Unusual Illness, including Deliberate or Accidental Releases: Cardinal Signs and Tips for Key Biological Agents

If you see any of the following:

- **New or unusual clusters of infections with a number of ill people presenting at around the same time**
- **Cluster of patients with a similar syndrome with unusual characteristics or unusually high morbidity and mortality**
- **Unexplained increase in the incidence of a common syndrome above seasonally expected levels or occurring in an unusual setting or key sector of the community**
- **Single case of disease with unusual or unusually severe symptoms and no history suggesting an explanation for illness**

STOP/ THINK/ ACT!

! CONTACT:

☎ **Medical Microbiologist and/ or Infectious Disease (ID) Consultant through the hospital switchboard IMMEDIATELY**

☎ Director of Infection Prevention and Control (DIPC) through the hospital switchboard/ Infection Control Team

☎ Consultant in Communicable Disease Control (CCDC) at the local Health Protection Unit (HPU)

☎ 24hr Duty Doctor at HPA Colindale
Tel. 020 8200 4400 or 6868

Key Biological Agents	*Infection Control – Protection and Personal Protective Equipment (PPE) for health care workers caring for patients*
Not or rarely transmissible person-to-person: **Anthrax (Inhalational), Botulism, Tularemia, Glanders, Melioidosis, Q-fever, Brucellosis**	**Standard precautions:** Always use standard infection control procedures according to local policy. PPE comprises; single-use apron or if risk of extensive contamination full-length impermeable gown, gloves, wear surgical mask and eye protection for taking blood and splash hazards.
Transmissible from person-to-person via respiratory droplets: **Pneumonic Plague**	**Respiratory precautions:** PPE comprises; full-length gown or single-use apron, gloves, surgical mask, eye protection for taking blood and splash hazards.
Transmissible from person-to-person via airborne route and from contaminated fomites: **Smallpox, VHF**	**Airborne protection:** PPE comprises; single-use impermeable gown, apron, gloves, boots, head cover, correctly fitting respirator mask (ENV149 FFP3), face shield, visor, or goggles. Strict patient and environmental hygiene (washing, spillage management etc).
Decontamination of surfaces and/or spills: As per local protocol. Autoclave or incinerate clinical waste.	

Health Protection Agency

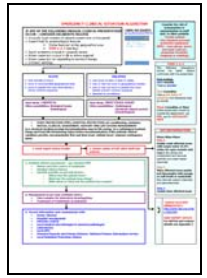
DH Department of Health

For information on **accessing stocks or pods** (containers with sufficient equipment, antidotes and antibiotics to meet the needs of 100 people) for immediate response in a major incident:
http://www.dh.gov.uk/en/Policyandguidance/Emergencyplanning/DH_4069610
Other modes of prophylaxis may also be available.
For links to **agent specific guidelines** and the **Investigation and Management of Unusual Illness** document: http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/DeliberateReleases/

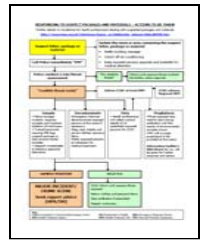
Key Documents

accessible at:
hpa.org.uk/deliberate_accidental_releases/biological

CBRN Incidents



Emergency Clinical Situations Algorithm



Suspect Packages and Materials Algorithm

Disease	Incubation in days (d)	Possible Presenting Symptoms	Clinical Features	Diagnostic Samples (use appropriate sterile container(s)) **SEEK ADVICE FROM MICROBIOLOGIST on diagnostic assays**	Infection Control	Initial Treatment (symptomatic and supportive therapy is essential in all cases) **SEEK ADVICE FROM ID CONSULTANT on treatment**	Post-exposure Prophylaxis **SEEK ADVICE FROM ID CONSULTANT on treatment**
ANTHRAX (INHALATIONAL) ***Bacillus anthracis***	1-6d (up to 60d)	**Initially flu-like** (fever, headache, myalgia and non-productive cough) May appear to be an exacerbation of chronic airways disease, unresponsive to usual treatment 2-4d later, **abrupt onset respiratory failure**	More likely with inhalation anthrax than other flu-like illness: nausea, vomiting, cyanosis, sweating, altered mental status and raised red blood cell count **Chest X-ray: widened mediastinum and/ or pleural effusions**	*Ideally samples should be taken before antibiotic treatment* Blood culture Clotted blood Respiratory samples (e.g. sputum, pleural fluid, lung aspirate) CSF	**No person-to-person transmission** **Standard precautions**	AVOID CEPHALOSPORINS **Adults:** Ciprofloxacin 400mg IV bd (oral dose 500mg bd) or Doxycycline 100mg oral bd Plus one or two other antibiotics e.g: rifampicin, gentamicin, chloramphenicol, penicillin, amoxicillin. **Children:** Ciprofloxacin 10mg/kg IV bd or 15mg/kg oral bd or Doxycycline 100mg oral bd (NB: >8yrs and >45kg only) Plus one or two other antibiotics **NB: Change to single antibiotic oral therapy when condition improves and susceptibility known** **Duration: 60d**	**CEPHALOSPORINS ARE INEFFECTIVE** **Adults:** Initial 5d in pods: Ciprofloxacin 500mg oral bd Further 55d: Ciprofloxacin 500mg oral bd or Doxycycline 100mg oral bd or Amoxicillin 500mg oral tds **Children:** Initial 5d: Ciprofloxacin 15mg/kg oral bd Further 55d: Ciprofloxacin 15mg/kg oral bd or Doxycycline 100mg oral bd (NB: >8yrs and >45kg only) or Amoxicillin 80mg/kg in tds

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BOTULISM ***Clostridium botulinum* neurotoxins**	Hours – 8d (depends on type and dose of toxin)	May be few or no symptoms before **sudden respiratory paralysis** Nausea, vomiting, diarrhoea follow ingestion of toxin	**Symmetrical descending flaccid paralysis with prominent bulbar palsies, afebrile and no change in sensory awareness** **Double or blurred vision and speech difficulties are common** Respiratory paralysis may be fatal Gastrointestinal symptoms progress from vomiting/ diarrhoea to constipation	*Botulism is primarily a clinical diagnosis* Clotted blood (at least 10ml) Faeces/ vomit Bronchoalveolar lavage Wound pus or wound tissue	**No person-to-person transmission** **Standard precautions**	May need early intubation and ventilation **Antitoxin** - slow IV infusion Give on suspicion of diagnosis **as soon as possible** after symptoms start Contact 24 hr Duty Doctor at HPA Colindale on 0208200 6868 for details of how to get anti-toxin	None

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BRUCELLOSIS ***Brucella spp.***	5-30d (up to 6 months)	Variable symptoms onset may be acute or insidious Persistent fever, fatigue, joint pain	**Prolonged fever, debilitation, weight loss, general malaise, muscle and joint pain, sweating** Dry cough, hepato-splenomegaly, arthritis, lympha-denopathy, orchitis, meningo-encephalitis or endocarditis	*Ideally samples should be taken before antibiotic treatment* Blood culture or bone marrow Aspirate or biopsy of enlarged lymph nodes, liver, CSF, or joint fluid	**Person-to-person transmission documented but very rare** **Standard precautions**	**Adults:** Doxycycline 100mg oral bd plus either Rifampicin 600mg oral daily or Gentamicin 5mg/kg IV daily **Pregnant or breast-feeding women:** Rifampicin 600mg oral daily **Children:** Cotrimoxazole (sulfamethoxazole 40mg/kg + trimethoprim 8mg/kg) oral daily plus either Rifampicin 10-15mg/kg oral daily or Gentamicin 5mg/kg IV daily **Duration: 6 weeks (2 wks for gentamicin)**	**Adults:** Doxycycline 100mg oral bd plus either Rifampicin 600mg oral daily or Cotrimoxazole 960mg oral bd **Pregnant or breast-feeding women:** Rifampicin 600mg oral daily **Children:** Cotrimoxazole (sulfamethoxazole 40mg/kg + trimethoprim 8mg/kg) oral daily plus Rifampicin 10-15mg/kg oral daily **Duration: 3 weeks**

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MELIOIDOSIS ***Burkholderia pseudomallei*** (GLANDERS) *(Burkholderia mallei)*	1-21d (long latent intervals – may be years)	Fever Focal sepsis, eg empyaema, often with bacteraemia Variable, may be acute with rapid progression	Pneumonia Skin or soft tissue infection with multiple abscesses possible Sepsis syndrome	*Ideally samples should be taken before antibiotic treatment* Blood culture Clotted blood Pus Sputum Urine	**Person-to-person transmission is extremely rare** **Standard precautions**	Initial treatment with: Ceftazidime 120mg/kg/day tds IV or Meropenem 50mg/kg/day tds IV or Imipenem with cilastin 50mg/kg/day tds IV **Duration: 14d** Followed by oral eradication treatment: Doxycycline 4mg/kg/day plus Cotrimoxazole (sulfamethoxazole 40mg/kg + trimethoprim 8mg/kg) or Coamoxiclav 60/15 mg/kg/day **Duration: 20 weeks**	Doxycycline 100mg oral bd or Cotrimoxazole 960mg oral bd **Duration: 7d**

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PNEUMONIC PLAGUE ***Yersinia pestis***	1-4d	Sudden onset **severe febrile respiratory illness**	**Fulminant pneumonia** often with haemoptysis Rapid progression of respiratory failure, septicaemia and shock **Chest X-ray pneumonic consolidation** (and haemoptysis) distinguishes plague from inhalational anthrax Complications include septicaemic plague and plague meningitis	*Ideally samples should be taken before antibiotic treatment* Blood culture Clotted blood Sputum	**Transmissible from person-to-person by the droplet route or by aerosol-generating procedures** **Respiratory precautions**	**Adults:** Gentamicin (first choice in pregnancy) 5mg/kg IM or IV daily or Doxycycline 100mg oral bd or Ciprofloxacin 400mg IV bd or 500mg oral bd Or for meningitis: Chloramphenicol 25mg/kg qds **Children:** Ciprofloxacin 10mg/kg IV bd or 15mg/kg oral bd or Doxycycline 100mg oral bd (NB: >8yrs and >45kg only) **Duration: 14d**	**Adults:** Initial 5 days in pods: Ciprofloxacin 500mg oral bd Further 2 days: Ciprofloxacin 500mg oral bd **Children:** Initial 5d: Ciprofloxacin 15mg/kg oral bd Further 2d: Ciprofloxacin 15mg/kg oral bd or Doxycycline 100mg oral bd (NB: >8yrs and >45kg only) **Duration: 7d**

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Q-FEVER ***Coxiella burnetii***	7-30d	Flu-like illness, fever, cough	**Pneumonia**, may also get hepatitis, neurological symptoms, thyroiditis, anaemia, gastroenteritis, rash, endocarditis, glomerulonephritis **Chronic malaise and fatigue** may last for months	Clotted blood	**Person-to-person transmission is rare** **Standard precautions**	**Adults:** Tetracycline 500mg qds or Doxycycline 100mg bd or Cotrimoxazole 960mg bd **Children:** Cotrimoxazole (sulfamethoxazole 40mg/kg + trimethoprim 8mg/kg) oral daily **Duration: 7-14d** (continue treatment for at least 3d after remission of fever)	**Prophylaxis is not effective if given within 7d of exposure and may prolong onset if given within this time period** **Adults:** Doxycycline 100mg bd or Cotrimoxazole 960mg bd **Children:** Cotrimoxazole (sulfamethoxazole 40mg/kg and trimethoprim 8mg/kg) oral daily **Duration: 7d** NB : start 8-12d post-exposure

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SMALLPOX **Variola Virus**	7-17d	**Sudden onset high fever** 2-3d later **maculo-papular rash**	**Vesicular Rash** more prominent on face and extremities than trunk - erupts simultaneously (Not in crops) Maculo-papular to vesicular to pustular with deep seated lesions in dermis - progresses to scabs	Vesicular/ pustular fluid Scab biopsy Pharyngeal swab Clotted blood	**Transmissible droplets or fomites** **Airborne precautions** **Immediate isolation** (negative pressure, HEPA filtration) Infectious from onset of fever until last scab falls off **Identify contacts –** vaccination and monitoring as appropriate	*Consult Smallpox Diagnosis Expert through the local ambulance service* Vaccination is highly effective in the first 4d of incubation period Antibiotics for secondary infection Consider antivirals	Vaccine within 3d of exposure Monitor for fever and symptoms for 16d

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TULAREMIA ***Francisella tularensis***	1-21d (usually 2-5d)	Pneumonic forms a flu-like illness, then systemic symptoms 3-5d later 3 main forms: • **Pneumonic** • **Typhoidal** • **Septicaemic**	**Pneumonic:** fever, non-productive cough, pharyngitis, pleuritic chest pain, and hilar lymphadenopathy, progressing to severe pneumonitis and pleural effusion. **Typhoidal:** diarrhoea and vomiting. **Septicaemic:** acute Gram negative sepsis Also possible ocular lesions, skin ulcers, oropharyngeal or glandular disease	*Ideally samples should be taken before antibiotic treatment* Blood culture Clotted blood Sputum or pharyngeal washings Pleural fluid Fasting gastric aspirate	**No person-to-person transmission** **Standard precautions**	**Adults:** Gentamicin First choice in pregnancy. 5mg/kg IM or IV daily or Ciprofloxacin 400mg IV bd (oral dose 500mg bd) **Children:** Gentamicin 2.5mg/kg IM/IV tds Ciprofloxacin 15mg/kg IV bd, then oral 10-15 mg/kg bd	**Adults:** Initial 5d in pods: Ciprofloxacin 500mg oral bd Further 9d: Ciprofloxacin 500mg oral bd or Doxycycline 100mg oral bd **Children:** Initial 5d: Ciprofloxacin 15mg/kg oral bd Further 9d: Ciprofloxacin 15mg/kg oral bd or Doxycycline 100mg oral bd (NB: >8yrs and >45kg only) Doxycycline 2.2 mg/kg oral bd **Duration: 14d**

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VHF (Viral Haemorrhagic Fever) **Lassa fever, Crimean/Congo fever (CCHF), Ebola and Marburg viruses**	Lassa fever 3-21d CCHF 1-12d Ebola HF 2-21d Marburg HF 3-16d	Acute febrile illness with prostration and signs of increased vascular permeability and circulatory failure **NB: Clinical symptoms and features vary with infecting agent-onset may be flu-like with sustained high temperature** **Haemorrhage is marked in CCHF, with nose and gum bleeding as first signs, otherwise it is often a late feature**	**Febrile illness with facial oedema and tendency to haemorrhage (e.g. nosebleed)** Vomiting and diarrhoea (may be bloody) and petechial or purpuric rashes are common Warning signs are rapid rise in Aspartate transaminase and sometimes a rapid fall in platelet count.	Blood culture Clotted blood	**Person-to-person transmission only through blood and body fluids (via coughing or vomiting)** **Airborne precautions** Patients should be admitted to a designated high security infectious disease unit or an intermediate isolation facility **Identify contacts -** make aware of signs and symptoms - Local HPU organise follow-up	Supportive care with hydration maintenance Minimal trauma (injections or parenteral interventions) Replacement of coagulation factors and platelets may be of value Ribavirin (Lassa fever and CCHF): Loading dose 30 mg/kg IV; first 4d 16 mg/kg IV every 6 hrs; next 6d 8 mg/kg IV every 8 hrs **Duration: 10d**	PEP is only based on an appropriate risk assessment after discussion with consultant specialist