CRISIS CPCCRN Protocol 003
Endpoint Determination

I. Introduction

The CRISIS Protocol 003 Endpoint Committee will comprise the DCC Principal Investigator and members of the CPCCRN Steering Committee. The adjudication process will consist of an initial review and determination of the endpoint status by the CPCCRN site investigator. He/she will be responsible for initially classifying all nosocomial sepsis and infection events. All cases will then be presented to and reviewed by the Endpoint Committee at the quarterly Steering Committee meetings. For all cases, information regarding nosocomial sepsis and infection events will be reviewed in a blinded manner (without any information regarding the identity of the treatment assignment).

Classification principles will be established by the Committee before the classification and adjudication process begins.

II. Study Efficacy Variables

The CRISIS Protocol 003 Endpoint Committee is responsible for the adjudication and classification of all nosocomial sepsis and infection events which are the primary study endpoints defined in this trial. The primary endpoint of this study is the time (hours) between admission to the PICU and occurrence of nosocomial infection or clinical sepsis in PICU patients who have endotracheal tubes, central venous catheters, or urinary catheters.

The definitions of nosocomial infection and clinical sepsis are as follows:

Nosocomial: defined as occurrence 48 hours after admission until 5 days after discharge from the PICU.

Infection: microbiologically (culture, antigen, PCR, or antibody) proven infection in a patient with fever, hypothermia, chills, or hypotension.

Clinical Sepsis: must meet at least one of the following two criteria:

1. Criterion 1

- Patient has at least *one* of the following clinical signs or symptoms with no other recognized cause: fever (≥ 38° C), hypotension (systolic BP ≤ 90 mm Hg), or oliguria (≤ 20 cc/hr); AND
- Blood culture *not* done or *no* organisms or antigen detected in blood; AND
- No apparent infection at another site; AND
- Physician institutes treatment for sepsis

2. Criterion 2
   - Patient ≤ 1 year of age has at least *one* of the following clinical signs or symptoms with no other recognized cause: fever (≥ 38°C), hypothermia (≤ 37°C), apnea, or bradycardia; AND
   - Blood culture *not* done or *no* organisms or antigen detected in blood; AND
   - No apparent infection at another site; AND
   - Physician institutes treatment for sepsis

Lymphopenia: will be defined as an absolute lymphocyte count of less than 1000 per mm^3.

Prolonged lymphopenia: will be defined as an absolute lymphocyte count of less than 1000 per mm^3 occurring for greater than seven PICU days.

PICU day: will be defined as a calendar day during any part of which the child is an in-patient in the PICU.

Ventilated day: will be defined as a PICU day during any part of which the child requires mechanical ventilation support greater than chronic baseline settings by endotracheal tube, tracheostomy, or face mask.

Resistant organism: is defined according to CDC criteria e.g. MRSA, ESBL, VRE, Fluconazole resistant candida/fungus etc, and/or the presence of MICs which are > 1 for all antibiotics listed in the susceptibility chart.

CDC Definitions of Nosocomial Infections are listed in the Appendix B.

The study period is defined as the period from the first dose of randomized medication (study day 1) to study day 28. For patients who are prematurely withdrawn from study medication, the study period is still the same. These patients will continue to be reviewed for adverse events until discharge from the hospital, or for 28 days following enrollment because this study is designed as an intention-to-treat study.

III. Study Endpoints and Reporting Procedures

All study endpoints will be recorded by the responsible investigator on the appropriate TrialDB forms and, together with supportive documentation, provided to the sponsor in a timely fashion. The protocol provides guidance to the investigator in the identification of study endpoints and delineates their reporting responsibilities.

IV. Study Endpoint Case Report Forms

Each Endpoint event will be systematically reviewed and validated by the Endpoint Committee. For this purpose, the CPCCRN Protocol 003 Endpoint Form (see Appendix A) has been created.

The investigator at each site will be responsible for the timely completion and transmission of final status forms which includes their assessment of nosocomial sepsis and infection. The DCC is responsible for the archiving of TrialDB forms and supportive documentation and their provision to the members of the Endpoint Committee prior to each scheduled committee meeting.

All endpoint forms and supportive documents, such as, discharge notes, admission notes, autopsy and postmortem notes, clinical laboratory tests and medical surgical studies will be in the English language.

V. Endpoint Documentation and Data Flow

The DCC will review all data in TrialDB including the Investigator's Final Assessment of Nosocomial Sepsis and Infection and supportive documentation for accuracy, consistency and completeness and contact the site regarding queries and/or deficiencies, as needed. The DCC will request additional supportive information, as deemed necessary. Each individual endpoint will be reviewed in advance of the scheduled Committee meeting by the DCC Principal Investigator and independently compared to the endpoint determination made by data generated from TrialDB.

At a Committee meeting each study endpoint scheduled for adjudication will be presented to the full Committee by the DCC Principal investigator. The Endpoint/Steering Committee will provide comments on the DCC review. The DCC will be responsible for the documentation of the outcome of each adjudicated event on the appropriate Endpoint Committee Classification Form. If due to incomplete or inadequate

information pertaining to an event the Committee is unable to complete the adjudication process, that endpoint will be tabled and placed on the agenda for review at the next Committee meeting, pending the provision of the additional information requested.

Once the adjudication and classification process is completed for an endpoint, the DCC PI will complete, sign and date the appropriate Endpoint Committee Classification Form. The original completed and signed classification forms will be maintained by the DCC. The forms will be entered into the CPCCRN Protocol 003 trial TrialDB system by DCC staff.

A. Supportive Documentation

During the course of the trial, study investigators are instructed to provide the DCC with pertinent data and documentation detailing the succession of events, supportive diagnoses, and descriptions of interventions and/or procedures that pertain to a study event submitted for adjudication. Documentation that may prove helpful to Committee members in the adjudication and classification of sepsis and infection events includes, but is not limited to, the following:

1. Physician Narrative
2. Physician Referral Letter
3. Admitting Hospital Note
4. Lab Results
5. Imaging studies
6. Discharge Summary
7. Autopsy Report
8. Death Certificate

Any of this documentation that is not already uploaded into TrialDB may be requested by the Endpoint Committee if necessary to complete their review.

Appendix A: Endpoint Committee Classification Forms

Endpoint Summary

TrialDB number: _____ Date of birth: _____
Date of PICU admission: _____ Date of randomization: _____
Date patient last evaluated: _____ Date of Death: _____

Patient Status

☐ Completed Patient ☐ Early Withdrawal

☐ Existing Sepsis ☐ Existing Infection

Endpoint Status

Yes	No			
☐	☐	Nosocomial Clinical Sepsis	Number of Sepsis Events	_____
☐	☐	Nosocomial Clinical Infection	Number of Infection Events	_____

Type of Event	Date	Time

Type of Event	Date	Time

Endpoint Definitions

The primary endpoint of this study is the time (hours) between admission to the PICU and occurrence of nosocomial infection or clinical sepsis in PICU patients who have endotracheal tubes, central venous catheters, or urinary catheters:

Nosocomial Clinical Sepsis: Patient has at least one of the following clinical signs or symptoms with no other recognized cause:
Fever (≥ 38°C), hypotension (systolic BP ≤ 90 mm Hg), or oliguria (≤ 20cc/hr); AND Blood culture *not* done or *no* organisms or antigen detected in blood; AND no apparent infection at another site; AND physician institutes treatment for sepsis

Nosocomial Clinical Infection: Microbiologically (culture, antigen, PCR, or antibody) proven infection in a patient with:
Fever, hypothermia, chills, hypotension

Comments:

_____

_____

_____

_____

Signature:_____ Date:_____

Data Coordinating Center PI, CRISIS Protocol 003

Appendix B: CDC Definitions of Nosocomial Infections

From: Horan TC, Gaynes RP. Surveillance of nosocomial infections. In:Hospital Epidemiology and Infection Control, 3rd ed., Mayhall CG, editor. Philadelphia:Lippincott Williams & Wilkins, 2004:1659-1702.

APPENDIX A-1. CDC DEFINITIONS OF NOSOCOMIAL INFECTIONS [EXCLUDING PNEUMONIA (SEE APPENDIX A-2)]

Listing of Major and Specific Site Codes and Descriptions

UTI **Urinary Tract Infection**
- SUTI Symptomatic urinary tract infection
- ASB Asymptomatic bacteriuria
- OUTI Other infections of the urinary tract

SSI **Surgical Site Infection**
- SKIN Superficial incisional site, except after CBGB[1]
- SKNC After CBGB, report SKNC for superficial incisional infection at chest incision site
- SKNL After CBGB, report SKNL for superficial incisional infection at leg (donor) site
- ST Deep incisional surgical site infection, except after CBGB
- STC After CBGB, report STC for deep incisional surgical site infection at chest incision site
- STL After CBGB, report STL for deep incisional surgical site infection at leg (donor) site
- Organ/Space Surgical Site Infection
  Indicate specific site:
  BONE, BRST, CARD, DISC, EAR, EMET, ENDO, EYE, GIT, IAB, IC, JNT, LUNG, MED, MEN, ORAL, OREP, OUTI, SA, SINU, UR, VASC, VCUP.

PNEU **Pneumonia (See Appendix A:2)**
- PNU 1
- PNU 2
- PNU 3

BSI **Bloodstream Infection**
- LCBI Laboratory-confirmed bloodstream infection
- CSEP Clinical sepsis

BJ **Bone and Joint Infection**
- BONE Osteomyelitis
- JNT Joint or bursa
- DISC Disc space

CNS **Central Nervous System Infection**
- IC Intracranial infection
- MEN Meningitis or ventriculitis
- SA Spinal abscess without meningitis

CVS **Cardiovascular System Infection**
- VASC Arterial or venous infection
- ENDO Endocarditis
- CARD Myocarditis or pericarditis
- MED Mediastinitis

EENT **Eye, Ear, Nose, Throat, or Mouth Infection**
- CONJ Conjunctivitis
- EYE Eye Other than conjunctivitis
- EAR Ear Mastoid
- ORAL Oral Cavity (mouth, tongue, or gums)
- SINU Sinusitis
- UR Upper respiratory tract, pharyngitis, laryngitis, epiglottitis

GI **Gastrointestinal System Infection**
- GE Gastroenteritis
- GIT Gastrointestinal (GI) tract
- HEP Hepatitis
- IAB Intraabdominal, not specified elsewhere
- NEC Necrotizing enterocolitis

LRI **Lower Respiratory Tract Infection, Other Than Pneumonia**
- BRON Bronchitis, tracheobronchitis, tracheitis, without evidence of pneumonia
- LUNG Other infections of the lower respiratory tract

REPR **Reproductive Tract Infection**
- EMET Endometritis
- EPIS Episiotomy
- VCUF Vaginal cuff
- OREP Other infections of the male or female reproductive tract

SST **Skin and Soft Tissue Infection**
- SKIN Skin
- ST Soft tissue
- DECU Decubitus ulcer
- BURN Burn
- BRST Breast abscess or mastitis
- UMB Omphalitis
- PUST Infant pustulosis
- CIRC Newborn circumcision

SYS **Systemic Infection**
- DI Disseminated infection

Definitions of Infection Sites

INFECTION SITE: Symptomatic urinary tract infection
CODE: UTI-SUTI
DEFINITION: A symptomatic urinary tract infection must meet at least one of the following criteria:

Criterion 1: Patient has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness
and
patient has a positive urine culture, that is, $\geq 10^5$ microorganisms per cm^3 of urine with no more than two species of microorganisms.

Criterion 2: Patient has at least *two* of the following signs or

[1] CBGB, coronary artery bypass graft with both chest and donor site incisions.

symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness
and
at least *one* of the following:
a. Positive dipstick for leukocyte esterase and/or nitrate
b. Pyuria (urine specimen with ≥10 WBC/mm^3 or ≥3 WBC/high power field of unspun urine)
c. Organisms seen on Gram stain of unspun urine
d. At least *two* urine cultures with repeated isolation of the same uropathogen (gram-negative bacteria or *S. saprophyticus*) with ≥10^2 colonies/mL in nonvoided specimens
e. ≤10^5 colonies/mL of a single uropathogen (gram-negative bacteria or *S. saprophyticus*) in a patient being treated with an effective antimicrobial agent for a urinary tract infection
f. Physician diagnosis of a urinary tract infection
g. Physician institutes appropriate therapy for a urinary tract infection

Criterion 3: Patient ≤1 year of age has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting
and
patient has a positive urine culture, that is, ≥10^5 microorganisms per cm^3 of urine with no more than two species of microorganisms.

Criterion 4: Patient ≤1 year of age has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting
and
at least *one* of the following:
a. Positive dipstick for leukocyte esterase and/or nitrate
b. Pyuria (urine specimen with ≥10 WBC/mm^3 or ≥3 WBC/high power field of unspun urine)
c. Organisms seen on Gram stain of unspun urine
d. At least *two* urine cultures with repeated isolation of the same uropathogen (gram-negative bacteria or *S. saprophyticus*) with ≥10^2 colonies/mL in nonvoided specimens
e. ≤10^5 colonies/mL of a single uropathogen (gram-negative bacteria or *S. saprophyticus*) in a patient being treated with an effective antimicrobial agent for a urinary tract infection
f. Physician diagnosis of a urinary tract infection
g. Physician institutes appropriate therapy for a urinary tract infection

COMMENTS:

- A positive culture of a urinary catheter tip is *not* an acceptable laboratory test to diagnose a urinary tract infection.
- Urine cultures must be obtained using appropriate technique, such as clean catch collection or catheterization.
- In infants, a urine culture should be obtained by bladder catheterization or suprapubic aspiration; a positive urine culture from a bag specimen is unreliable and should be confirmed by a specimen aseptically obtained by catheterization or suprapubic aspiration.

INFECTION SITE: Asymptomatic bacteriuria
CODE: UTI-ASB
DEFINITION: An asymptomatic bacteriuria must meet at least one of the following criteria:

Criterion 1: Patient has had an indwelling urinary catheter within 7 days before the culture
and
patient has a positive urine culture, that is, ≥10^5 microorganisms per cm^3 of urine with no more than two species of microorganisms
and
patient has *no* fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness.
Criterion 2: Patient has *not* had an indwelling urinary catheter within 7 days before the first positive culture
and
patient has had at least *two* positive urine cultures, that is, ≥10^5 microorganisms per cm^3 of urine with repeated isolation of the same microorganism and no more than two species of microorganisms
and
patient has *no* fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness.

COMMENTS:

- A positive culture of a urinary catheter tip is *not* an acceptable laboratory test to diagnose bacteriuria.
- Urine cultures must be obtained using appropriate technique, such as clean catch collection or catheterization.

INFECTION SITE: Other infections of the urinary tract (kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric spaces)
CODE: SUTI-OUTI
DEFINITION: Other infections of the urinary tract must meet at least one of the following criteria:

Criterion 1 Patient has organisms isolated from culture of fluid (other than urine) or tissue from affected site.
Criterion 2: Patient has an abscess or other evidence of infection seen on direct examination, during a surgical operation, or during a histopathologic examination.

Criterion 3: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), localized pain, or localized tenderness at the involved site
and
at least *one* of the following:
a. Purulent drainage from affected site

b. Organisms cultured from blood that are compatible with suspected site of infection
c. Radiographic evidence of infection, for example, abnormal ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), or radiolabel scan (gallium, technetium)
d. Physician diagnosis of infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space
e. Physician institutes appropriate therapy for an infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space

Criterion 4: Patient ≤1 year of age has at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, lethargy, or vomiting
and
at least *one* of the following:
a. Purulent drainage from affected site
b. Organisms cultured from blood that are compatible with suspected site of infection
c. Radiographic evidence of infection, for example, abnormal ultrasound, CT, MRI, or radiolabel scan (gallium, technetium)
d. Physician diagnosis of infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space
e. Physician institutes appropriate therapy for an infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space

REPORTING INSTRUCTION:

- Report infections following circumcision in newborns as SST-CIRC.

INFECTION SITE: Surgical site infection (superficial incisional)
CODE: SSI-(SKIN) except following the NNIS operative procedure, CBGB. For CBGB[a] only, if infection is at chest site, use SKNC (skin-chest) or if at leg (donor) site, use SKNL (skin-leg)
DEFINITION: A superficial SSI must meet the following criteria:
Infection occurs within 30 days after the operative procedure
and
involves only skin and subcutaneous tissue of the incision
and
patient has at least *one* of the following:
a. Purulent drainage from the superficial incision
b. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
c. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, *and* superficial incision is deliberately opened by surgeon, *unless* incision is culture-negative
d. Diagnosis of superficial incisional SSI by the surgeon or attending physician

REPORTING INSTRUCTIONS:

- Do *not* report a stitch abscess (minimal inflammation and discharge confined to the points of suture penetration) as an infection.
- Do not report a localized stab wound infection as SSI, instead report as skin or soft tissue infection, depending on its depth.
- Report infection of the circumcision site in newborns as SST-CIRC. Circumcision is not an NNIS operative procedure.
- Report infection of the episiotomy site as REPR-EPIS. Episiotomy is not an NNIS operative procedure.
- Report infected burn wound as SST-BURN.
- If the incisional site infection involves or extends into the fascial and muscle layers, report as a deep incisional SSI.
- Classify infection that involves *both* superficial and deep incision sites as deep incisional SSI.
- Report culture specimen from superficial incisions as ID (incisional drainage).

INFECTION SITE: Surgical site infection (deep incisional)
CODE: SSI-[ST (soft tissue)] except following the NNIS operative procedure, CBGB. For CBGB only, if infection is at chest site, use STC (soft tissue-chest) or if at leg (donor) site, use STL (soft tissue-leg)
DEFINITION: A deep incisional SSI must meet the following criteria:
Infection occurs within 30 days after the operative procedure if no implant[b] is left in place or within 1 year if implant is in place and the infection appears to be related to the operative procedure
and
involves deep soft tissues (e.g., fascial and muscle layers) of the incision
and
patient has at least *one* of the following:
a. Purulent drainage from the deep incision but not from the organ/space component of the surgical site
b. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C) or localized pain or tenderness, *unless* incision is culture-negative
c. An abscess or other evidence of infection involving the deep incision is found on direct

[a] CBGB, coronary artery bypass graft with both chest and donor site incisions.

[b] A nonhuman-derived implantable foreign body (e.g., prosthetic heart valve, nonhuman vascular graft, mechanical heart, or hip prosthesis) that is permanently placed in a patient during surgery.

examination, during reoperation, or by histopathologic or radiologic examination
d. Diagnosis of a deep incisional SSI by a surgeon or attending physician

REPORTING INSTRUCTIONS:

- Classify infection that involves *both* superficial and deep incision sites as deep incisional SSI.
- Report culture specimen from deep incisions as ID.

INFECTION SITE: Surgical site infection (organ/space)
CODE: SSI-(Specific site of organ/space)
DEFINITION: An organ/space SSI involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure. Specific sites are assigned to organ/space SSI to further identify the location of the infection. Listed later are the specific sites that must be used to differentiate organ/space SSI. An example is appendectomy with subsequent subdiaphragmatic abscess, which would be reported as an organ/space SSI at the intraabdominal specific site (SSI-IAB).
An organ/space SSI must meet the following criteria:
Infection occurs within 30 days after the operative procedure if no implant[b] is left in place or within 1 year if implant is in place and the infection appears to be related to the operative procedure
and
infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure
and
patient has at least *one* of the following:
a. Purulent drainage from a drain that is placed through a stab wound into the organ/space
b. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
c. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination
d. Diagnosis of an organ/space SSI by a surgeon or attending physician

REPORTING INSTRUCTIONS:

- Occasionally, an organ/space infection drains through the incision. Such infection generally does not involve reoperation and is considered a complication of the incision. Therefore, it is classified as a deep incisional SSI.
- Report culture specimen from organ/space as DD (deep drainage).

The following are specific sites of an organ/space SSI:

Code	Site
BONE	Osteomyelitis
BRST	Breast abscess or mastitis
CARD	Myocarditis or pericarditis
DISC	Disc space
EAR	Ear, mastoid
EMET	Endometritis
ENDO	Endocarditis
EYE	Eye, other than conjunctivitis
GIT	GI tract
IAB	Intraabdominal, not specified elsewhere
IC	Intracranial, brain abscess or dura
JNT	Joint or bursa
LUNG	Other infections of the lower respiratory tract
MED	Mediastinitis
MEN	Meningitis or ventriculitis
ORAL	Oral cavity (mouth, tongue, or gums)
OREP	Other male or female
OUTI	Other infections of the urinary tract
SA	Spinal abscess without meningitis
SINU	Sinusitis
UR	Upper respiratory tract
VASC	Arterial or venous infection
VCUF	Vaginal cuff

INFECTION SITE: Pneumonia (See Appendix A-2)
INFECTION SITE: Laboratory-confirmed bloodstream infection
CODE: BSI-LCBI
DEFINITION: Laboratory-confirmed bloodstream infection must meet at least one of the following criteria:
Criterion 1: Patient has a recognized pathogen cultured from one or more blood cultures
and
organism cultured from blood is *not* related to an infection at another site.
Criterion 2: Patient has at least *one* of the following signs or symptoms: fever (>38°C), chills, or hypotension
and
at least *one* of the following:
a. Common skin contaminant (e.g., diphtheroids, *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci, or micrococci) is cultured from two or more blood cultures drawn on separate occasions
b. Common skin contaminant (e.g., diphtheroids, *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci, or micrococci) is cultured from at least one blood culture from a patient with an intravascular line, and the physician institutes appropriate antimicrobial therapy
c. Positive antigen test on blood (e.g., *Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis,* or group B *Streptococcus*)
and
signs and symptoms and positive laboratory results are *not* related to an infection at another site.
Criterion 3: Patient ≤1 year of age has at least *one* of the following signs or symptoms: fever (>38°C), hypothermia (<37°C), apnea, or bradycardia
and
at least *one* of the following:
a. Common skin contaminant (e.g., diphthe-

roids, *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci, or micrococci) is cultured from *two* or more blood cultures drawn on separate occasions

b. Common skin contaminant (e.g., diphtheroids, *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci, or micrococci) is cultured from at least one blood culture from a patient with an intravascular line, and physician institutes appropriate antimicrobial therapy

c. Positive antigen test on blood (e.g., *H. influenzae, S. pneumoniae, N. meningitidis,* or group B *Streptococcus*)
and
signs and symptoms and positive laboratory results are *not* related to an infection at another site.

REPORTING INSTRUCTIONS:

- Report purulent phlebitis confirmed with a positive semiquantitative culture of a catheter tip, but with either negative or no blood culture, as CVS-VASC.
- Report organisms cultured from blood as BSI-LCBI when no other site of infection is evident.
- Pseudobacteremias are not nosocomial infections.

INFECTION SITE: Clinical sepsis
CODE: BSI-CSEP
DEFINITION: Clinical sepsis must meet at least one of the following criteria:

Criterion 1: Patient has at least *one* of the following clinical signs or symptoms with no other recognized cause: fever (>38°C), hypotension (systolic pressure ≤ 90 mm Hg), or oliguria (<20 cm^3/hr)
and
blood culture *not* done or *no* organisms or antigen detected in blood
and
no apparent infection at another site
and
physician institutes treatment for sepsis.

Criterion 2: Patient ≤1 year of age has at least *one* of the following clinical signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, or bradycardia
and
blood culture *not* done or *no* organisms or antigen detected in blood
and
no apparent infection at another site
and
physician institutes treatment for sepsis.

REPORTING INSTRUCTION:

- Report culture-positive infections of the bloodstream as BSI-LCBI.

INFECTION SITE: Osteomyelitis
CODE: BJ-BONE
DEFINITION: Osteomyelitis must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from bone.

Criterion 2: Patient has evidence of osteomyelitis on direct examination of the bone during a surgical operation or histopathologic examination.

Criterion 3: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), localized swelling, tenderness, heat, or drainage at suspected site of bone infection
and
at least *one* of the following:

a. Organisms cultured from blood
b. Positive blood antigen test (e.g., *H. influenzae, S. pneumoniae*)
c. Radiographic evidence of infection, for example, abnormal findings on x-ray, CT, MRI, radiolabeled scan (gallium, technetium, etc.)

INFECTION SITE: Joint or bursa
CODE: BJ-JNT
DEFINITION: Joint or bursa infections must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from joint fluid or synovial biopsy.

Criterion 2: Patient has evidence of joint or bursa infection seen during a surgical operation or histopathologic examination.

Criterion 3: Patient has at least *two* of the following signs or symptoms with no other recognized cause: joint pain, swelling, tenderness, heat, evidence of effusion or limitation of motion
and
at least *one* of the following:

a. Organisms *and* white blood cells seen on Gram stain of joint fluid
b. Positive antigen test on blood, urine, or joint fluid
c. Cellular profile and chemistries of joint fluid compatible with infection and *not* explained by an underlying rheumatologic disorder
d. Radiographic evidence of infection, for example, abnormal findings on x-ray, CT, MRI, radiolabel scan (gallium, technetium, etc.)

INFECTION SITE: Disc space
CODE: BJ-DISC
DEFINITION: Vertebral disc space infection must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from vertebral disc space tissue obtained during a surgical operation or needle aspiration.

Criterion 2: Patient has evidence of vertebral disc space infection seen during a surgical operation or histopathologic examination.

Criterion 3: Patient has fever (>38°C) with no other recog-

nized cause or pain at the involved vertebral disc space
and
radiographic evidence of infection, e.g., abnormal findings on x-ray, CT, MRI, radiolabel scan with gallium or technetium.
Criterion 4: Patient has fever (>38°C) with no other recognized cause and pain at the involved vertebral disc space
and
positive antigen test on blood or urine (e.g., *H. influenzae, S. pneumoniae, N. meningitidis,* or group B *Streptococcus*)

INFECTION SITE: Intracranial infection (brain abscess, subdural or epidural infection, encephalitis)
CODE: CNS-IC
DEFINITION: Intracranial infection must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from brain tissue or dura.

Criterion 2: Patient has an abscess or evidence of intracranial infection seen during a surgical operation or histopathologic examination.

Criterion 3: Patient has at least *two* of the following signs or symptoms with no other recognized cause: headache, dizziness, fever (>38°C), localizing neurologic signs, changing level of consciousness, or confusion
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy
and
at least *one* of the following:
a. Organisms seen on microscopic examination of brain or abscess tissue obtained by needle aspiration or by biopsy during a surgical operation or autopsy
b. Positive antigen test on blood or urine
c. Radiographic evidence of infection, for example, abnormal findings on ultrasound, CT, MRI, radionuclide brain scan, or arteriogram
d. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

Criterion 4: Patient ≤1 year of age has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, localizing neurologic signs, or changing level of consciousness
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy
and
at least *one* of the following:
a. Organisms seen on microscopic examination of brain or abscess tissue obtained by needle aspiration or by biopsy during a surgical operation or autopsy
b. Positive antigen test on blood or urine
c. Radiographic evidence of infection, for example, abnormal findings on ultrasound CT, MRI, radionuclide brain scan, or arteriogram
d. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

REPORTING INSTRUCTION:

- If meningitis and a brain abscess are present together, report the infection as IC.

INFECTION SITE: Meningitis or ventriculitis
CODE: CNS-MEN
DEFINITION: Meningitis or ventriculitis must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from cerebrospinal fluid (CSF).

Criterion 2: Patient has at least *one* of the following signs of symptoms with no other recognized cause: fever (>38°C), headache, stiff neck, meningeal signs, cranial nerve signs, or irritability
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy
and
at least *one* of the following:
a. Increased white cells, elevated protein and/or decreased glucose in CSF
b. Organisms seen on Gram stain of CSF
c. Organisms cultured from blood
d. Positive antigen test of CSF, blood, or urine
e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

Criterion 3: Patient ≤1 year of age has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, stiff neck, meningeal signs, cranial nerve signs, or irritability
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy
and
at least *one* of the following:
a. Positive CSF examination with increased white cells, elevated protein, and/or decreased glucose
b. Positive Gram stain of CSF
c. Organisms cultured from blood
d. Positive antigen test of CSF, blood, or urine
e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

REPORTING INSTRUCTIONS:

- Report meningitis in the newborn as nosocomial *unless* there is compelling evidence indicating the meningitis was acquired transplacentally.
- Report CSF shunt infection as SSI-MEN if it occurs ≤1 year of placement; if later, report as CNS-MEN.
- Report meningoencephalitis as MEN.
- Report spinal abscess with meningitis as MEN.

INFECTION SITE: Spinal abscess without meningitis
CODE: CNS-SA
DEFINITION: An abscess of the spinal epidural or subdural space, without involvement of the CSF or adjacent bone structures, must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from abscess in the spinal epidural or subdural space.

Criterion 2: Patient has an abscess in the spinal epidural or subdural space seen during a surgical operation or at autopsy of evidence of an abscess seen during a histopathologic examination.

Criterion 3: Patient has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), back pain, focal tenderness, radiculitis, paraparesis, or paraplegia
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy
and
at least *one* of the following:
a. Organisms cultured from blood
b. Radiographic evidence of a spinal abscess, for example, abnormal findings on myelography, ultrasound, CT, MRI, or other scans (gallium, technetium, etc.)

REPORTING INSTRUCTION:

- Report spinal abscess *with* meningitis as MEN.

INFECTION SITE: Arterial or venous infection
CODE: CVS-VASC
DEFINITION: Arterial or venous infection must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from arteries or veins removed during a surgical operation
and
blood culture *not* done or *no* organisms cultured from blood.

Criterion 2: Patient has evidence of arterial or venous infection seen during a surgical operation or histopathologic examination.

Criterion 3: Patient has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), pain, erythema, or heat at involved vascular size
and
more than 15 colonies cultured from intravascular cannula tip using semiquantitative culture method
and
blood culture *not* done or *no* organisms cultured from blood.

Criterion 4: Patient has purulent drainage at involved vascular site
and
blood culture *not* done or *no* organisms cultured from blood.

Criterion 5: Patient ≤1 year of age has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, lethargy, or pain, erythema, or heat at involved vascular site
and
more than 15 colonies cultured from intravascular cannula tip using semiquantitative culture method
and
blood culture *not* done or *no* organisms cultured from blood.

REPORTING INSTRUCTIONS:

- Report infections of an arteriovenous graft, shunt, or fistula or intravascular cannulation site without organisms cultured from blood as CVS-VASC.
- Report intravascular infections with organisms cultured from the blood as BSI-LCBI.

INFECTION SITE: Endocarditis involving either a natural or prosthetic heart valve
CODE: CVS-ENDO
DEFINITION: Endocarditis of a natural or prosthetic heart valve must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from valve or vegetation.

Criterion 2: Patient has *two* or more of the following signs or symptoms with no other recognized cause: fever (>38°C), new or changing murmur, embolic phenomena, skin manifestations (i.e., petechiae, splinter hemorrhages, painful subcutaneous nodules), congestive heart failure, or cardiac conduction abnormality
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy
and
at least *one* of the following:
a. Organisms cultured from *two* or more blood cultures
b. Organisms seen on Gram stain of valve when culture is negative or *not* done
c. Valvular vegetation seen during a surgical operation or autopsy
d. Positive antigen test on blood or urine (e.g., *H. influenzae, S. pneumoniae, N. meningitidis,* or group B *Streptococcus*)
e. Evidence of new vegetation seen on echocardiogram

Criterion 3: Patient ≤1 year of age has *two* or more of the following signs or symptoms with no other recognized cause fever (>38°C), hypothermia (<37°C), apnea, bradycardia, new or changing murmur, embolic phenomena skin manifestations (i.e., petechiae, splinter hemorrhages, painful subcutaneous nodules), congestive heart failure, or cardiac conduction abnormality
and
if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy

and

at least *one* of the following:

a. Organisms cultured from *two* or more blood cultures
b. Organisms seen on Gram stain of valve when culture is negative or *not* done
c. Valvular vegetation seen during a surgical operation or autopsy
d. Positive antigen test on blood or urine (e.g., *H. influenzae, S. pneumoniae, N. meningitidis,* or group B *Streptococcus*)
e. Evidence of new vegetation seen on echocardiogram

INFECTION SITE: Myocarditis or pericarditis
CODE: CVS-CARD
DEFINITION: Myocarditis or pericarditis must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from pericardial tissue or fluid obtained by needle aspiration or during a surgical operation.

Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), chest pain, paradoxical pulse, or increased heart size

and

at least *one* of the following:

a. Abnormal electrocardiogram (ECG) consistent with myocarditis or pericarditis
b. Positive antigen test on blood (e.g., *H. influenzae, S. pneumoniae*)
c. Evidence of myocarditis or pericarditis on histologic examination of heart tissue
d. Fourfold rise in type-specific antibody with or without isolation of virus from pharynx or feces
e. Pericardial effusion identified by echocardiogram, CT, MRI, or angiography

Criterion 3: Patient ≤1 year of age has at least *two* of the following signs of symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, paradoxical pulse, or increased heart size

and

at least *one* of the following:

a. Abnormal ECG consistent with myocarditis or pericarditis
b. Positive antigen test on blood (e.g., *H. influenzae, S. pneumoniae*)
c. Histologic examination of heart tissue shows evidence of myocarditis or pericarditis
d. Fourfold rise in type-specific antibody with or without isolation of virus from pharynx or feces
e. Pericardial effusion identified by echocardiogram, CT, MRI, or angiography

COMMENT:

- Most cases of postcardiac surgery or postmyocardial infarction pericarditis are not infectious.

INFECTION SITE: Mediastinitis
CODE: CVS-MED
DEFINITION: Mediastinitis must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from mediastinal tissue or fluid obtained during a surgical operation or needle aspiration.

Criterion 2: Patient has evidence of mediastinitis seen during a surgical operation of histopathologic examination.

Criterion 3: Patient has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), chest pain, or sternal instability

and

at least *one* of the following:

a. Purulent discharge from mediastinal area
b. Organisms cultured from blood or discharge from mediastinal area
c. Mediastinal widening on x-ray

Criterion 4: Patient ≤1 year of age has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, or sternal instability

and

at least one of the following:

a. Purulent discharge from mediastinal area
b. Organisms cultured from blood or discharge from mediastinal area
c. Mediastinal widening on x-ray

REPORTING INSTRUCTION:

- Report mediastinitis following cardiac surgery that is accompanied by osteomyelitis as SSI-MED rather than SSI-BONE.

INFECTION SITE: Conjunctivitis
CODE: EENT-CONJ
DEFINITION: Conjunctivitis must meet at least one of the following criteria:

Criterion 1: Patient has pathogens cultured from purulent exudate obtained from the conjunctiva or contiguous tissues, such as eyelid, cornea, meibomian glands, or lacrimal glands.

Criterion 2: Patient has pain or redness of conjunctiva or around eye

and

at least *one* of the following:

a. WBCs and organisms seen on Gram stain of exudate
b. Purulent exudate
c. Positive antigen test [e.g., enzyme-linked immunosorbent assay (ELISA) or immunofluorescence (IF) for *Chlamydia trachomatis,* herpes simplex virus, adenovirus) on exudate or conjunctival scraping
d. Multinucleated giant cells seen on microscopic examination of conjunctival exudate or scrapings
e. Positive viral culture
f. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

REPORTING INSTRUCTIONS:

- Report other infections of the eye as EYE.
- Do *not* report chemical conjunctivitis caused by silver nitrate ($AgNO_3$) as a nosocomial infection.
- Do *not* report conjunctivitis that occurs as a part of a more widely disseminated viral illness (e.g., measles, chickenpox, or a URI).

INFECTION SITE: Eye, other than conjunctivitis
CODE: EENT-EYE
DEFINITION: An infection of the eye, other than conjunctivitis, must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from anterior or posterior chamber of vitreous fluid.

Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: eye pain, visual disturbance, or hypopyon
and
at least *one* of the following:
a. Physician's diagnosis of an eye infection
b. Positive antigen test on blood (e.g., *H. influenzae, S. pneumoniae*)
c. Organisms cultured from blood

INFECTION SITE: Ear, mastoid
CODE: EENT-EAR
DEFINITION: Ear and mastoid infections must meet the following applicable criteria:
Otitis externa must meet at least one of the following criteria:

Criterion 1: Patient has pathogens cultured from purulent drainage from ear canal.

Criterion 2: Patient has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), pain, redness, or drainage from ear canal
and
organisms seen on Gram stain of purulent drainage.

Otitis media must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from fluid from middle ear obtained by tympanocentesis or at surgical operation.

Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C) pain in the eardrum, inflammation, retraction or decreased mobility of eardrum, or fluid behind eardrum.

Otitis interna must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from fluid from inner ear obtained at surgical operation.

Criterion 2: Patient has a physician's diagnosis of inner ear infection.

Mastoiditis must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from purulent drainage from mastoid.

Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), pain, tenderness, erythema, headache, or facial paralysis
and
at least *one* of the following:
a. Organisms seen on Gram stain of purulent material from mastoid
b. Positive antigen test on blood

INFECTION SITE: Oral cavity (mouth, tongue, or gums)
CODE: EENT-ORAL
DEFINITION: Oral cavity infections must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from purulent material from tissues of oral cavity.

Criterion 2: Patient has an abscess or other evidence of oral cavity infection seen on direct examination, during a surgical operation, or during a histopathologic examination.

Criterion 3: Patient has at least *one* of the following signs or symptoms with no other recognized cause: abscess, ulceration, or raised white patches on inflamed mucosa, or plaques on oral mucosa
and
at least *one* of the following:
a. Organisms seen on Gram stain
b. Positive potassium hydroxide (KOH) stain
c. Multinucleated giant cells seen on microscopic examination of mucosal scrapings
d. Positive antigen test on oral secretions
e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen
f. Physician diagnosis of infection and treatment with topical or oral antifungal therapy

REPORTING INSTRUCTION:

- Report nosocomial primary herpes simplex infections of the oral cavity as ORAL; recurrent herpes infections are *not* nosocomial.

INFECTION SITE: Sinusitis
CODE: EENT-SINU
DEFINITION: Sinusitis must meet at least one of the following criteria:

Criterion 1: Patient has organisms cultured from purulent material obtained from sinus cavity.

Criterion 2: Patient has at least *one* of the following signs or symptoms with no other recognized cause: fever (>38°C), pain or tenderness over the involved sinus, headache, purulent exudate, or nasal obstruction
and
at least *one* of the following:
a. Positive transillumination
b. Positive radiographic examination

INFECTION SITE: Upper respiratory tract, pharyngitis, laryngitis, epiglottitis
CODE: EENT-UR
DEFINITION: Upper respiratory tract infections must meet at least one the following criteria:

Criterion 1: Patient has at least *two* of the following signs or

symptoms with no other recognized cause: fever (>38°C), erythema of pharynx, sore throat, cough, hoarseness, of purulent exudate in throat
and
at least *one* of the following:
a. Organisms cultured from the specific site
b. Organisms cultured from blood
c. Positive antigen test on blood or respiratory secretions
d. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen
e. Physician's diagnosis of an upper respiratory infection

Criterion 2: Patient has an abscess seen on direct examination, during a surgical operation, or during a histopathologic examination.

Criterion 3: Patient ≤1 year of age has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, nasal discharge, or purulent exudate in throat
and
at least *one* of the following:
a. Organisms cultured from the specific site
b. Organisms cultured from blood
c. Positive antigen test on blood or respiratory secretions
d. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen
e. Physician's diagnosis of an upper respiratory infection

INFECTION SITE: Gastroenteritis
CODE: GI-GE
DEFINITION: Gastroenteritis must meet at least one of the following criteria:

Criterion 1: Patient has an acute onset of diarrhea (liquid stools for more than 12 hours) with or without vomiting or fever (>38°C) and no likely noninfectious cause (e.g., diagnostic tests, therapeutic regimen, acute exacerbation of a chronic condition, or psychologic stress).

Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: nausea, vomiting, abdominal pain, or headache
and
at least *one* of the following:
a. An enteric pathogen is cultured from stool or rectal swab
b. An enteric pathogen is detected by routine or electron microscopy
c. An enteric pathogen is detected by antigen or antibody assay on blood or feces
d. Evidence of an enteric pathogen is detected by cytopathic changes in tissue culture (toxin assay)
e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

INFECTION SITE: GI tract (esophagus, stomach, small and large bowel, and rectum) excluding gastroenteritis and appendicitis
CODE: GI-GIT
DEFINITION: Gastrointestinal tract infections, excluding gastroenteritis and appendicitis, must meet at least one of the following criteria:

Criterion 1: Patient has an abscess or other evidence of infection seen during a surgical operation or histopathologic examination.

Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause and compatible with infection of the organ or tissue involved: fever (>38°C), nausea, vomiting, abdominal pain, or tenderness
and
at least *one* of the following:
a. Organisms cultured from drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain
b. Organisms seen on Gram or KOH stain or multinucleated giant cells seen on microscopic examination of drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain
c. Organisms cultured from blood
d. Evidence of pathologic findings on radiologic examination
e. Evidence of pathologic findings on endoscopic examination (e.g., *Candida* esophagitis or proctitis)

INFECTION SITE: Hepatitis
CODE: GI-HEP
DEFINITION: Hepatitis must meet the following criterion:
Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), anorexia, nausea, vomiting, abdominal pain, jaundice, or history of transfusion within the previous 3 months
and
at least *one* of the following:
a. Positive antigen or antibody test for hepatitis A, hepatitis B, hepatitis C, or delta hepatitis
b. Abnormal liver function tests (e.g., elevated alanine/aspartate aminotransferases, bilirubin)
c. Cytomegalovirus detected in urine or oropharyngeal secretions

REPORTING INSTRUCTIONS:

- Do *not* report hepatitis or jaundice of noninfectious origin (alpha-1 antitrypsin deficiency, etc.).
- Do *not* report hepatitis or jaundice that results from exposure to hepatotoxins (alcoholic or acetaminophen-induced hepatitis, etc.).
- Do *not* report hepatitis or jaundice that results from biliary obstruction (cholecystitis).

INFECTION SITE: Intraabdominal, including gallbladder, bile ducts, liver (excluding viral hepatitis), spleen, pancreas, perito-

neum, subphrenic or subdiaphragmatic space, or other intraabdominal tissue or area *not* specified elsewhere
CODE: GI-IAB
DEFINITION: Intraabdominal infections must meet at least one of the following criteria:
Criterion 1: Patient has organisms cultured from purulent material from intraabdominal space obtained during a surgical operation or needle aspiration.
Criterion 2: Patient has abscess or other evidence of intraabdominal infection seen during a surgical operation or histopathologic examination.
Criterion 3: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), nausea, vomiting, abdominal pain, or jaundice
and
at least *one* of the following:
a. Organisms cultured from drainage from surgically placed drain (e.g., closed suction drainage system, open drain, T-tube drain)
b. Organisms seen on Gram stain of drainage or tissue obtained during surgical operation or needle aspiration
c. Organisms cultured from blood and radiographic evidence of infection, for example, abnormal findings on ultrasound, CT, MRI, or radiolabel scans (gallium, technetium, etc.) or on abdominal x-ray

REPORTING INSTRUCTION:

- Do *not* report pancreatitis (an inflammatory syndrome characterized by abdominal pain, nausea, and vomiting associated with high serum levels of pancreatic enzymes) unless it is determined to be infectious in origin.

INFECTION SITE: Necrotizing enterocolitis
CODE: GI-NEC
DEFINITION: Necrotizing enterocolitis in infants must meet the following criteria:
Infant has at least *two* of the following signs or symptoms with no other recognized cause: vomiting, abdominal distention, or prefeeding residuals
and
persistent microscopic or gross blood in stools
and
at least *one* of the following abdominal radiographic abnormalities:
a. Pneumoperitoneum
b. Pneumatosis intestinalis
c. Unchanging ''rigid'' loops of small bowel

INFECTION SITE: Bronchitis, tracheobronchitis, bronchiolitis, tracheitis, without evidence of pneumonia
CODE: LRI-BRON
DEFINITION: Tracheobronchial infections must meet at least one of the following criteria:
Criterion 1: Patient has *no* clinical or radiographic evidence of pneumonia
and
patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), cough, new or increased sputum production, rhonchi, wheezing
and
at least *one* of the following:
a. Positive culture obtained by deep tracheal aspirate or bronchoscopy
b. Positive antigen test on respiratory secretions
Criterion 2: Patient ≤1 year of age has *no* clinical or radiographic evidence of pneumonia
and
patient has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), cough, new or increased sputum production, rhonchi, wheezing, respiratory distress, apnea, or bradycardia
and
at least *one* of the following:
a. Organisms cultured from material obtained by deep tracheal aspirate or bronchoscopy
b. Positive antigen test on respiratory secretions
c. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

REPORTING INSTRUCTION:

- Do *not* report chronic bronchitis in a patient with chronic lung disease as an infection unless there is evidence of an acute secondary infection, manifested by change in organism.

INFECTION SITE: Other infections of the lower respiratory tract
CODE: LRI-LUNG
DEFINITION: Other infections of the lower respiratory tract must meet at least one of the following criteria:
Criterion 1: Patient has organisms seen on smear or cultured from lung tissue or fluid, including pleural fluid.
Criterion 2: Patient has a lung abscess or empyema seen during a surgical operation or histopathologic examination.
Criterion 3: Patient has an abscess cavity seen on radiographic examination of lung.

REPORTING INSTRUCTIONS:

- Report concurrent lower respiratory tract infection and pneumonia with the same organism(s) as PNEU.
- Report lung abscess or empyema without pneumonia as LUNG.

INFECTION SITE: Endometritis
CODE: REPR-EMET
DEFINITION: Endometritis must meet at least one of the following criteria:
Criterion 1: Patient has organisms cultured from fluid or tissue from endometrium obtained during surgical operation, by needle aspiration, or by brush biopsy.
Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: fever

(>38°C), abdominal pain, uterine tenderness, or purulent drainage from uterus.

REPORTING INSTRUCTION:

- Report postpartum endometritis as a nosocomial infection *unless* the amniotic fluid is infected at the time of admission or the patient was admitted 48 hours after rupture of the membrane.

INFECTION SITE: Episiotomy
CODE: REPR-EPIS
DEFINITION: Episiotomy infections must meet at least one of the following criteria:
Criterion 1: Postvaginal delivery patient has purulent drainage from the episiotomy.
Criterion 2: Postvaginal delivery patient has an episiotomy abscess.

REPORTING INSTRUCTION:

- Episiotomy is not a NNIS operative procedure; do not report as an SSI.

INFECTION SITE: Vaginal cuff
CODE: REPR-VCUF
DEFINITION: Vaginal cuff infections must meet at least one of the following criteria:
Criterion 1: Posthysterectomy patient has purulent drainage from the vaginal cuff.
Criterion 2: Posthysterectomy patient has an abscess at the vaginal cuff.
Criterion 3: Posthysterectomy patient has pathogens cultured from fluid or tissue obtained from the vaginal cuff.

REPORTING INSTRUCTION:

- Most vaginal cuff infections are SSI-VCUF.
- Report only late onset (>30 days after hysterectomy) VCUF as REPR-VCUF.

INFECTION SITE: Other infections of the male or female reproductive tract (epididymis, testes, prostate, vagina, ovaries, uterus, or other deep pelvic tissues, excluding endometritis or vaginal cuff infections)
CODE: REPR-OREP
DEFINITION: Other infections of the male or female reproductive tract must meet at least one of the following criteria:
Criterion 1: Patient has organisms cultured from tissue or fluid from affected site.
Criterion 2: Patient has an abscess or other evidence of infection of affected site seen during a surgical operation or histopathologic examination.
Criterion 3: Patient has *two* of the following signs or symptoms with no other recognized cause: fever (>38°C), nausea, vomiting, pain, tenderness, or dysuria
and
at least *one* of the following:
a. Organisms cultured from blood
b. Diagnosis by physician

REPORTING INSTRUCTIONS:

- Report endometritis as EMET.
- Report vaginal cuff infections as VCUF.

INFECTION SITE: Skin
CODE: SST-SKIN
DEFINITION: Skin infections must meet at least one of the following criteria:
Criterion 1: Patient has purulent drainage, pustules, vesicles, or boils.
Criterion 2: Patient has at least *two* of the following signs or symptoms with no other recognized cause: pain or tenderness, localized swelling, redness, or heat
and
at least *one* of the following:
a. Organisms cultured from aspirate or drainage from affected site; if organisms are normal skin flora (e.g., coagulase negative staphylococci, micrococci, diphtheroids) they must be a pure culture
b. Organisms cultured from blood
c. Positive antigen test performed on infected tissue or blood (e.g., herpes simplex, varicella zoster, *H. influenzae, N. meningitidis*)
d. Multinucleated giant cells seen on microscopic examination of affected tissue
e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

COMMENT:

- Nosocomial skin infections may be the result of exposure to a variety of procedures performed in the hospital. Superficial incisional infections after surgery are identified separately as SSI-SKIN unless the operative procedure is a CBGB. If the chest incision site after a CBGB becomes infected, the specific site is denoted SKNC; if the donor site becomes infected, the specific site is denoted SKNL. Other skin infections associated with important exposures are identified with their own sites and are listed in the section on reporting instructions.

REPORTING INSTRUCTIONS:

- Report omphalitis in infants as UMB.
- Report infections of the circumcision site in newborns as CIRC.
- Report pustules in infants as PUST.
- Report infected decubitus ulcers as DECU.
- Report infected burns as BURN.
- Report breast abscesses or mastitis as BRST.

INFECTION SITE: Soft tissue (necrotizing fascitis, infectious gangrene, necrotizing cellulitis, infectious myositis, lymphadenitis, or lymphangitis)
CODE: SST-ST
DEFINITION: Soft tissue infections must meet at least one of the following criteria:
Criterion 1: Patient has organisms cultured from tissue or drainage from affected site.
Criterion 2: Patient has purulent drainage at affected site.
Criterion 3: Patient has an abscess or other evidence of infec-

tion seen during a surgical operation or histopathologic examination.

Criterion 4: Patient has at least *two* of the following signs of symptoms at the affected site with no other recognized cause: localized pain or tenderness, redness, swelling, or heat
and
at least *one* of the following:
a. Organisms cultured from blood
b. Positive antigen test performed on blood or urine (e.g., *H. influenzae, S. pneumoniae, N. meningitidis,* group B *Streptococcus, Candida* sp.)
c. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen

REPORTING INSTRUCTIONS:

- Report surgical site infections that involve both the skin and deep soft tissue (at or beneath the fascial or muscle layer) as SSI-ST (soft tissue) unless the operative procedure is a CBGB. For CBGB, if skin and deep soft tissue at the chest incision site become infected, the specific site is STC and if skin and deep soft tissue at the donor site become infected, the specific site is STL.
- Report infected decubitus ulcers as DECU.
- Report infection of deep pelvic tissues as OREP.

INFECTION SITE: Decubitus ulcer, including both superficial and deep infections
CODE: SST-DECU
DEFINITION: Decubitus ulcer infections must meet the following criterion:
Patient has at least *two* of the following signs or symptoms with no other recognized cause: redness, tenderness, or swelling of decubitus wound edges
and
at least *one* of the following:
a. Organisms cultured from properly collected fluid or tissue (see later)
b. Organisms cultured from blood

COMMENTS:

- Purulent drainage alone is not sufficient evidence of an infection.
- Organisms cultured from the surface of a decubitus ulcer are not sufficient evidence that the ulcer is infected. A properly collected specimen from a decubitus ulcer involves needle aspiration of fluid or biopsy of tissue from the ulcer margin.

INFECTION SITE: Burn
CODE: SST-BURN
DEFINITION: Burn infections must meet one of the following criteria:

Criterion 1: Patient has a change in burn wound appearance or character, such as rapid eschar separation; dark brown, black, or violaceous discoloration of the char; or edema at wound margin
and
histologic examination of burn biopsy shows invasion of organisms into adjacent viable tissue.

Criterion 2: Patient has a change in burn wound appearance or character, such as rapid eschar separation; dark brown, black, or violaceous discoloration of the eschar; or edema at wound margin
and
at least *one* of the following:
a. Organisms cultured from blood in the absence of other identifiable infection
b. Isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy or visualization of viral particles by electron microscopy in biopsies or lesion scrapings

Criterion 3: Patient with a burn has at least *two* of the following signs or symptoms with no other recognized cause: fever (>38°C) or hypothermia (<36°C), hypotension, oliguria (<20 cm^3/hr), hyperglycemia at previously tolerated level of dietary carbohydrate, or mental confusion
and
at least *one* of the following:
a. Histologic examination of burn biopsy shows invasion of organisms into adjacent viable tissue
b. Organisms cultured from blood
c. Isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles electron microscopy in biopsies or lesion scrapings

COMMENTS:

- Purulence alone at the burn wound site is *not* adequate for the diagnosis of burn infection; such purulence may reflect incomplete wound care.
- Fever alone in a burn patient is *not* adequate for the diagnosis of a burn infection because fever may be the result of tissue trauma or the patient may have an infection at another site.
- Surgeons in Regional Burn Centers who take care of burn patients exclusively, may require Criterion 1 for diagnosis burn infection.
- Hospitals with Regional Burn Centers may further divide burn infections into the following: burn wound site, burn graft site, burn donor site, burn donor site-cadaver; the NNIS system, however, will code all of these as BURN.

INFECTION SITE: Breast abscess or mastitis
CODE: SST-BRST
DEFINITION: A breast abscess or mastitis must meet at least one of the following criteria:

Criterion 1: Patient has a positive culture of affected breast tissue or fluid obtained by incision and drainage or needle aspiration.

Criterion 2: Patient has a breast abscess or other evidence of infection seen during a surgical operation or histopathologic examination.

Criterion 3: Patient has fever (>38°C) and local inflammation of the breast
and
physician's diagnosis of breast abscess.

COMMENT:

- Breast abscesses occur most frequently after childbirth. Those that occur within 7 days after childbirth should be considered nosocomial.

INFECTION SITE: Omphalitis
CODE: SST-UMB
DEFINITION: Omphalitis in a newborn (≤30 days old) must meet at least one of the following criteria:

Criterion 1: Patient has erythema and/or serous drainage from umbilicus
and
at least *one* of the following:
a. Organisms cultured from drainage or needle aspirate
b. Organisms cultured from blood.

Criterion 2: Patient has both erythema and purulence at the umbilicus.

REPORTING INSTRUCTIONS:

- Report infection of the umbilical artery or vein related to umbilical catheterization as CVS-VASC if blood culture is negative or not done.
- Report as nosocomial if infection occurs in a newborn within 7 days of hospital discharge.

INFECTION SITE: Infant pustulosis
CODE: SST-PUST
DEFINITION: Pustulosis in an infant (≤12 months old) must meet at least one of the following criteria:

Criterion 1: Infant has *one* or more pustules
and
physician diagnosis of skin infection.

Criterion 2: Infant has *one* or more pustules
and
physician institutes appropriate antimicrobial therapy.

REPORTING INSTRUCTIONS:

- Do *not* report erythema toxicum and noninfectious causes of pustulosis.
- Report as nosocomial if pustulosis occurs in an infant within 7 days of hospital discharge.

INFECTION SITE: Newborn circumcision
CODE: SST-CIRC
DEFINITION: Circumcision infection in a newborn (≤30 days old) must meet at least one of the following criteria:

Criterion 1: Newborn has purulent drainage from circumcision site.

Criterion 2: Newborn has at least *one* of the following signs or symptoms with no other recognized cause at circumcision site: erythema, swelling, or tenderness
and
pathogen cultured from circumcision site.

Criterion 3: Newborn has at least *one* of the following signs or symptoms with no other recognized cause at circumcision site: erythema, swelling, or tenderness
and
skin contaminant (coagulase-negative staphylococci, diphtheroids, *Bacillus* sp., or micrococci) is cultured from circumcision site
and
physician diagnosis of infection or physician institutes appropriate therapy.

REPORTING INSTRUCTION:

- Newborn circumcision is not an NNIS operative procedure; do not report as an SSI.

INFECTION SITE: Disseminated infection
CODE: SYS-DI
DEFINITION: Disseminated infection is infection involving multiple organs or systems, without an apparent single site of infection, usually of viral origin, and with signs or symptoms with no other recognized cause and compatible with infectious involvement of multiple organs or systems.

REPORTING INSTRUCTIONS:

- This code should be used primarily for viral infections involving multiple organ systems (e.g., measles, mumps, rubella, varicella, erythema infectiosum). These infections often can be identified by clinical criteria alone. Do *not* use this code for nosocomial infections with multiple metastatic sites, such as with bacterial endocarditis; only the primary site of these infections should be reported.
- Do not report fever of unknown origin (FUO) as DI-SYS.
- Report neonatal ''sepsis'' as BSI-CSEP.
- Report viral exanthems or rash illness as DI-SYS.

APPENDIX A-2. CRITERIA FOR DEFINING NOSOCOMIAL PNEUMONIA

General Comments Applicable to All Pneumonia Specific Site Criteria

1. Physician's diagnosis of pneumonia alone is *not* an acceptable criterion for nosocomial pneumonia.
2. Although specific criteria are included for infants and children, pediatric patients may meet any of the other pneumonia specific site criteria.
3. Ventilator-associated pneumonia (i.e., pneumonia in persons who had a device to assist or control respiration continuously through a tracheostomy or by endotracheal intubation within the 48-hour period before the onset of infection) should be so designated when reporting pneumonia data.
4. When assessing a patient for presence of pneumonia, it is important to distinguish between changes in clinical status resulting from other conditions such as myocardial infarction, pulmonary embolism, respiratory distress syndrome, atelectasis, malignancy, chronic obstructive pulmonary disease, hyaline membrane disease, bronchopulmonary dysplasia, and so forth. Also, care must be taken when assessing intubated patients to distinguish between tracheal colonization, upper

respiratory tract infections (e.g., tracheobronchitis), and early onset pneumonia. Finally, it should be recognized that it may be difficult to determine nosocomial pneumonia in the elderly, infants, and immunocompromised patients because such conditions may mask typical signs or symptoms associated with pneumonia. Alternate specific criteria for the elderly, infants and immunocompromised patients have been included in this definition of nosocomial pneumonia.

5. Nosocomial pneumonia can be characterized by its onset: early or late. Early onset pneumonia occurs during the first 4 days of hospitalization and is often caused by *Moraxella catarrhalis, H. influenzae,* and *S. pneumoniae.* Causative agents of late onset pneumonia are frequently gram-negative bacilli or *Staphylococcus aureus,* including methicillin-resistant *S. aureus.* Viruses (e.g., influenza A and B or respiratory syncytial virus) can cause early and late onset nosocomial pneumonia, whereas yeasts, fungi, legionellae, and *Pneumocystis carinii* are usually pathogens of late onset pneumonia.
6. Pneumonia resulting from gross aspiration (e.g., in the setting of intubation in the emergency room or operating room) is considered nosocomial if it meets any specific criteria and was not clearly present or incubating at the time of admission to the hospital.
7. Multiple episodes of nosocomial pneumonia may occur in critically ill patients with lengthy hospital stays. When determining whether to report multiple episodes of nosocomial pneumonia in a single patient, look for evidence of resolution of the initial infection. The addition of or change in pathogen alone is *not* indicative of a new episode of pneumonia. The combination of new signs and symptoms and radiographic evidence or other diagnostic testing is required.
8. Positive Gram stain for bacteria and positive KOH mount for elastin fibers and/or fungal hyphae from appropriately collected sputum specimens are important clues that point toward the etiology of the infection. However, sputum samples are frequently contaminated with airway colonizers and, therefore, must be interpreted cautiously. In particular, *Candida* is commonly seen on stain but infrequently causes nosocomial pneumonia.

Abbreviations

BAL—bronchoalveolar lavage
EIA—enzyme immunoassay
FAMA—fluorescent-antibody staining of membrane antigen
IFA—immunofluorescent antibody
LRT—lower respiratory tract
PCR—polymerase chain reaction
PMN—polymorphonuclear leukocyte
RIA—radioimmunoassay

Reporting Instructions

- There is a hierarchy of specific site categories within the major site pneumonia. Even if a patient meets criteria for more than one specific site, report only one:
  - If a patient meets criteria for both PNU1 and PNU2, report PNU2.
  - If a patient meets criteria for both PNU2 and PNU3, report PNU3.
  - If a patient meets criteria for both PNU1 and PNU3, report PNU3.
- Report concurrent lower respiratory tract infection (e.g., abscess or empyema) and pneumonia with the same organism(s) as pneumonia.
- Report lung abscess or empyema *without* pneumonia as LUNG.
- Report acute bronchitis, tracheitis, tracheobronchitis, or bronchiolitis *without* pneumonia as BRON.

APPENDIX A-2. PNEUMONIA ALGORITHMS

Major Site: Pneumonia (PNEU)
Site-Specific Algorithms for Clinically Defined Pneumonia (PNU1)

Radiology	Signs/symptoms/laboratory	Code
Two or more serial chest radiographs with at least *one* of the following[1,2]: • New or progressive • *and* persistent infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old	FOR ANY PATIENT, at least *one* of the following: • Fever (>38°C or >100.4°F) with no other recognized cause • Leukopenia (<4,000 WBC/mm^3) *or* leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause *and* At least *two* of the following: • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilation demand)	PNU1
NOTE: In patients without underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), *one definitive* chest radiograph is acceptable[1].	ALTERNATE CRITERIA FOR INFANT ≤1 YEAR OLD: Worsening gas exchange (e.g., O_2 desaturations, increased oxygen requirements, or increased ventilator demand) *and* at least *three* of the following: • Temperature instability with no other recognized cause • Leukopenia (<4,000 WBC/mm^3) *or* leukocytosis (≥15,000 WBC/mm^3) and left shift (≥10% band forms) • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • Apnea, tachypnea[5], nasal flaring with retraction of chest wall, or grunting • Wheezing, rales[6], or rhonchi • Cough • Bradycardia (<100 beats/min) or tachycardia (>170 beats/min) ALTERNATE CRITERIA FOR CHILD >1 OR ≤12 YEARS OLD, at least *three* of the following: • Fever (>38.4°C or >101.1°F) or hypothermia (<37°C or <97.7°F) with no other recognized cause • Leukopenia (<4,000 WBC/mm^3) *or* leukocytosis (≥15,000 WBC/mm^3) • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough or dyspnea, apnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., pulse oximetry <94%], increased oxygen requirements, or increased ventilation demand)	

Major Site: Pneumonia (PNEU)
Specific Site Algorithms for Pneumonia with Common Bacterial or Filamentous Fungal Pathogens and Specific Laboratory Findings (PNU2)

Radiology	Signs/symptoms	Laboratory	Code
Two or more serial chest radiographs with at least *one* of the following[1,2]: • New or progressive *and* persistent infiltrate • Consolidation • Cavitation	At least *one* of the following: • Fever (>38°C or >100.4°F) with no other recognized cause • Leukopenia (<4,000 WBC/mm^3) *or* leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause *and* At least *one* of the following: • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilation demand)	At least *one* of the following: • Positive growth in blood culture[8] not related to another source of infection • Positive growth in culture of pleural fluid • Positive quantitative culture[9] from minimally contaminated LRT specimen (e.g., BAL or protected specimen brushing) • ≥5% BAL-obtained cells contain intracellular bacteria on direct microscopic exam (e.g., Gram stain) • Histopathologic exam shows at least *one* of the following evidences of pneumonia: Abscess formation or foci of consolidation with intense PMN accumulation in bronchioles and alveoli Positive quantitative culture[9] of lung parenchyma Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae	PNU2
NOTE: In patients without underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), *one definitive* chest radiograph is acceptable[1].			

Major Site: Pneumonia (PNEU)
Specific Site Algorithms for Pneumonia with Viral, *Legionella, Chlamydia, Mycoplasma*, and Other Uncommon Pathogens and Specific Laboratory Findings (PNU2)

Radiology	Signs/symptoms	Laboratory	Code
Two or more serial chest radiographs with at least *one* of the following[1,2]: • New or progressive *and* persistent infiltrate • Consolidation • Cavitation NOTE: In patients without underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), *one definitive* chest radiograph is acceptable[1].	At least *one* of the following: • Fever (>38°C or >100.4°F) with no other recognized cause • Leukopenia (<4,000 WBC/mm^3) *or* leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause *and* At least *one* of the following: • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., $PaO_2/FiO_2 \leq 240$][7], increased oxygen requirements, or increased ventilation demand)	At least *one* of the following[10–12]: • Positive culture of virus or *Chlamydia* from respiratory secretions • Positive detection of viral antigen or antibody from respiratory secretions (e.g., EIA, FAMA, shell vial assay, PCR) • Fourfold rise in paired sera (IgG) for pathogen (e.g., influenza viruses, *Chlamydia*) • Positive PCR for *Chlamydia* or *Mycoplasma* • Positive micro-IF test for *Chlamydia* • Positive culture or visualization by micro-IF of *Legionella* spp. from respiratory secretions or tissue • Detection of *Legionella pneumophila* serogroup 1 antigens in urine by RIA or EIA • Fourfold rise in *L. pneumophila* serogroup **1** antibody titer to ≥1:128 in paired acute and convalescent sera by indirect IFA	PNU2

Major Site: Pneumonia (PNEU)
Specific Site Algorithm for Pneumonia in Immunocompromised Patients (PNU3)

Radiology	Signs/symptoms	Laboratory	Code
Two or more serial chest radiographs with at least *one* of the following[1,2]: • New or progressive *and* persistent infiltrate • Consolidation • Cavitation NOTE: In patients without underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), *one definitive* chest radiograph is acceptable[1].	Patient who is immunocompromised[13] has at least *one* of the following: • Fever (>38°C or >100.4°F) with no other recognized cause • For adults ≥70 years old, altered mental status with no other recognized cause • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., $PaO_2/FiO_2 \leq 240$][7], increased oxygen requirements, or increased ventilation demand) • Hemoptysis • Pleuritic chest pain	At least *one* of the following: • Matching positive blood and sputum cultures with *Candida* spp.[14,15] • Evidence of fungi or *Pneumocytis carinii* from minimally contaminated LRT specimen (e.g., BAL or protected specimen brushing) from *one* of the following: – Direct microscopic exam – Positive culture of fungi Any of the following from: LABORATORY CRITERIA DEFINED UNDER PNU2	PNU3

1. Occasionally, in nonventilated patients, the diagnosis of nosocomial pneumonia may be quite clear on the basis of symptoms, signs, and a single definitive chest radiograph. However, in patients with pulmonary or cardiac disease (e.g., interstitial lung disease or congestive heart failure), the diagnosis of pneumonia may be particularly difficult. Other noninfectious conditions (e.g., pulmonary edema from decompensated congestive heart failure) may simulate the presentation of pneumonia. In these more difficult cases, serial chest radiographs must be examined to help separate infectious from noninfectious pulmonary processes. To help confirm difficult cases, it may be useful to review radiographs on the day of diagnosis, 3 days prior to the diagnosis, and on days 2 and 7 after the diagnosis. Pneumonia may have rapid onset and progression but does not resolve quickly. Radiographic changes of pneumonia persist for several weeks. As a result, rapid radiograph resolution suggests that the patient does *not* have pneumonia but rather a noninfectious process such as atelectasis or congestive heart failure.
2. Note that there are many ways of describing the radiographic appearance of pneumonia. Examples include, but are not limited to, air-space disease, focal opacification, and patchy areas of increased density. Although perhaps not specifically delineated as pneumonia by the radiologist, in the appropriate clinical setting these alternative descriptive wordings should be seriously considered as potentially positive findings.
3. Purulent sputum is defined as secretions from the lungs, bronchi, or trachea that contain ≥25 neutrophils and ≤10 squamous epithelial cells per low power field (×100). If your laboratory reports these data qualitatively (e.g., many WBCs or few squames), be sure their descriptors match this definition of purulent sputum. This laboratory confirmation is required because written clinical descriptions of purulence are highly variable.
4. A single notation of either purulent sputum or change in character of the sputum is not meaningful; repeated notations over a 24-hour period would be more indicative of the onset of an infectious process. Change in character of sputum refers to the color, consistency, odor, and quantity.

Footnotes Continued.

5. In adults, tachypnea is defined as respiration rate >25 breaths per minute. Tachypnea is defined as >75 breaths per minute in premature infants born at <37 weeks' gestation and until the 40th week; >60 breaths per minute in patients <2 months old; >50 breaths per minute in patients 2–12 months old; and >30 breaths per minute in children >1 year old.
6. Rales may be described as crackles.
7. This measure of arterial oxygenation is defined as the ratio of the arterial tension (PaO_2) to the inspiratory fraction of oxygen (FiO_2).
8. Care must be taken to determine the etiology of pneumonia in a patient with positive blood cultures and radiographic evidence of pneumonia, especially if the patient has invasive devices in place such as intravascular lines or an indwelling urinary catheter. In general, in an immunocompetent patient, blood cultures positive for coagulase negative staphylococci, common skin contaminants, and yeasts will not be the etiologic agent of the pneumonia.
9. Refer to Table A-2.1 for threshold values of bacteria from cultured specimens. An endotracheal aspirate is not a minimally contaminated specimen. Therefore, an endotracheal aspirate does not meet the laboratory criteria.
10. Once laboratory-confirmed cases of pneumonia due to respiratory syncytial virus (RSV), adenovirus, or influenza virus have been identified in a hospital, clinician's presumptive diagnosis of these pathogens in subsequent cases with similar clinical signs and symptoms is an acceptable criterion for presence of nosocomial infection.
11. Scant or watery sputum is commonly seen in adults with pneumonia due to viruses and *Mycoplasma* although sometimes the sputum may be mucopurulent. In infants, pneumonia due to RSV or influenza yields copious sputum. Patients, except premature infants, with viral or mycoplasmal pneumonia may exhibit few signs or symptoms, even when significant infiltrates are present on radiographic exam.
12. Few bacteria may be seen on stains of respiratory secretions from patients with pneumonia due to *Legionella* spp, *Mycoplasma*, or viruses.
13. Immunocompromised patients include those with neutropenia (absolute neutrophil count <500/mm^3), leukemia, lymphoma, HIV with CD4 count <200, or splenectomy; those who are in their transplant hospital stay; and those who are on cytotoxic chemotherapy, high dose steroids, or other immunosuppressives daily for >2 weeks [e.g., >40mg of prednisone or its equivalent (>160mg hydrocortisone, >32mg methylprednisolone, >6mg dexamethasone, >200mg cortisone)].
14. Blood and sputum specimens must be collected within 48 hours of each other.
15. Semiquantitative or nonquantitative cultures of sputum obtained by deep cough, induction, aspiration, or lavage are acceptable. If quantitative culture results are available, refer to algorithms that include such specific laboratory findings.

TABLE A-2.1. THRESHOLD VALUES FOR CULTURED SPECIMENS USED IN THE DIAGNOSIS OF PNEUMONIA

Specimen Collection/Technique	Values	Comment
Lung parenchyma	$\geq 10^4$ CFU/g tissue	1
Bronchoscopically (B) obtained specimens		
Bronchoalveolar lavage (B-BAL)	$\geq 10^4$ CFU/mL	
Protected BAL (B-PBAL)	$\geq 10^4$ CFU/mL	
Protected specimen brushing (B-PSB)	$\geq 10^3$ CFU/mL	
Nonbronchoscopically (NB) obtained (blind) specimens		
NB-BAL	$\geq 10^4$ CFU/mL	
NB-PSB	$\geq 10^3$ CFU/mL	

1, open-lung biopsy specimens and immediate postmortem specimens obtained by transthoracic or transbronchial biopsy; CFU, colony-forming units; g, gram; mL, milliliter.