Appendix D: Infections always regarded as serious and their reference standards

- Pneumonia:[1-3]
  Infiltrate on chest radiograph or computed tomography (CT) within 7 days after inclusion
- Infectious acute exacerbation of COPD:[4]
  An acute worsening of symptoms such as dyspnoea, cough and/or sputum production in a patient with a spirometry confirmed COPD (post bronchodilator $FEV_1/FVC < 0.70$), resulting in hospital admission and anti-infectious treatment
- Influenza infection requiring hospital admission:[5]

  Confirmation of the presence of influenza virus (type A or B) in an upper respiratory tract specimen by the use of reverse transcription polymerase chain reaction (RT-PCR) in a hospitalised patient
- Severe Acute Respiratory Syndrome Corona virus (SARS-CoV-2) infection requiring hospital admission:

  Confirmation of the presence of SARS-CoV-2 infection in a nasopharyngeal specimen by the use of reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay in a patient who was hospitalised because of a suspicion of SARS-CoV-2 infection.
- Sepsis:[6]
  Suspected or blood culture proven infection and an acute increase of ≥2 SOFA points (organ dysfunction), following the Sepsis-3 guidelines
- Complicated UTI:[7]
  Uropathogen growth of at least 10^5 colony forming units/ml in urine culture, with clinical symptoms and signs attributable to a complicated UTI, or abnormal imaging results such as CT, DMSA scans or ultrasound
- Infectious encephalitis/meningitis:[8]
  Pleocytosis and pathogen identification from cerebrospinal fluid (viral or bacterial) via culture or PCR
- Osteomyelitis:[7]
  - Single pathogen from bone aspirate
    OR
  - radiographic imaging compatible with osteomyelitis combined with a positive blood culture
- Prosthetic joint infections:[9]

Radiolucency surrounding prosthesis on radiography

- Septic (infectious) arthritis:[10,11]
  Single pathogen from synovial fluid aspirate
- Infective endocarditis (IE):[12,13]
  A diagnosis of infective endocarditis is definite if the following pathological OR clinical criteria are met (modified Duke criteria):

    - One of these pathological criteria:

    - Histology or culture of a cardiac vegetation, an embolized vegetation, or intracardiac abscess from the heart finds microorganisms
    - Active endocarditis

    - One of these combinations of clinical criteria:
    - 2 major clinical criteria
    - 1 major and 3 minor criteria
    - 5 minor criteria
      (Major clinical criteria: Positive blood culture with typical IE microorganism, evidence of endocardial involvement with positive echocardiogram)
      (Minor clinical criteria: e.g. a predisposing factor, fever >38°C, immunological phenomena, microbiological phenomena…)

- Infectious cholecystitis:[14]
    - combination of clinical features such as right epigastric pain, a palpable gallbladder, and Murphy's sign, and positive findings on imaging: abdominal ultrasound or abdominal CT with intravenous contrast
      OR
    - pathological confirmation after surgery
- Infectious spondylitis or spondylodiscitis:[15]
    - Magnetic resonance imaging (MRI) of the spine.
    - If an MRI cannot be obtained: CT scan or a positron emission tomography (PET) scan.
- Appendicitis:[16]
    - Positive findings on CT or MRI. Ultrasound imaging serves as a second choice.
      OR
    - pathological confirmation after surgery
- Complicated diverticulitis:[17-22]

Clinical assessment including signs of peritonitis, ileus, rectal bleeding, local muscular resistance, hypotension with or without laboratory tests such as CRP>100 mg/L, followed by:

  - CT-scan of abdomen and pelvis

    OR

  - ultrasound imaging if CT not available

    OR

  - pathological confirmation after surgery

- Cellulitis: acute, suppurated inflammation of the subcutaneous tissues

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