (BSAC)</u> and/or <u>EUCAST</u> quidelines.

4.8 Referral for outbreak investigations

N/A

4.9 Referral to reference laboratories

For information on the tests offered, turn around times, transport procedure and the other requirements of the reference laboratory <u>click here for user manuals and request</u> forms.

Organisms with unusual or unexpected resistance, and whenever there is a laboratory or clinical problem, or anomaly that requires elucidation should be sent to the appropriate reference laboratory.

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

England and Wales

https://www.gov.uk/specialist-and-reference-microbiology-laboratory-tests-and-services

Scotland

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

Northern Ireland

http://www.publichealth.hscni.net/directorate-public-health/health-protection

5 Reporting procedure

5.1 Microscopy

Report microscopy on the CSF (see <u>B 27 - Investigation of cerebrospinal fluid</u>), or pus from external surface.

5.1.1 Microscopy reporting time

Urgent microscopy results to be telephoned or sent electronically.

5.2 Culture

Report organisms isolated or

Report absence of growth.

5.3 Antimicrobial susceptibility testing

Report susceptibilities as clinically indicated. Prudent use of antimicrobials according to local and national protocols is recommended.

6 Notification to PHE^{33,34} or equivalent in the devolved administrations³⁵⁻³⁸

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.

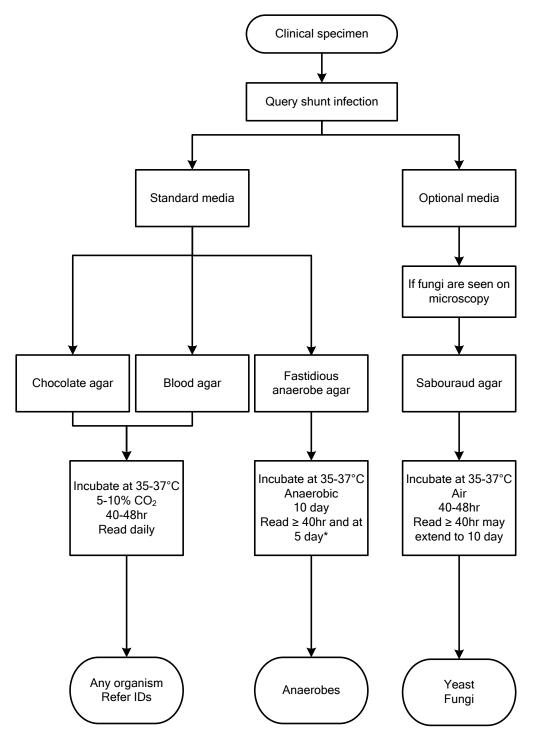
Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to PHE. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to PHE and many PHE Health protection Teams have agreements with local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

https://www.gov.uk/government/organisations/public-health-england/about/ourgovernance#health-protection-regulations-2010

Other arrangements exist in <u>Scotland</u>^{35,36}, <u>Wales</u>³⁷ and <u>Northern Ireland</u>³⁸.

Appendix: Investigation of cerebrospinal fluid shunts



^{*}if using an anaerobic incubator/cabinet. Otherwise the first reading should be at 5 days

References

- 1. Khan AA, Jabbar A, Banerjee A, Hinchley G. Cerebrospinal shunt malfunction: recognition and emergency management. Br J Hosp Med (Lond) 2007;68:651-5.
- 2. Gardner P, Leipzig T, Phillips P. Infections of central nervous system shunts. Med Clin North Am 1985;69:297-314.
- 3. Mayhall CG, Archer NH, Lamb VA, Spadora AC, Baggett JW, Ward JD, et al. Ventriculostomy-related infections. A prospective epidemiologic study. N Engl J Med 1984;310:553-9.
- 4. Sampedro MF, Patel R. Infections associated with long-term prosthetic devices. Infect Dis Clin North Am 2007;21:785-819, x.
- 5. Setz U, Frank U, Anding K, Garbe A, Daschner FD. Shunt nephritis associated with Propionibacterium acnes. Infection 1994;22:99-101.
- 6. Garbarini-Maywood C, Mulligan ME. Ventriculoperitoneal shunt infection due to anaerobic and facultative bacteria: case report. Clin Infect Dis 1995;20 Suppl 2:S240-S241.
- 7. Sanchez-Portocarrero J, Martin-Rabadan P, Saldana CJ, Perez-Cecilia E. Candida cerebrospinal fluid shunt infection. Report of two new cases and review of the literature. Diagn Microbiol Infect Dis 1994;20:33-40.
- 8. Chiou CC, Wong TT, Lin HH, Hwang B, Tang RB, Wu KG, et al. Fungal infection of ventriculoperitoneal shunts in children. Clin Infect Dis 1994;19:1049-53.
- 9. Bayston R, Ashraf W, Barker-Davies R, Tucker E, Clement R, Clayton J, et al. Biofilm formation by Propionibacterium acnes on biomaterials in vitro and in vivo: impact on diagnosis and treatment. J Biomed Mater Res A 2007;81:705-9.
- 10. Fux CA, Quigley M, Worel AM, Post C, Zimmerli S, Ehrlich G, et al. Biofilm-related infections of cerebrospinal fluid shunts. Clin Microbiol Infect 2006;12:331-7.
- 11. Stevens NT, Greene CM, O'Gara JP, Bayston R, Sattar MT, Farrell M, et al. Ventriculoperitoneal shunt-related infections caused by Staphylococcus epidermidis: pathogenesis and implications for treatment. Br J Neurosurg 2012;26:792-7.
- 12. European Parliament. UK Standards for Microbiology Investigations (SMIs) use the term "CE marked leak proof container" to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: "The design must allow easy handling and, where necessary, reduce as far as possible contamination of, and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes".
- 13. Official Journal of the European Communities. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices. 7-12-1998. p. 1-37.
- 14. Health and Safety Executive. Safe use of pneumatic air tube transport systems for pathology specimens. 9/99.
- 15. Department for transport. Transport of Infectious Substances, 2011 Revision 5. 2011.
- 16. World Health Organization. Guidance on regulations for the Transport of Infectious Substances 2013-2014. 2012.

- 17. Home Office. Anti-terrorism, Crime and Security Act. 2001 (as amended).
- 18. Advisory Committee on Dangerous Pathogens. The Approved List of Biological Agents. Health and Safety Executive. 2013. p. 1-32
- 19. Advisory Committee on Dangerous Pathogens. Infections at work: Controlling the risks. Her Majesty's Stationery Office. 2003.
- 20. Advisory Committee on Dangerous Pathogens. Biological agents: Managing the risks in laboratories and healthcare premises. Health and Safety Executive. 2005.
- 21. Advisory Committee on Dangerous Pathogens. Biological Agents: Managing the Risks in Laboratories and Healthcare Premises. Appendix 1.2 Transport of Infectious Substances Revision. Health and Safety Executive. 2008.
- 22. Centers for Disease Control and Prevention. Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories. MMWR Surveill Summ 2012;61:1-102.
- 23. Health and Safety Executive. Control of Substances Hazardous to Health Regulations. The Control of Substances Hazardous to Health Regulations 2002. 5th ed. HSE Books; 2002.
- 24. Health and Safety Executive. Five Steps to Risk Assessment: A Step by Step Guide to a Safer and Healthier Workplace. HSE Books. 2002.
- 25. Health and Safety Executive. A Guide to Risk Assessment Requirements: Common Provisions in Health and Safety Law. HSE Books. 2002.
- 26. Health Services Advisory Committee. Safe Working and the Prevention of Infection in Clinical Laboratories and Similar Facilities. HSE Books. 2003.
- 27. British Standards Institution (BSI). BS EN12469 Biotechnology performance criteria for microbiological safety cabinets. 2000.
- 28. British Standards Institution (BSI). BS 5726:2005 Microbiological safety cabinets. Information to be supplied by the purchaser and to the vendor and to the installer, and siting and use of cabinets. Recommendations and guidance. 24-3-2005. p. 1-14
- 29. Allen BW. Survival of tubercle bacilli in heat-fixed sputum smears. J Clin Pathol 1981;34:719-22.
- 30. Baron EJ, Miller JM, Weinstein MP, Richter SS, Gilligan PH, Thomson RB, Jr., et al. A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2013 Recommendations by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM). Clin Infect Dis 2013;57:e22-e121.
- 31. Bayston R. Diagnosis of shunt infection: Laboratory Procedures. In: Bayston R, editor. Hydrocephalus Shunt Infections. London: Chapman and Hall; 1989. p. 71-8.
- 32. Arnell K, Cesarini K, Lagerqvist-Widh A, Wester T, Sjolin J. Cerebrospinal fluid shunt infections in children over a 13-year period: anaerobic cultures and comparison of clinical signs of infection with Propionibacterium acnes and with other bacteria. J Neurosurg Pediatr 2008;1:366-72.
- 33. Public Health England. Laboratory Reporting to Public Health England: A Guide for Diagnostic Laboratories. 2013. p. 1-37.
- 34. Department of Health. Health Protection Legislation (England) Guidance. 2010. p. 1-112.
- 35. Scottish Government. Public Health (Scotland) Act. 2008 (as amended).

Investigation of Cerebrospinal Fluid Shunts

- 36. Scottish Government. Public Health etc. (Scotland) Act 2008. Implementation of Part 2: Notifiable Diseases, Organisms and Health Risk States. 2009.
- 37. The Welsh Assembly Government. Health Protection Legislation (Wales) Guidance. 2010.
- 38. Home Office. Public Health Act (Northern Ireland) 1967 Chapter 36. 1967 (as amended).