9.5.5 Data collection on cases

- A line-listing of all possible, probable or definite cases should be maintained and updated. This should include as a minimum dataset: case identification, classification of case, date of presentation, location, contact details for clinician in charge of case, investigations, outcome of case (recovery, death etc).
- An epicurve of cases should be constructed and updated regularly by the incident information officer. The shape of the epicurve can give important clues as to the cause; point source versus continuing source versus propagated source.
- A proforma should be developed to gather additional epidemiological and clinical information about possible cases that need further evaluation.
- By agreement, the proforma should be completed by the patient's clinician from the case notes and where appropriate by further interview of the patient.
- The incident clinical adviser should be responsible for collating all the more detailed information.

9.5.6 Data collection on exposed but not ill people

Decisions will need to be made about how to define exposure. A list should be compiled of those who have been potentially exposed but who are not as yet ill. This should include not only the general public at risk but also health care workers and professionals from other agencies who may have been involved with the incident. The list should include name, address, and date of birth, contact details and GP details along with a classification of exposure risk.

9.5.7 Producing best available current advice on management of individual cases

- Guidance on appropriate individual management will initially be based on the working theory of aetiology.
- Advice sheets should be produced for clinicians who may encounter cases. This task would be best done by the expert advisors to the incident team and will probably need regular updating. These could be disseminated via a website such as that of the HPA.

9.5.8 Producing best available current advice for public health protection

- Guidance on appropriate public health management will initially be based on the working theory of aetiology, including how to manage exposed but not ill people.
- Information for the public should also be prepared, and this and the guidance for health care professionals should be disseminated via websites, so that it can be readily updated.

9.5.9 Assessment of whether cases may be the result of deliberate action

- On the basis of the clinical and epidemiological evidence as it evolves, repeated assessments should be made of whether cases may be the result of deliberate action.
- If deliberate action is a possibility, this should be discussed with the police immediately.
- Remember that initial cases may be the perpetrators of the crime. Seek forensic advice early if deliberate release is a possibility

9.5.10 Communication

- A focal point for contact about the incident should be identified.
- Effective communication with all those who need to know is crucial to the management of any outbreak/ incident.
- Systems need to be set up from the outset to ensure that regular updates and communications are built into investigation and management.
- A full list of all essential contact details should be compiled and disseminated to all parties involved by a nominated individual. This should be updated regularly.
- The incident information officer should disseminate regular updates of summary data and developments to all parties involved in management.
- For a list of those who may need to be alerted see checklist 4.
- A nominated press office should handle all media enquiries for the incident.

9.6 Incident control team

An incident control team (ICT) is likely to be necessary for either type of incident. This would usually be chaired by the CCDC, Regional Director or national epidemiologist, depending upon the scale and geographical spread of the incident. It should include: representatives from key organisations involved

in the management of the incident with the necessary seniority and expertise to be able to take decisions, the designated press officer and secretarial support. A suggested agenda for the first meeting is given in checklist 5.

It is not possible in this document to provide guidance beyond these initial stages of incident investigation and management, however throughout the incident the team will need to re-appraise:

- evidence regarding cause
- investigations required
- measures to manage individual cases and for public health protection
- risk assessment for public health
- likelihood of deliberate action
- resource requirements
- communications

In the event of an emergency where there is likely to be a requirement for coordinated scientific or technical advice a Science and Technical Advice Cell (STAC) should be established (arrangements for the STAC will have been agreed through the Local Resilience Forum). The STAC will provide the best possible advice in a timely, coordinated and understandable format to those involved in the response. **It will also need to consider:**

- criteria for declaring the outbreak/ incident over and dissemination of this information
- post incident report writing, including any lessons identified
- post incident health monitoring, particularly where the causative agent was chemical or radiological

Checklist 5: Suggested agenda for first ICT meeting

1.Purpose/ objectives

- Agree facts as currently known
- Agree a case definition
- Ensure that care of cases is appropriate given current knowledge of aetiology
- Decide how others should be protected given current knowledge of aetiology, who will be responsible for this and how it will be resourced
- Define measures necessary to identify the cause of the illnesses, including environmental sampling as appropriate

2. Incident/ assessment and planning

- Examine available evidence re aetiology and consider whether the incident may be the result of deliberate action
- Risk assessment -assess risks to public health given current knowledge of aetiology
- Consider who else is at risk, including health professionals and other agencies who may have been involved in managing the incident

3. Decisions/ actions

- Define mechanisms for data collection and collation
- Determine whether active case finding is necessary and how this will be done
- Define measures necessary to monitor the effectiveness of containment
- Summarise actions and those responsible

4. Allocation of roles

- Define roles and responsibilities
- Identify personnel and other resources necessary to manage the outbreak/ incident
- Identify additional expert assistance which may be required for investigation or management of the illnesses
- Assign functions both within and outside the ICT

5. Communications

- Identify who needs to know
- Agree lines of communication
- Define measures for communication to the public, press and other organisations and individuals

6. AOB

- Decide the necessary frequency of meetings

APPENDICES

Appendix 1

USEFUL CONTACT NUMBERS FOR HEALTH PROFESSIONALS ONLY

1a. Expert support agencies
1b. Specialist reference Laboratories

For contact details of local HPUs – office & out of hours telephone numbers see
http://www.hpa.org.uk/lars_homepage.htm

Appendix 1a – Expert Support Agencies

AGENCY	PHONE (24 HR)	FAX (9AM TO 5PM) E-MAIL
HPA Centre for Emergency Preparedness and Response (CEPR)	01980 612100	01980 612968 erd@hpa.org.uk
National Public Health Service for Wales	01443 824160	01443 824161 general.enquiries@nphs.wales.nhs.uk
Communicable Disease Surveillance Centre Northern Ireland	02890 263765	02890 263511 cdscni@hpa.org.uk
Health Protection Scotland	0141 300 1100 0141 211 3600	0141 300 1170 (general) hpsenquiries@HPS.scot.nhs.uk
INFECTIOUS DISEASES **HPA Centre for Infections (Cfl)**	020 8200 4400 020 8200 6868	020 8200 7874 DrComments@hpa.org.uk
CHEMICAL HAZARDS **HPA Chemical Hazards and Poisons Division (CHaPD)**	National on-call number: 0870 6064444	01235 822614 chemicals@hpa.org.uk
National Poisons Information Service (NPIS)	0870 2432241	
RADIOLOGICAL HAZARDS **HPA Radiation Protection Division (RPD)**	01235 831600	01235 833891 (general) rpd@hpa.org.uk
Radiation and Environmental Monitoring Scotland	0141 440 2201	0141 440 0820 HPAScotland@hpa.org.uk

Appendix 1b - specialist reference laboratories for unknowns or deliberate release agents

Further information and links to specialist microbiology tests and reference services can be found at, http://www.hpa.org.uk/cfi/reference_tests_index.htm
Specific information and guidelines on deliberate release agents see http://www.hpa.org.uk/infections/topics_az/deliberate_release/default.htm

DISEASE	LABORATORY	PHONE (24 HR unless otherwise stated)
UNKNOWN	Contact EIZ department at HPA CfI in the first instance (see section 8.2.4) Also see undiagnosed protocol	020 8200 4400 / 6868 020 8327 7483 (9am-5pm)
ANTHRAX	Special Pathogens Reference Unit, HPA CEPR	01980 612100 01980 612224 (9am-5pm)
BOTULISM	Food Safety Microbiology Laboratory, HPA CfI	020 8200 4400 / 6868 020 8327 7116/ 7117 (9am-5pm)
BRUCELLOSIS	Brucella Reference Unit, HPA Collaborating Laboratory, University Hospital Aintree, Liverpool OR Department of Statutory and Exotic Bacterial Diseases, Veterinary Laboratory Agency, Weybridge	0151 529 4900 OR 0193 234 1111
GLANDERS AND MELIOIDOSIS	Laboratory of Health Care Associated Infection, HPA CfI	020 8200 4400 / 6868 020 8327 7224 (9am-5pm)
PLAGUE	Laboratory of Enteric Pathogens, HPA CfI	020 8200 4400 / 6868 020 8327 6173 (9am-5pm)
Q FEVER	HPA South West, Bristol Royal Infirmary OR Special Pathogens Reference Unit, HPA CEPR	0117 928 3242 OR 01980 612100 01980 612224 (9am-5pm)
SMALLPOX	Virus Reference Department, HPA CfI OR Special Pathogens Reference Unit, HPA CEPR	020 8200 4400 / 6868 020 8327 3117 (9am-5pm) OR 01980 612100
TULAREMIA	Special Pathogens Reference Unit, HPA CEPR	01980 612100 01980 612224 (9am-5pm)
VIRAL HAEMORRHAGIC FEVERS	Virus Reference Department, HPA CfI OR Special Pathogens Reference Unit, HPA CEPR	020 8200 4400 / 6868 020 8327 3117 (9am-5pm) OR 01980 612100
CHEMICALS	CHaPD	National on-call number: 0870 6064444
RADIATION	HPA RPD	01235 831600

Appendix 2 - Documentation
Appendix 2a - Chemical incident analysis request form for use with Toxi-Boxes or ChEAKs (Chemical Exposure Assessment Kits)

CHEMICAL INCIDENT ANALYSIS REQUEST FORM

Unless you are certain which samples are required and to which analytical toxicology laboratory they should be sent, please check first with HPA CHaPD (0870 606 4444)

PLEASE COMPLETE IN BLOCK CAPITALS

REQUESTNG LABORATORY (Req Lab):

ANALYTICAL TOXICOLOGY LABORATORY (ATL):

PATIENT DETAILS	Surname:	First name:	Sex:
Hospital number:		Date of birth:	Age:
Hospital/Trust:		Ward/Unit:	
Analysis requested by:		Consultant:	

SAMPLE DETAILS

Sample date	Sample time	Sample type	Req Lab No	ATL No
		Heparinised blood (10ml)		
		EDTA blood (10ml)		
		Heparinised blood (5ml) glass		
		Urine (30ml)		

Name and address for report:

EXPOSURE DETAILS

Place and nature of exposure:

Date (dd/mm/yy) of exposure:	
Time exposure occurred (24 hr clock):	
Exposed to (give name of chemical or CAS number if available):	
Length of exposure (estimate duration in minutes):	

Telephone number:

Clinical features (Please describe these as fully as possible):

Name and address for invoice:

Brief Description of Incident
(Incident Reference Number if relevant)

Telephone number:

CHAIN OF EVIDENCE FORM	A form has been completed and accompanies these specimens (Yes/No):

BEFORE REFERRING THESE SPECIMENS, PLEASE NOTIFY THE ANALYTICAL TOXICOLOGY LABORATORY AND KEEP A KEEP A COPY THE COMPLETED REQUEST FORM

Appendix 2b - Chain of evidence documentation

Chain of evidence form				
HOSPITAL/TRUST				
PATIENT DETAILS	Patient name:		Sex:	Date of birth:
	Hospital number:	Postcode:		Ward:
Requesting doctor:		Bleep number:		Consultant:
SAMPLE DETAILS				
Sample type/description	Sample date	Sample time	Laboratory/ specimen number	
HANDOVER DETAILS				
Person handing the sample(s) over		**Person receiving the sample(s)**		
Name:	Grade:	Name:		Grade:
Signature:	Date & time:	Signature:		Date & time:
Person authorising the transfer				
Name:	Signature:			Date:
Address:				Form number:

- To be used where deliberate release is suspected or other forensic considerations are important
- Please note that **a separate form must be filled in every time samples change hands**, starting from the doctor taking the samples
- All forms should be kept together and numbered in sequence
- Any break in the chain of evidence documentation may compromise the evidential value of the sample
- The consultant in charge of the case should authorise the transfer of sample(s) to the laboratory and this may be verbal as samples should not be delayed – but the consultant must sign the form as soon as practically possible
- Laboratories will have their own local protocols for who is sufficiently senior to authorise sample handover and these should be adhered to

Appendix 3 - Information to record in case(s) of unusual illness

Name of clinician recording information with contact details
Hospital
Number of cases
Is deliberate release suspected?
Is there any information about others who might be exposed/ at risk (including staff)?

For each case:

- Name
- Address
- Sex
- Age
- Occupation
- GP details
- Date and time of presentation
- Mode of presentation (walk-in, ambulance, GP referral etc.)
- Name of senior clinician in charge
- Ward
- Date/time of onset of symptoms
- Nature of symptoms/severity of illness
- Has there been an expert clinical assessment? By whom?
- Clinical findings (who performed assessment?)
- Any risk factors/exposures identified?
- Relevant past medical history/ drug history?
- Vaccination status
- Samples taken
- Investigations undertaken and results available
- Working diagnosis
- Management: decontamination, treatment
- Outcome
- Autopsy – if done where?

What is being done to prevent the development of further cases e.g. patient containment/ staff protection?

Record all staff in contact with the patient with their personal contact details.

HPA Protocol for UNDIAGNOSED SERIOUS ILLNESS:

A MICROBIOLOGICAL APPROACH TO INVESTIGATION

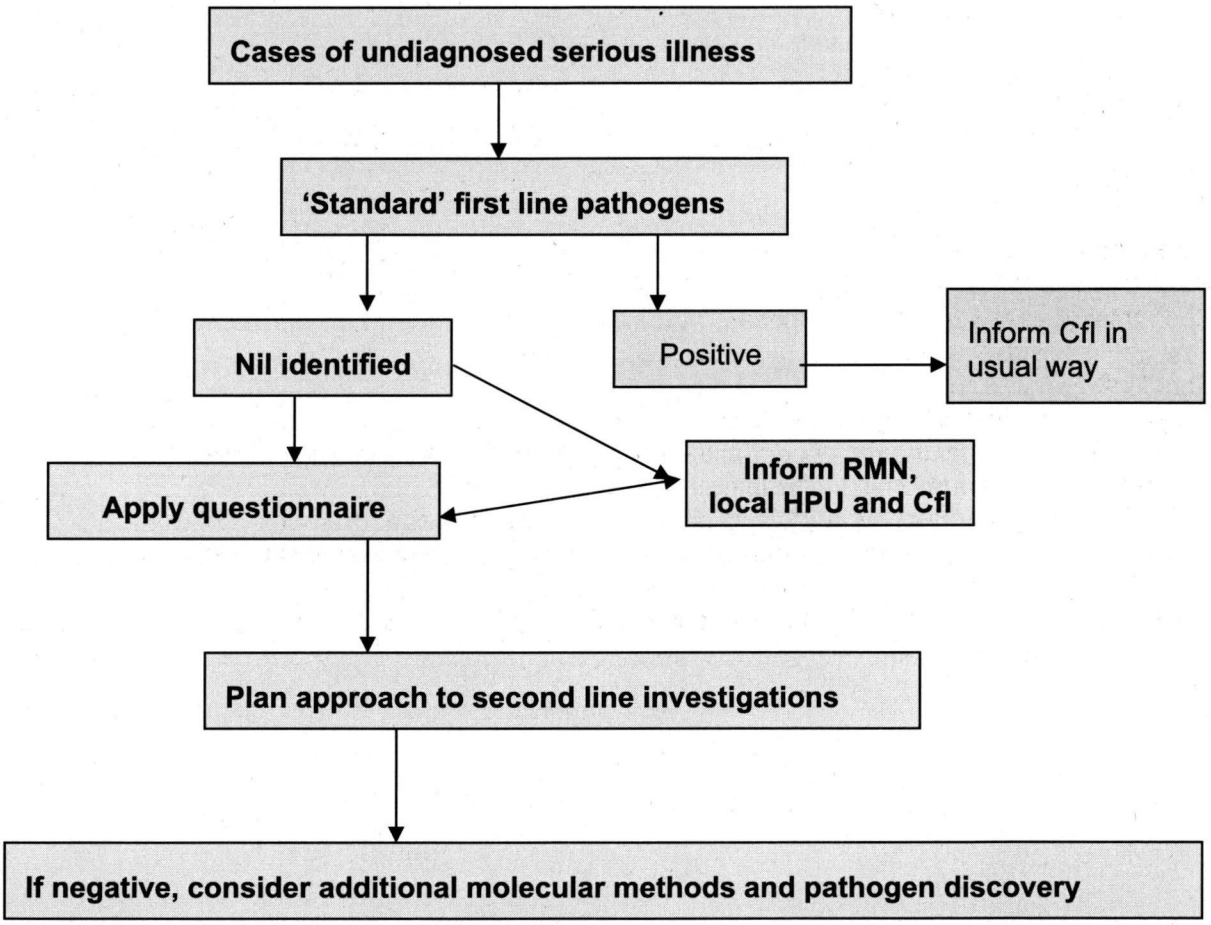
CONTENTS

Introduction

Outbreaks and incidents of "unusual" illnesses might have any of a number of causes, including infectious, chemical, nutritional, or radiological. The aetiological agent may remain undetermined, it may be that a novel organism is responsible, or that there has been an accidental or deliberate release of a chemical, biological or radiological agent. This document outlines the approach for the microbiological investigation of cases or clusters of serious undiagnosed illness.

Failure to identify a "conventional aetiology" should result in a direct approach to the Regional Microbiologist and to the Duty Officer at the local HPU, and then to the HPA Centre for Infections (CfI). The first points of contact at CfI for reporting the existence of a patient(s) who has presented with an unexplained illness of suspected infectious aetiology are given below. Specific microbiological or public health advice should be obtained from the relevant experts (see page 3). Clinical and epidemiological observation together with consultation and expert advice should result in one or more presumptive diagnoses, which can then be investigated appropriately.

The following diagram indicates the proposed investigation algorithm.



At CFI, please inform Mandy Walsh, Emerging Infections and Zoonoses Section (☎ 020 8327 7483), or if out of hours, the Duty Doctor at CfI (☎020 8200 4400)

Case definitions

For the purpose of focusing microbiological investigations and surveillance for an "unknown" infectious agent, it is essential to document in detail the clinical and epidemiological features of suspected cases. A working case definition should also be developed based on the initial clinical/epidemiological observations at the time. The following 'starting point' case definition encompasses the type of patient for which this guidance is appropriate. A cluster is defined here as two or more cases related in time and space. Single cases may be considered if they are severely ill, as may clusters of very severe or prolonged gastrointestinal disease.

A suitable case is :-

- aged between 1 and 60 years
- previously healthy
- has died or been admitted
- with a serious illness suggestive of an infectious process*
- with signs and symptoms relevant to these syndromes of interest

  Neurological: meningitis, encephalitis, encephalopathy, or neurological disturbance

  Respiratory: pneumonia, infiltrates, pneumonitis, or ARDS

  Sepsis: acute fulminating septicaemia, haemorrhagic disease, or shock

  Hepatitis/Jaundice: fulminant hepatitis, hepatic failure, or serious illness with jaundice

* Including for example: fever or history of fever, leucocytosis or leucopaenia, raised CRP or other marker of infection, histopathological evidence of an acute infectious process, or a physician-diagnosed syndrome consistent with an infectious aetiology.

Avian Influenza guidelines

Cases of severe respiratory disease may require to be investigated in order to rule out avian influenza. Appropriate algorithms for this can be found here:

http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1202115578855 (history of travel to endemic area)

http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1202115579653 (if not travelled to endemic area)

Recognising cases of unusual illness

The laboratory may become involved in investigating cases of unusual illness either before or after those cases have been recognised clinically as being unusual. If the laboratory is first to recognise such cases, please do the following:

- Liaise with the senior clinician in charge of the case and between you ensure that you have informed the local HPU, the Regional Microbiologist, and Mandy Walsh at CfI (☎ 020 8327 7483)
- Inform the infection control team, and ensure that appropriate infection control procedures are in place
- If appropriate, seek expert advice concerning the management of any potentially exposed laboratory staff. If relevant, make a list of staff who may have been exposed (name, age, address, contact details, their GP contact details, and type of exposure)
- Advice on the **initial investigation and management of outbreaks and incidents of unusual illnesses** is available on the HPA website. Sections of this document provide advice specifically for laboratories. Available at: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1201265888951
- Cases may be first recognised through post-mortem examinations, either coronial or routine. Section 7 of the above document provides advice on sampling by histopathology departments.

First line investigations

On receipt of enquiries about, or clinical material from, patients with 'undiagnosed' serious illness, the laboratory will naturally work through its own standard first line list of likely pathogens. This may require referral of samples, for example, for virology or PCR. Lists of first and second line pathogens are included overleaf for each of the clinical syndromes. *Please note that these lists are NOT intended to be a complete list of every possible pathogen, but rather some examples of rarer diagnoses to be considered.*

If first line diagnostic investigations are negative, use of the checklist *(below) and questionnaire (appendix 2) may guide the direction of further laboratory diagnostic testing, and ensure that small volume samples are reserved for the most appropriate tests.

Checklist

(see Appendix 2 for full questionnaire)

a) The patient	b) The samples
• What is the syndrome? ▪ **Neurological** :- meningitis, encephalitis, encephalopathy, or neurological disturbance ▪ **Respiratory**:- pneumonia, infiltrates, pneumonitis, or ARDS ▪ **Sepsis**:- acute fulminating septicaemia, haemorrhagic disease, or shock syndrome ▪ **Jaundice/Hepatitis**:- fulminant hepatitis, hepatic failure, or serious illness with jaundice • Rapidity of onset? Onset date? Duration of illness to date? (or to death) • Age, sex, and geographic location? • Contact with other sick people, at home or at work? • Occupational exposure? What do they do and where? How long have they worked there? • Hobbies or recreational exposure? Doing what, when, and where? • Animal exposure? Which animals/birds, where, and duration of exposure? Were the animals/birds sick or healthy? • Consumption of unpasteurised or 'unusual' food items, or home-processed foods? What, where, and how produced? When consumed? • National or foreign travel? If so where, how long for, and what type of exposure is likely to have occurred? • Compromised immune status, underlying disease or other risk factors?	• What samples are available? Or can be retrieved? • What tests have already been done? Negative on standard tests/cultures so far?* • What are now thought to be the most likely pathogens? • Is there a possibility of a BT agent? (particularly anthrax, smallpox, plague, tularemia, VHF, botulism) - **may require urgent referral to relevant labs at CFI or CEPR** • Consider referral of samples to other specialist or reference laboratory • Consider additional media or cell lines, atmosphere, range of temperatures, prolonged incubation etc. • Retain all samples * If an 'unidentifiable' organism has been isolated, refer to relevant reference lab (if known), or to laboratories at Cfl for identification (see below).

*** Identification of unknowns – please refer isolates to Cfl:**
1. Laboratory of Health Care Associated Infections for cellular fatty acid analysis (MIDI) and for 16S ribosomal DNA sequencing. (☎ 020 8327 7233)
2. Molecular Identification Services Unit (☎ 020 8327 7869)

Further diagnostic investigations

Once the first line pathogens have been excluded, samples can be referred as appropriate to a range of reference laboratories, and/or to laboratories at Cfl for additional expertise. In order that surveillance for Serious Undiagnosed Illness may be carried out more formally, and so that scientific/clinical advice and support may be given, please always notify one of the following:

Initial contact: Mandy Walsh, Emerging Infections and Zoonoses Section (☎ 020 8327 7483)

Virology: Dr. David Brown, Virus Reference Department (☎ 020 8327 6017)
Bacteriology: Dr. Robert George, Respiratory & Systemic Infections Department (☎ 020 8327 7222)
Public health: Dr. Dilys Morgan, Gastrointestinal, Emerging & Zoonotic Infections (☎ 020 8327 7474)

Molecular testing and a range of pathogen discovery options are also available at Cfl. The latter may be considered if there is a cluster of cases for whom a diagnosis cannot be reached. These options require further discussion with the Directors of the VRD and RSID (as above), and with the Molecular Identification Services Unit (☎ 020 8327 7869).

Reference laboratories are listed on page 7.
Specimen collection and storage guidance is in Appendix 1 on page 8.

1. Neurological :- meningitis, encephalitis, encephalopathy, or neurological disturbance

Likely 1st line

Streptococcus pneumoniae
Neisseria meningitidis
Haemophilus influenzae
Listeria monocytogenes
Staphylococcus aureus
ß-haemolytic streptococci
Enterobacteriaceae, including *Salmonella* spp

Mycobacterium spp

Clostridium botulinum

Herpes simplex virus
Varicella-Zoster virus
Enteroviruses
Parechovirus
Adenovirus
HHV6/7
Influenza viruses A&B

Cryptococcus neoformans

Examples of 2nd line organisms (depending on immune status, underlying disease, and possible exposures including travel history). *Note: this is not intended to be a complete list of possible aetiologies.*

Mycoplasma pneumoniae
Treponema pallidum
Borrelia spp
Leptospira spp
Nocardia spp

Brucella spp
Rickettsia spp
Ehrlichia spp
Bacillus anthracis
Yersinia pestis

Measles virus
Mumps virus
CMV
EBV
HIV

Lyssaviruses
Poliovirus
Arboviruses

LCMV
JC virus
Herpes B virus

Toxoplasma gondii

Acanthamoeba & *Naegleria* spp
Angiostrongylus cantonensis
Gnathostoma spinigerum
Baylisascaris procyonis

Candida spp
Histoplasma capsulatum
Coccidioides immitis

2. Respiratory:- pneumonia, infiltrates, pneumonitis, or ARDS

Likely 1st line

Streptococcus pneumoniae
Haemophilus influenzae
Moraxella catarrhalis
Staphylococcus aureus
Enterobacteriaceae

Mycoplasma pneumoniae
Legionella pneumophila
Mycobacterium spp

Influenza viruses A&B
Parainfluenza viruses
RSV
Adenoviruses
HSV
CMV

Pneumocystis jiroveci
Cryptococcus neoformans
Aspergillus fumigatus

Examples of 2nd line organisms (depending on immune status, underlying disease, and possible exposures including travel history). *Note: this is not intended to be a complete list of possible aetiologies.*

Chlamydophila pneumoniae
Chlamydophila psittaci
Coxiella burnetii
Pasteurella species
Neisseria meningitidis
Fusobacterium necrophorum and other anaerobes

Nocardia spp
Actinomyces spp

Bacillus anthracis
Yersinia pestis
Francisella tularensis
Burkholderia pseudomallei

Measles virus
VZV
EBV

Hantaviruses (e.g. Sin Nombre virus) [hantavirus pulmonary syndrome]

SARS coronavirus

Ascaris lumbricoides
Hookworms
Strongyloides stercoralis
Paragonimus westermanii

Candida species

Histoplasma capsulatum
Coccidiodes immitis
Blastomyces dermatitidis
Paracoccidioides brasiliensis
Cryptococcus gattii

3. Sepsis: Acute fulminating septicaemia, haemorrhagic disease, or shock

Likely 1st line

Escherichia coli
Streptococcus pneumoniae
Staphylococcus aureus
Other Enterobacteriaceae
Neisseria meningitidis
β-haemolytic streptococci

Pseudomonas aeruginosa and other non-fermentative GNRs

Haemophilus influenzae

Clostridium novyi and other clostridia

See 2nd line list – the possible viral agents require a relevant travel history

Examples of 2nd line organisms (depending on immune status, underlying disease, and possible exposures including travel history). *Note: this is not intended to be a complete list of possible aetiologies.*

Anaerobes including *Fusobacterium* (Lemierre's syndrome)
Leptospira spp
Salmonella Typhi & Paratyphi
Salmonella spp
Brucella spp
Vibrio spp

Mycobacterium species

Listeria monocytogenes
Streptococcus bovis
Bartonella species

Bacillus anthracis
Yersinia pestis
Francisella tularensis
Burkholderia mallei and *B. pseudomallei*

Dengue haemorrhagic fever/ Dengue shock syndrome

VHFs (CCHF, Lassa, Ebola, Marburg, New World Arenaviruses, etc)

Hantaviruses (Puumala, Dobrava, Seoul, Hantaan) [haemorrhagic fever with renal syndrome]

4. Hepatitis/Jaundice: Fulminant hepatitis, hepatic failure, or serious illness with jaundice

Likely 1st line

Leptospira spp

Pyogenic liver abscess (Enterobacteriaceae, *Staph aureus*, Anaerobes, Streptococcus *'milleri')*

HAV
HBV
HCV
HEV (Note: does NOT require a history of travel)
CMV
EBV

Examples of 2nd line organisms (depending on immune status, underlying disease, and possible exposures including travel history). *Note: this is not intended to be a complete list of possible aetiologies.*

Coxiella burnetii
Brucella spp
Rickettsia spp
Treponema pallidum
Borrelia burgdorferi
Salmonella Typhi

HSV

Haemorrhagic fever viruses
Yellow fever virus
Paramyxoviruses

Entamoeba histolytica
Toxoplasma gondii
Plasmodium falciparum

Specialist / Reference Laboratories

Links to all the laboratory-specific information can be found here http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1153846673361?p=1153846673361, or by selecting "Laboratories and Reference Facilities" from the left hand menu on the Infectious Diseases page on the HPA website www.hpa.org.uk

1. Colindale

- Virus Reference Department (VRD)
- Respiratory and Systemic Infections Laboratory (RSIL)
- Laboratory for Enteric Pathogens (LEP)
- Food Safety Microbiology Laboratory (FSML)
- Laboratory Health Care Associated infections (LHCAI)
- Sexually Transmitted Bacteria Reference Laboratory (STBRL)

2. Porton

- Special Pathogens Reference Unit (SPRU)

3. Other

- Anaerobe Reference Lab (Cardiff)
- Brucella Reference Unit (Liverpool)
- Leptospira Reference Unit (Hereford)
- Lyme Reference Unit (Southampton)
- Meningococcal Reference Unit (Manchester)
- Mycology Reference Laboratory (Bristol)
- Mycobacterium Reference Unit (London)
- Parasitology Reference Laboratory (London)
- Q fever Reference Laboratories (SPRU and Bristol)
- Toxoplasma Reference Laboratory (Swansea)

Appendix 1: Specimen Collection Protocol and Storage

The following is a guide for taking specimens from potential case-patients. In addition to examination in the local laboratory, it is likely that specimens will be referred to other laboratories for further microbiological analysis. A key objective of this guidance is to maximise the potential to identify an infective cause.

In the investigation of an unknown infection, in addition to culture techniques, it is likely that DNA amplification techniques to detect microbial specific nucleic acid (eg PCRs for eubacterial 16/23S rDNA, and specific/generic viral nucleic acids) will play a major role. Thus, normally sterile site samples are preferred wherever possible, providing they are relevant to the signs/symptoms displayed. Other investigations may include electron microscopy and serology.

The order of priority for specimen collection will in large part depend upon the clinical presentation.

Specimens should be collected and transported to the clinical microbiology laboratory as rapidly as possible for testing, storage, and possible subsequent transfer to a reference laboratory.

Samples

Blood cultures: for extended aerobic and anaerobic culture; ideally at least three sets of blood cultures collected over one hour, with at least one set prior to antibiotic administration. Consideration should be given to immediate post-mortem blood cultures if none have been collected in the previous few hours. Bottles negative after the standard incubation period should be retained for possible examination by PCR or other testing methods. Aliquot into 3x1ml containers and store at –70°C (or lowest temperature available).

Respiratory tract samples: sputum, broncho-alveolar lavage or similar, for standard cultures and virology. Nose and throat swabs may be appropriate depending upon signs and symptoms.

Biopsy tissues collected aseptically from local inflammatory lesion, necrosis or abscess, if surgical debridement is performed.

- as many samples as possible from multiple areas; quantity is important
- tissue placed in sterile containers for direct culture (aerobic and anaerobic) and storage
- formalin-fixed (10% buffered formalin) or paraffin embedded

Pus and vesicle fluid or swab of local lesion

- pus - as large a volume as feasible, placed in sterile containers for microscopy, aerobic and anaerobic cultures, and storage
- if no pus available, swab of lesion put immediately into transport medium
- vesicular fluid - should be swabbed and placed into viral transport medium and/or dried onto a microscope slide

Sera: acute (admission) and convalescent (near time of death, or on discharge) samples.

- optimal volume - 10 ml spun serum

Whole blood: acute and convalescent samples

- optimal volume - 10 ml whole blood (EDTA tube)

Urine: clean catch collection into sterile container

- optimal volume greater than 20ml

Body fluids: if clinically indicated - cerebrospinal, pleural, or pericardial fluids, or other specimens taken as part of the clinical workup.

Faeces/Stools. If ingestion of contaminated food or water is considered as a possible route of exposure, then faeces/stool samples should be collected for culture/microbial toxin detection whether GI symptoms are present or not.

Sample storage

Specimen	Requirements
Blood cultures	Negative blood culture bottles should be aliquoted into 3x1ml containers and stored at –70°C or lowest available temperature
Serum	Acute and convalescent samples. Store at –70°C or lowest available temperature
Whole blood in EDTA	Acute and convalescent samples, 2 x 5mls each if possible. ▪ Separate one, and keep both plasma and cell deposit. ▪ Store the other unseparated. All to be stored at –70°C or lowest temperature available
Respiratory samples	A portion of sputum, BAL or other respiratory sample, stored frozen at -70°C or lowest available temperature
Pus and tissue samples Tissues e.g.: • local inflammatory lesions or abscess material • liver • spleen • lung • kidney • heart • enlarged lymph nodes • bone marrow • other organs with gross pathologic changes • vitreous	Collect duplicate tissue fragments measuring ~ 1cc Pus or *non-fixed* tissue – store at -70°C or lowest available temperature Fixed samples (10% buffered formalin for 24 hours of fixation, and subsequent paraffin embedding. Antigenicity decreases for immuno-histochemical assays with prolonged formalin fixation), may be stored at room temperature
Stained and unstained slides	Stained slides may be kept at room temperature. Unstained slides should be frozen at the lowest available temperature
Urine	5mls, store at –70°C or lowest available temperature
Faeces/ stools	Store at –70°C or lowest available temperature
Other body fluids	e.g. cerebrospinal fluid, pleural fluid, pericardial fluid and other sterile site specimens. Store at –70°C or lowest available temperature

Appendix 2: Questionnaire

Completed by: .....
HPU / RMN / other
Date.....

a) The patient

- What is the syndrome?
  - **Neurological** :-

    Meningitis ☐ Encephalitis ☐ Encephalopathy ☐ Neurological disturbance ☐

    Details/other.....

  - **Respiratory**:-

    Pneumonia ☐ Infiltrates ☐ Pneumonitis ☐ ARDS ☐

    Details/Other.....

  - **Sepsis**:-

    Acute fulminating septicaemia ☐ Haemorrhagic disease ☐ Shock syndrome ☐

    Details/other .....

  - **Jaundice/Hepatitis**:-

    Fulminant hepatitis ☐ Hepatic failure ☐ Serious illness with jaundice ☐

    Details/other .....

- Age/DOB.....Sex: Male / Female... Ward.....
- Hospital .....
- HPU..... .....Region .....
- Where does the patient live ? .....
- Onset date? .... Rapidity of onset? .....
- Does the onset date relate to a possible exposure? .....
- Duration of illness to date? (or to death) .....
- **Contact with other sick people**? Y/N

If yes, Who? .....
Where? .....
Is their diagnosis known? Y/N If yes, please specify.....
Type of contact? .....
Duration of exposure? .....

- **Contact with sick animals or birds?** Y/ N

If yes, what animals/birds? (specify please) .....
Where? .....
What type of sickness did they have? .....
Type of contact. .....
Duration of exposure.....

- **Contact with healthy animals or birds?** Y / N

If yes, what animals/birds? .....
Where? .....
Type of contact.....
Duration of exposure .....

- **Occupational exposure?** Y / N

What occupation? .....
Where? .....
How long have they worked there? .....

- **Hobbies or recreational exposure?** Y / N

Doing what? .....
When? .....
Where? .....

- **Consumption of unpasteurised or 'unusual' food items, or home-processed foods**? Y / N

What? .....
How produced?... .....
Where consumed? .....When consumed? .....

- **National travel** Y / N **Foreign travel?** Y / N

Where? .....Where? .....
How long for? .....How long for? .....
What type of exposure likely? .....

- **Underlying disease or risk factors**? Y / N

(Please specify).....

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b) The samples (NB. Requirement for chain of evidence documentation if a deliberate release)

- What samples were taken?

Blood culture ☐ Urine ☐ Sputum ☐ CSF ☐ Pus ☐ Plasma ☐ Clot ☐ Buffy coat ☐ Other ☐
If other, please specify.....

- Which samples are still available?

Blood culture ☐ Urine ☐ Sputum ☐ CSF ☐ Pus ☐ Plasma ☐ Clot ☐ Buffy coat ☐ Other ☐
If other, please specify.....

- What tests have already been done?

Bacterial culture ☐ TB culture ☐ Viral culture ☐ Antigen detection ☐ PCR ☐ Serology ☐
Results?.....
.....
.....

- Negative on standard tests/cultures at source laboratory? Y / N
- Optimal methods used? Y/N
- What are now considered the most likely pathogens? .....
  .....

- Likelihood of BT agent? (particularly anthrax, smallpox, plague, tularemia, VHF, botulism) Y / N

Note:- may require urgent referral to relevant labs at HPA Cfl or HPA Porton (SPRU)

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.....

- Likelihood of an 'atypical' pathogen including zoonotic infections? (e.g. Q fever, chlamydiosis, leptospirosis, brucellosis, etc.)

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.....

- What samples/cultures have to be referred to other Specialist / Reference laboratories?
  .....
  .....
  .....
  .....
  .....