# Severe Acute Respiratory Syndrome (SARS): What Every Clinician Should Know About Diagnosis and Management

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SARS Preparedness Task Force
**National Center for Infectious Diseases**

# Objectives

- Review the importance of early recognition
- Review the clinical presentation of SARS
- Review key epidemiologic features of SARS
- Describe a strategy for early recognition and management that combines clinical and epidemiologic features
  - Before SARS activity is documented
  - After SARS activity is documented

# Importance of Early Recognition

- Simple infection control measures can dramatically reduce transmission of SARS-CoV
- Delays in clinical recognition and isolation of SARS patients contributed to transmission
- Early case detection and isolation will be critical in controlling future outbreaks of SARS

# Clinical Aspects of Severe Acute Respiratory Syndrome (SARS)

- Incubation period 2-10 days
  - Median 4-6
  - Rarely up to 14 days?
- Onset of fever, chills/rigors, headache, myalgias, malaise
  - Fever may resolve prior to respiratory symptoms
  - Diarrhea has been a prominent feature of early illness in some
- Respiratory symptoms often begin 3-7 days after symptom onset, peak in second week
  - 30% have respiratory symptoms at onset

# Symptoms Commonly Reported By Patients Presenting with SARS

| Symptom | Range (%) |
|---|---|
| Fever | 95-100 |
| Cough | 57-100 |
| Dyspnea | 20-100 |
| Chills/Rigor | 73-90 |
| Myalgias | 20-83 |
| Headache | 20-70 |
| Diarrhea | 10-67 |
| Nausea/Vomiting | 10-24 |

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| Diarrhea | 10-67 |
| Nausea/Vomiting | 10-24 |
| (Rhinorrhea) | 5-25 |
| (Sore Throat) | 5-25 |

# Common Clinical Findings in Patients with SARS

| Finding | Range (%) |
|---|---|
| **Physical Examination** | |
| Rales/Rhonci | 38-90 |
| Hypoxia | 60-83 |
| **Laboratory** | |
| Leukopenia | 17-34 |
| Lymphopenia | 70-95 |
| Thrombocytopenia | 30-50 |
| Prolonged aPTT | 40-60 |
| Increased ALT | 20-30 |
| Increased LDH | 70-94 |
| Increased CPK | 30-40 |

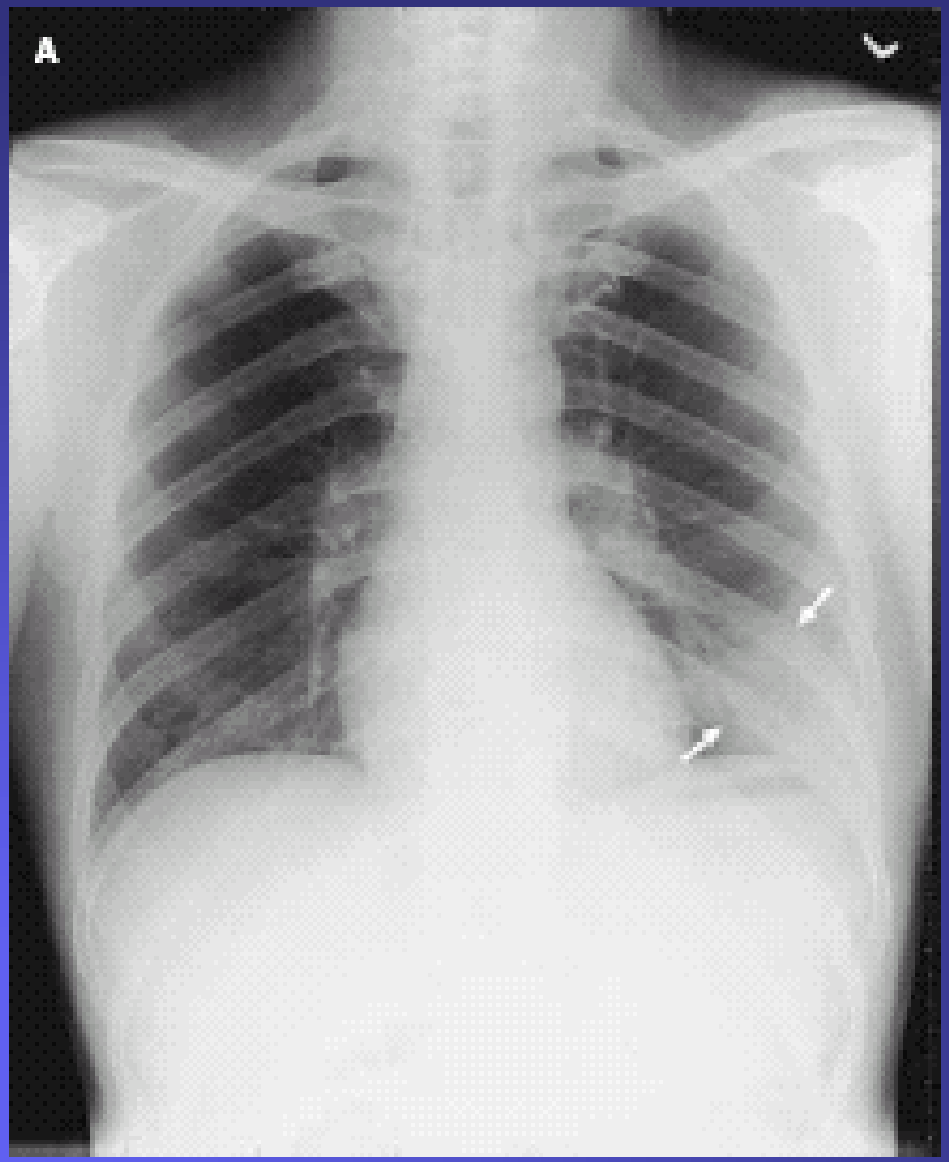
# Radiographic Features of SARS

- **Infiltrates develop on chest radiograph in nearly 100% of laboratory confirmed cases**
  - **At presentation, CXR normal in up to 30%**
- **How soon do abnormalities appear?**
  - **66% abnormal by day 3**
  - **97% abnormal by day 7**
  - **100% abnormal by day 10**

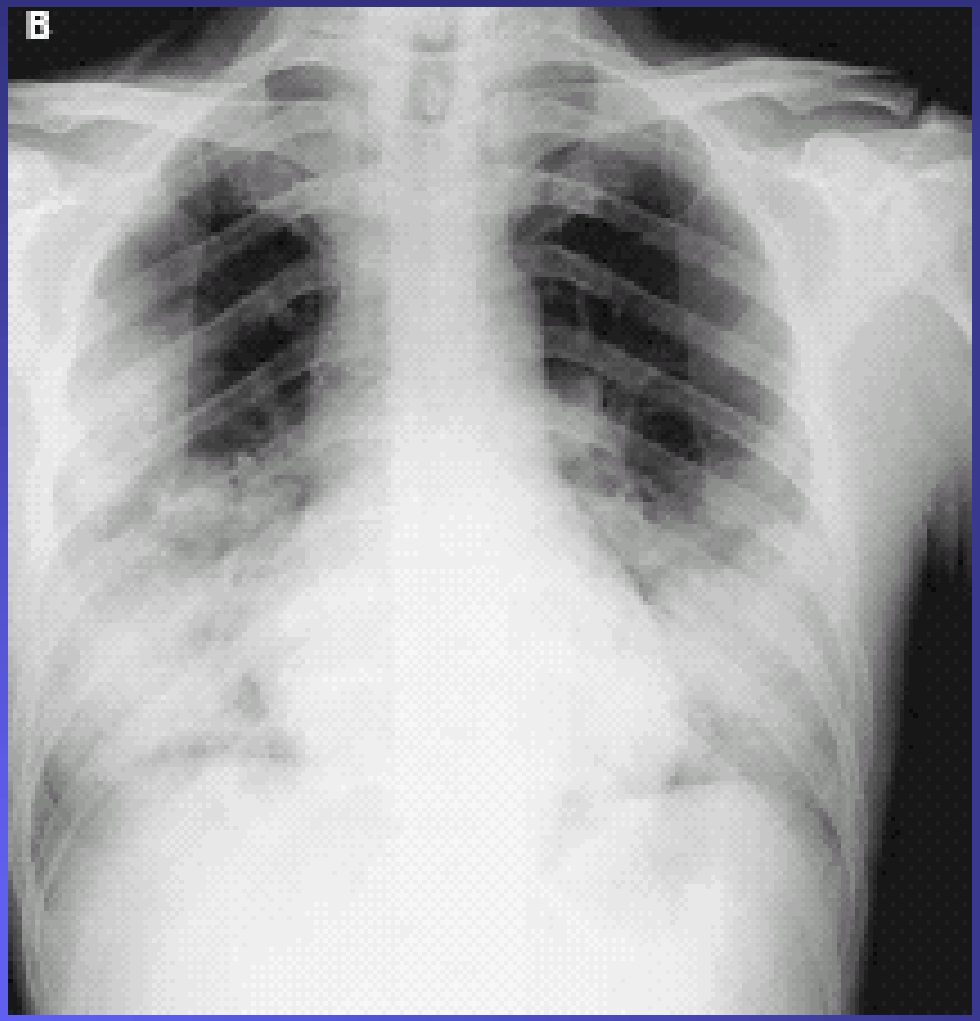

**Wong. Radiology 2003;228:401-6.**
**Wang. Proceedings of International Science Symposium on SARS. Beijing, China, 2003**
**Xue. Chin Med J 2003;116:819-822**
**Zhao. J Med Microbiol 2003;52:715-20.**
**Rainer. BMJ 2003;326:1354-8.**

# Radiographic Features of SARS

- **Infiltrates**
  - **initially focal, often peripheral lower lobes**
  - **interstitial**
  - **75% progress to involve multiple lobes or both lungs**
- **Computed tomography more sensitive than conventional radiography**
  - **Ground glass opacification**
  - **Peripheral lower lobes**




Lee N, et al NEJM 4/7/03

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# Common Clinical Features of the Severe Acute Respiratory Syndrome

| |
|---|
| Presenting Symptoms<br>Non-Respiratory Prodrome lasting 2-7 days characterized by one or more of the following:<br>Fever<br>Rigors<br>Headache<br>Malaise<br>Myalgia<br>Diarrhea/Nausea/Vomiting<br>Respiratory phase beginning 2-7 days after onset characterized by:<br>Non-productive cough<br>Dyspnea<br>Absence of upper respiratory symptoms |
| Laboratory Findings<br>Normal or low total white blood cell count<br>Lymphopenia<br>Elevated lactate dehydrogenase levels<br>Elevated creatine phospokinase levels<br>Elevated transaminase levels<br>Prolonged activated partial thromboplastin time |
| Radiographic Findings<br>Abnormal chest X-ray in almost all patients by day 7 of illness |

# Laboratory Diagnosis of SARS

- **SARS CoV testing**
  - **RNA detection by RT-PCR or real time PCR**
  - **Serology**

# Laboratory Diagnosis of SARS

- **Ability to detect SARS CoV early in illness limited**
  - **Low titer of virus in early specimens**
    - **< 50% positive by PCR 1st week**
    - **Testing multiple specimens may improve ability to diagnose**
      - **Respiratory, stool, serum/plasma**
      - **Stool may be best**
- **Antibody response can take up to 28 days**
    - **Detectable as early as 10-14 days**
- **False positive PCR assays a concern**

Currently, there are no specific clinical or laboratory findings which can distinguish with certainty SARS from other respiratory illnesses at the time of presentation

Early recognition will depend on the astute clinician's ability to combine clinical and epidemiologic features!

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- **Case clustering**
- **Association with healthcare**

# Key to Early Clinical Decision Making: Combining Clinical and Epidemiologic Features

- **Requires assessment of both:**
  - **clinical compatibility with SARS**

**AND**

  - **risk of exposure to SARS**
    - **depends upon level of SARS activity in the surrounding community and the world**
      - **No documented SARS transmission**
      - **Documented SARS transmission**

# Evaluating Patients When No SARS Transmission Documented Anywhere in the World

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- **Likelihood of SARS approaches zero unless presence of both the following:**
  - **Suggestive clinical presentation (i.e. severe unexplained pneumonia)**

    **AND**

  - **Epidemiologic features suggesting possibility of exposure to SARS-CoV**
    - **Travel to previously affected area OR clustering OR healthcare association**

# When SARS Transmission Has Not Been Documented Anywhere in the World.....

**SARS should only be considered in patients who:**

1. **Are hospitalized for pneumonia of unknown etiology <u>AND</u>**
2. **Have evidence of one of the following:**
   - **recent travel to a previously SARS-affected area or close contact with ill persons with a history of travel to such areas**
   - **Employment as a healthcare worker with recent direct patient contact**
   - **recent exposure to other persons with unexplained pneumonia**

# When SARS Transmission Has Not Been Documented Anywhere in the World.....

**If a patient hospitalized for pneumonia has at least one exposure risk factor, the clinician should:**

1. **Notify local health department**
2. **Use droplet precautions**
3. **Treat for common causes of community-acquired pneumonia**
4. **Perform diagnostic workup, including:**
   - **CBC with differential**
   - **Pulse oximetry**
   - **Blood cultures**
   - **Sputum Gram's stain and culture**
   - **Testing for viral respiratory pathogens**
   - **Urinary antigen testing: legionella and pneumococcal**
   - **Other tests: CPK, transaminase levels, LDH, aPTT, C-reactive protein**
5. **If no alternative diagnosis within 72 hours, consider need for SARS testing in consulation with local health department**

# Evaluating Patients Following Documented SARS Transmission Anywhere in the World

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- **Risk of exposure to SARS CoV varies based on presence of epidemiologic link to settings in which current SARS activity has been documented**

# Evaluating Patients Following Documented SARS Transmission Anywhere in the World

- No exposure to settings with current SARS activity
  - Very low risk
  - Higher threshold for clinical suspicion of SARS
    - Hospitalized for pneumonia

      plus
    - travel to *previously* SARS-affected area, clustering, or healthcare association
- Exposure to settings with documented SARS activity
  - Significant risk
  - Lower threshold for clinical suspicion of SARS
    - e.g. Fever *OR* respiratory illness

# After SARS Transmission Documented Anywhere in the World…

- **SARS should be considered among patients with both:**
  - **Early clinical features compatible with SARS (i.e. fever *OR* respiratory symptoms)**

    **AND**

  - **Evidence suggesting potential exposure to SARS CoV**
    - **Exposure to areas *currently* affected by SARS (foreign or domestic)**

      **OR**
    - **close contact to a suspected SARS case**

# After SARS Transmission Documented Anywhere in the World…

- Any patient with either fever OR respiratory symptoms should be asked about:
  - Recent exposure to a SARS-affected area or close contact with ill persons with exposure to such areas (foreign or domestic)
  - Recent exposure to a person suspected of having SARS

# After SARS Transmission Documented Anywhere in the World…

**If fever OR respiratory symptoms AND has at least one risk factor for exposure to SARS CoV:**

1. **Begin SARS isolation precautions**
2. **Notify local health department**
3. **Diagnostic workup**
   - **Chest X-ray**
   - **CBC with differential**
   - **Pulse oximetry**
   - **Blood cultures**
   - **Sputum Gram's stain and culture**
   - **Testing for viral respiratory pathogens**
   - **If pneumonia, then urinary antigen testing: legionella and pneumococcal**
   - **Other tests: CPK, transaminase levels, LDH, aPTT, C-reactive protein**
4. **Follow management algorithm……**

# Draft- Algorithm to Work Up and Isolate Symptomatic Persons who may have been Exposed to SARS

**Fever or Respiratory Illness in Adults Who May Have Been Exposed to SARS**

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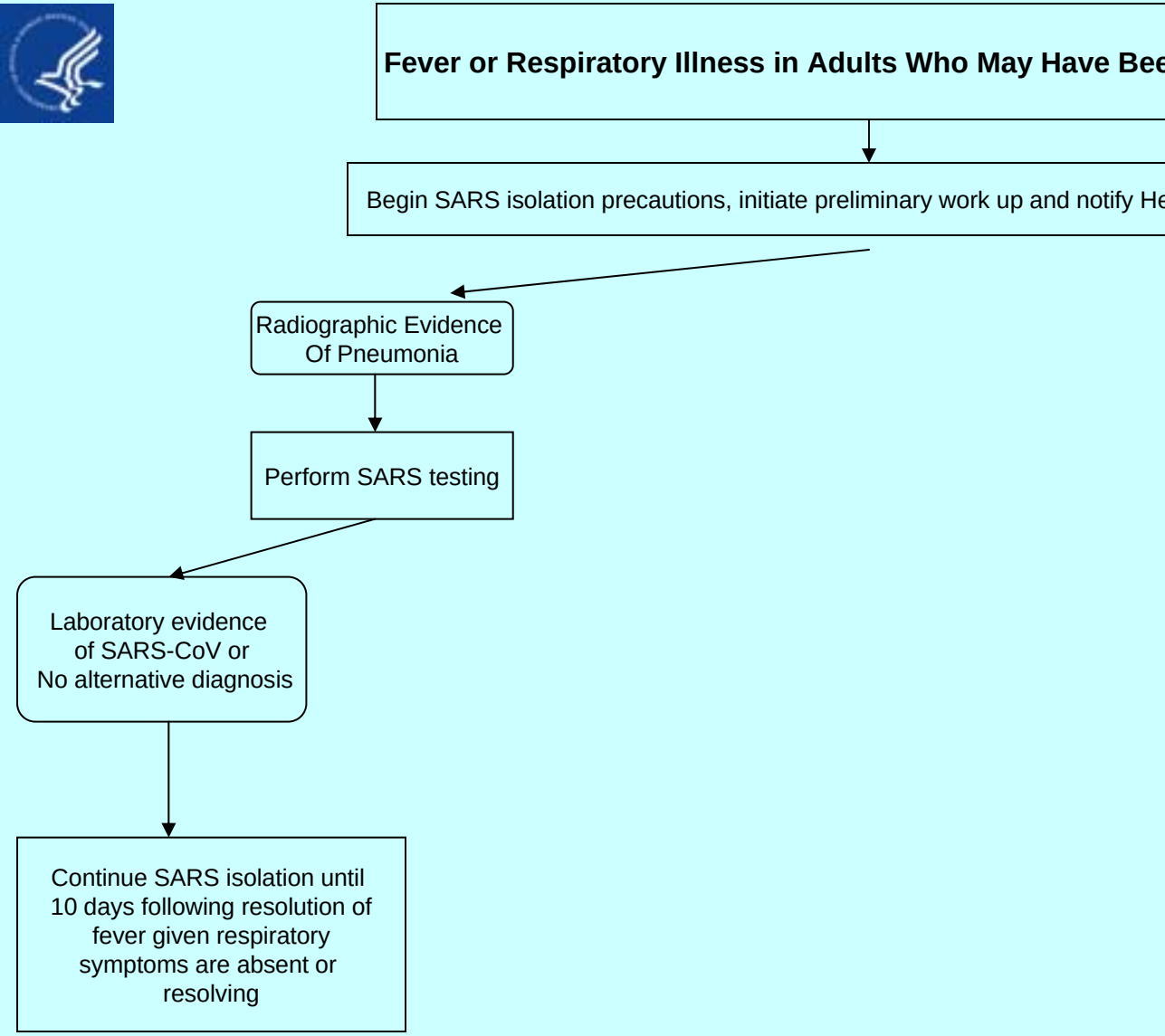
Begin SARS isolation precautions, initiate preliminary work up and notify Health Department

# Draft-Algorithm to Work Up and Isolate Symptomatic Persons who may have been Exposed to SARS



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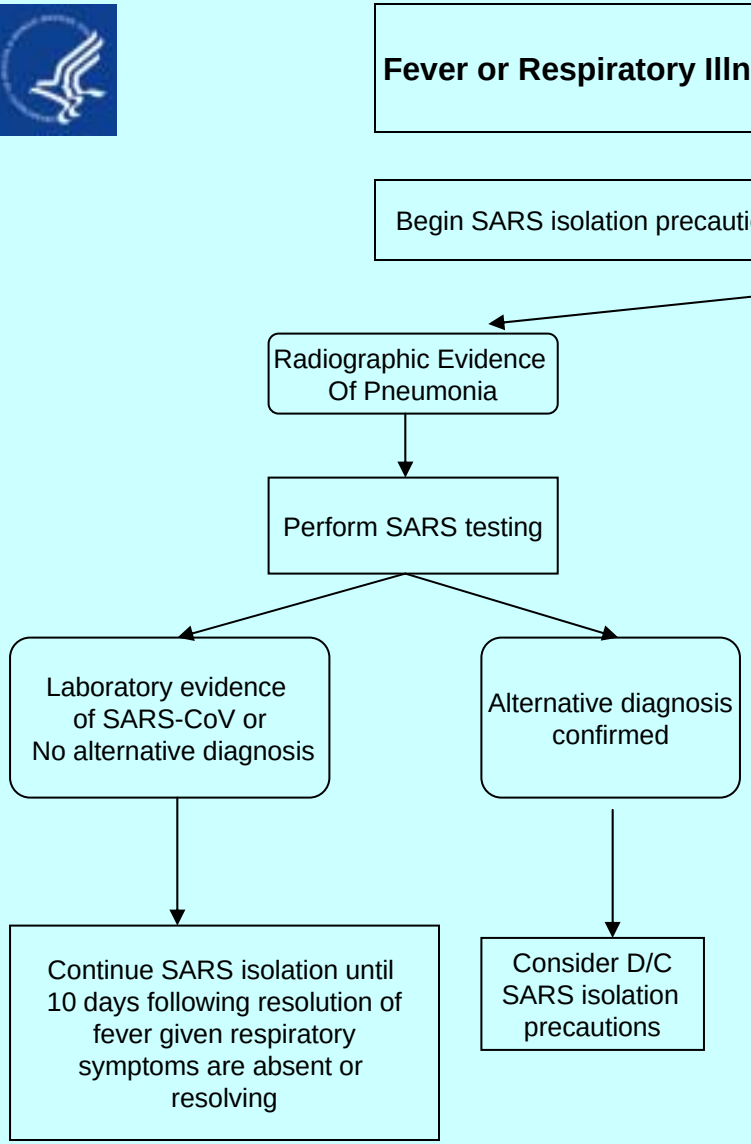

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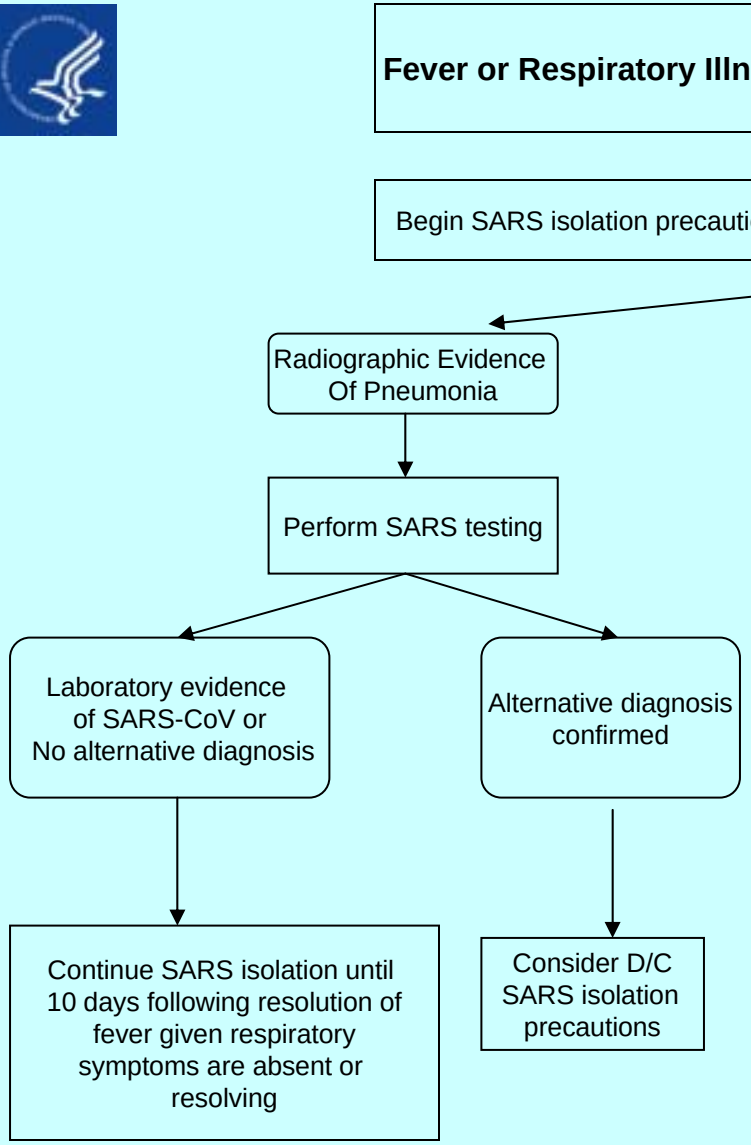


Using Alternative Diagnosis to "Rule Out" SARS

- Based on test with high positive predictive value
- Clinical course consistent
- No evidence of clustering
- No strong epidemiologic link

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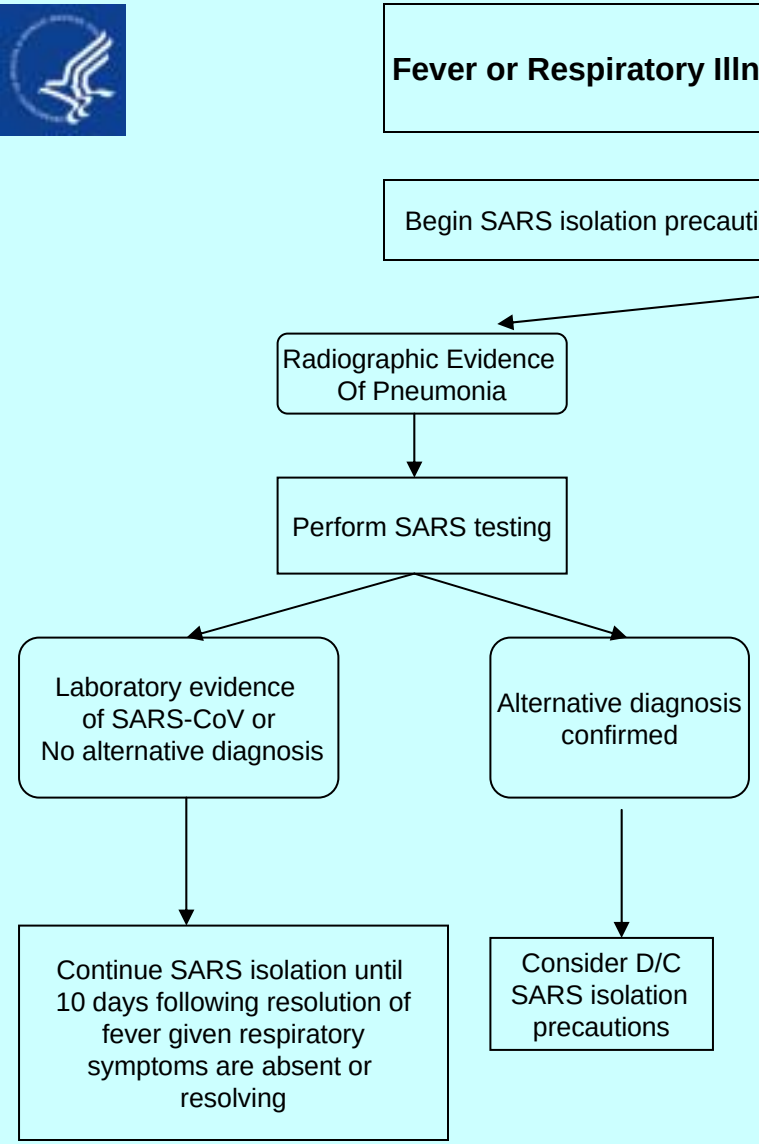

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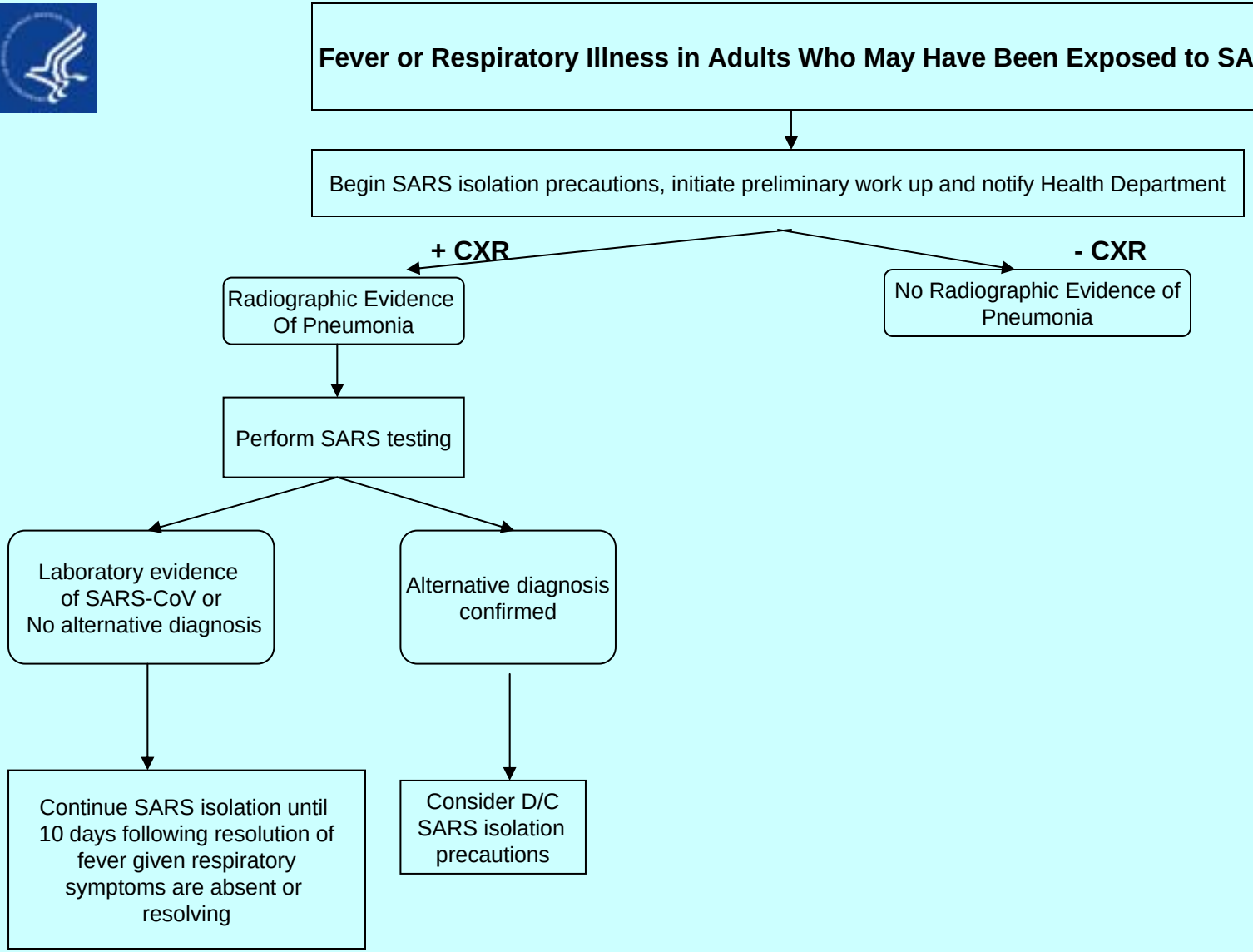

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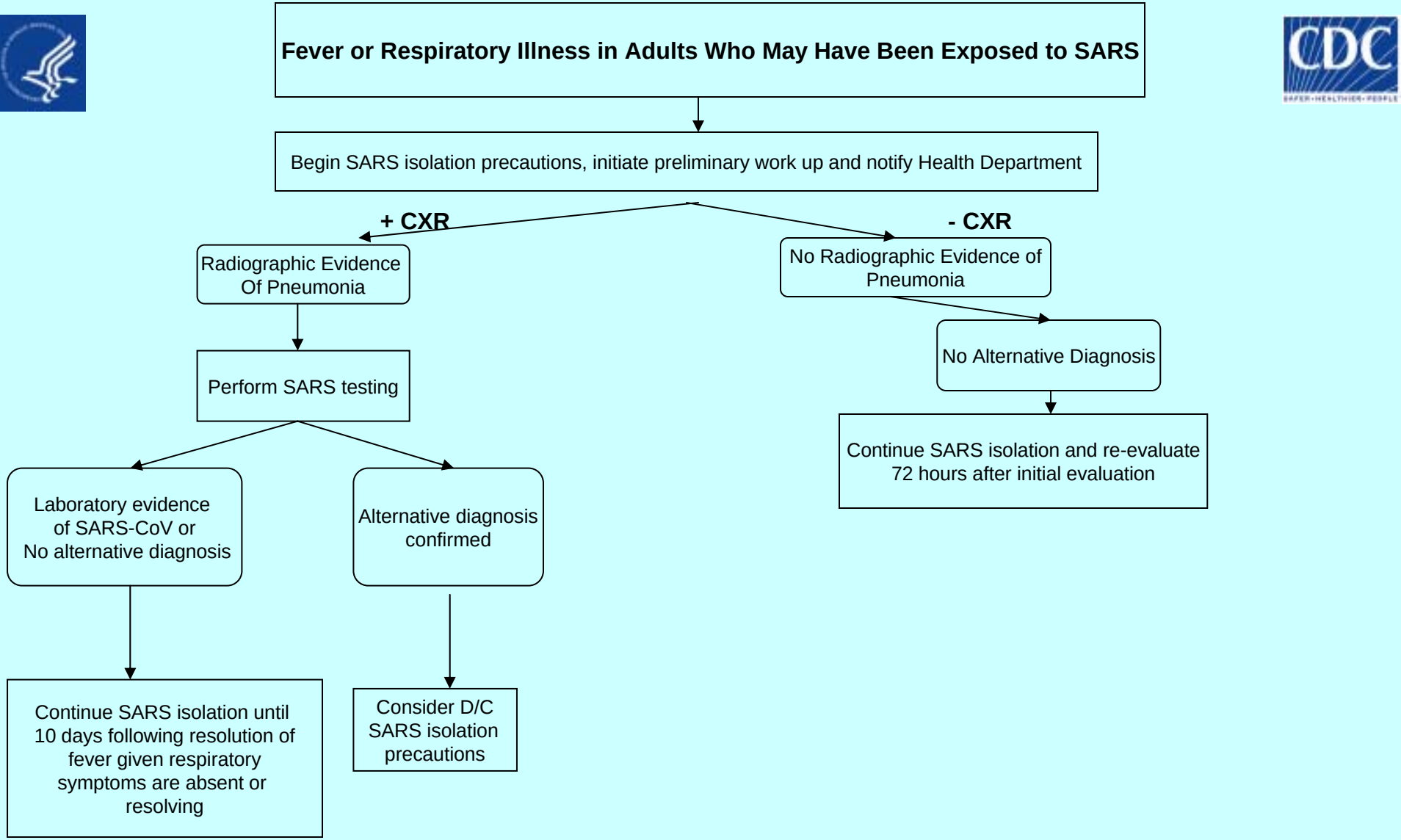

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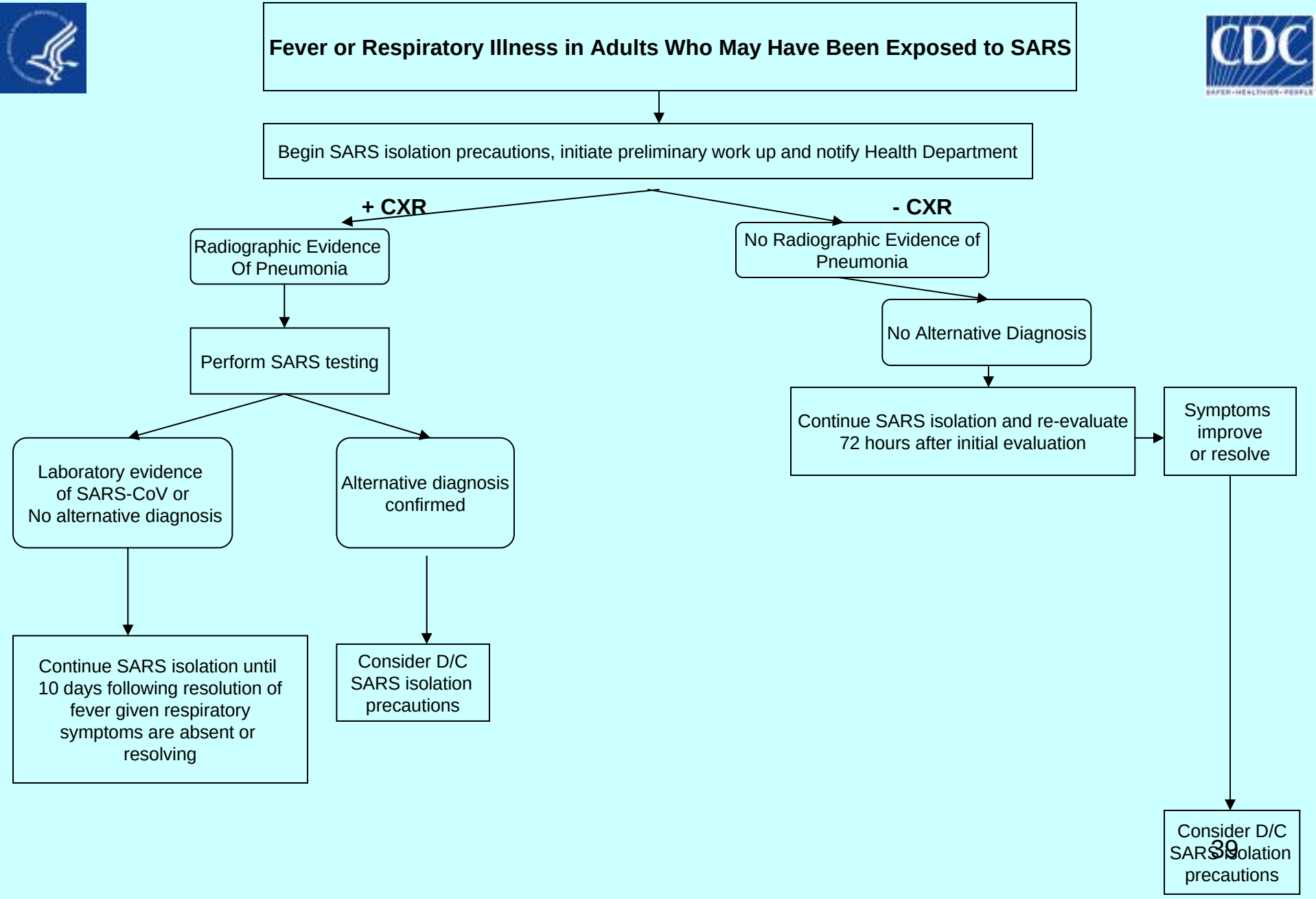

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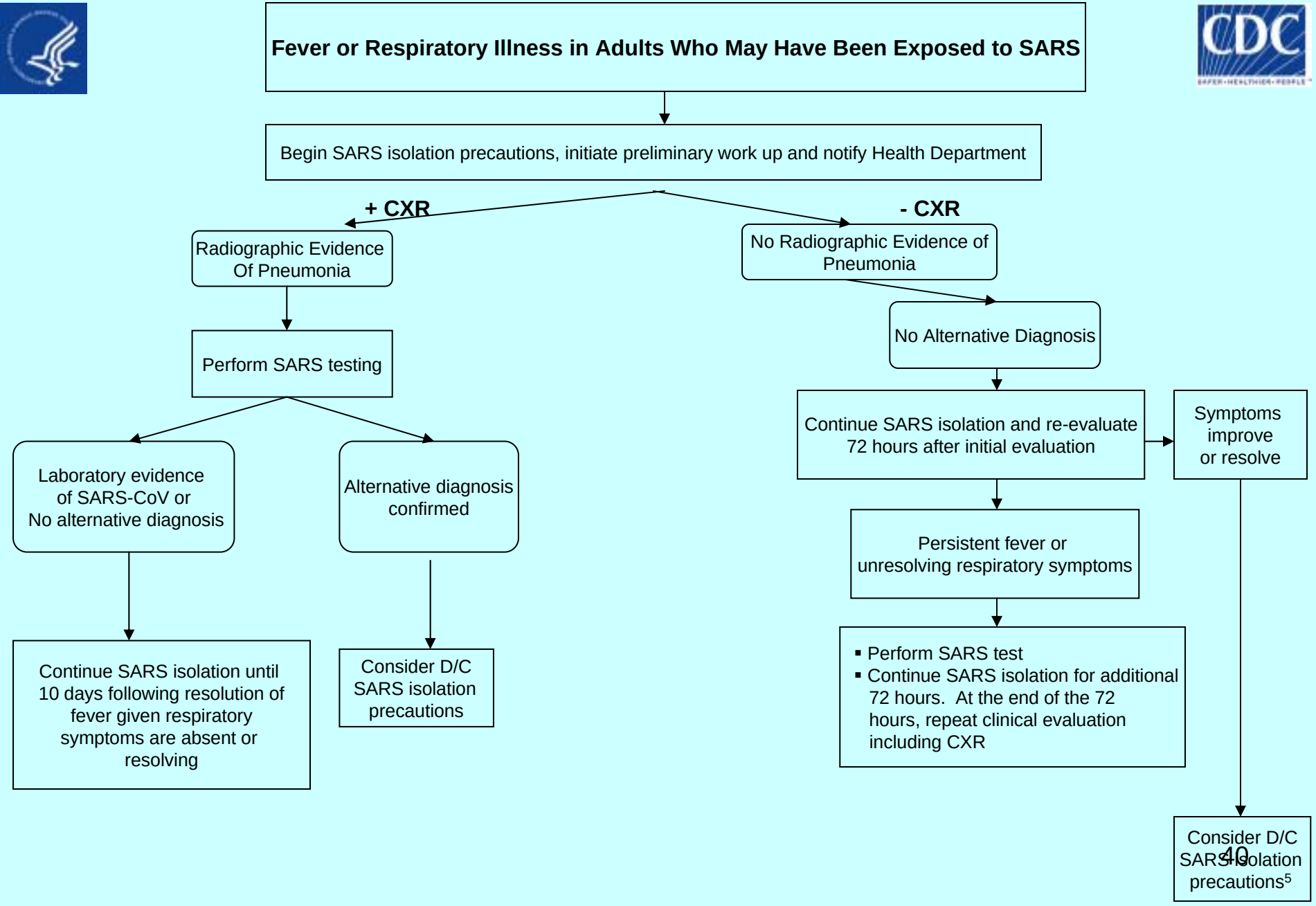

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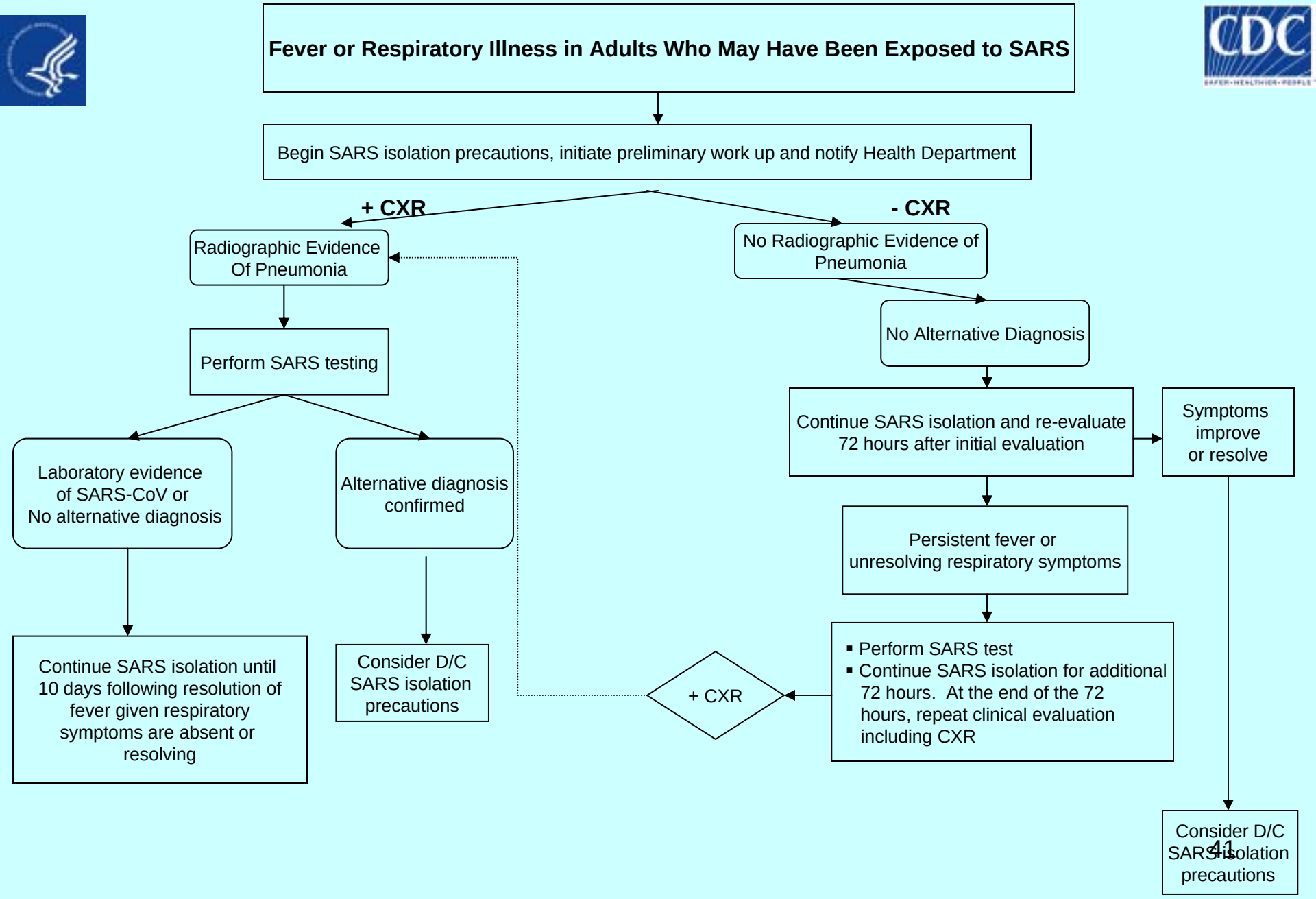

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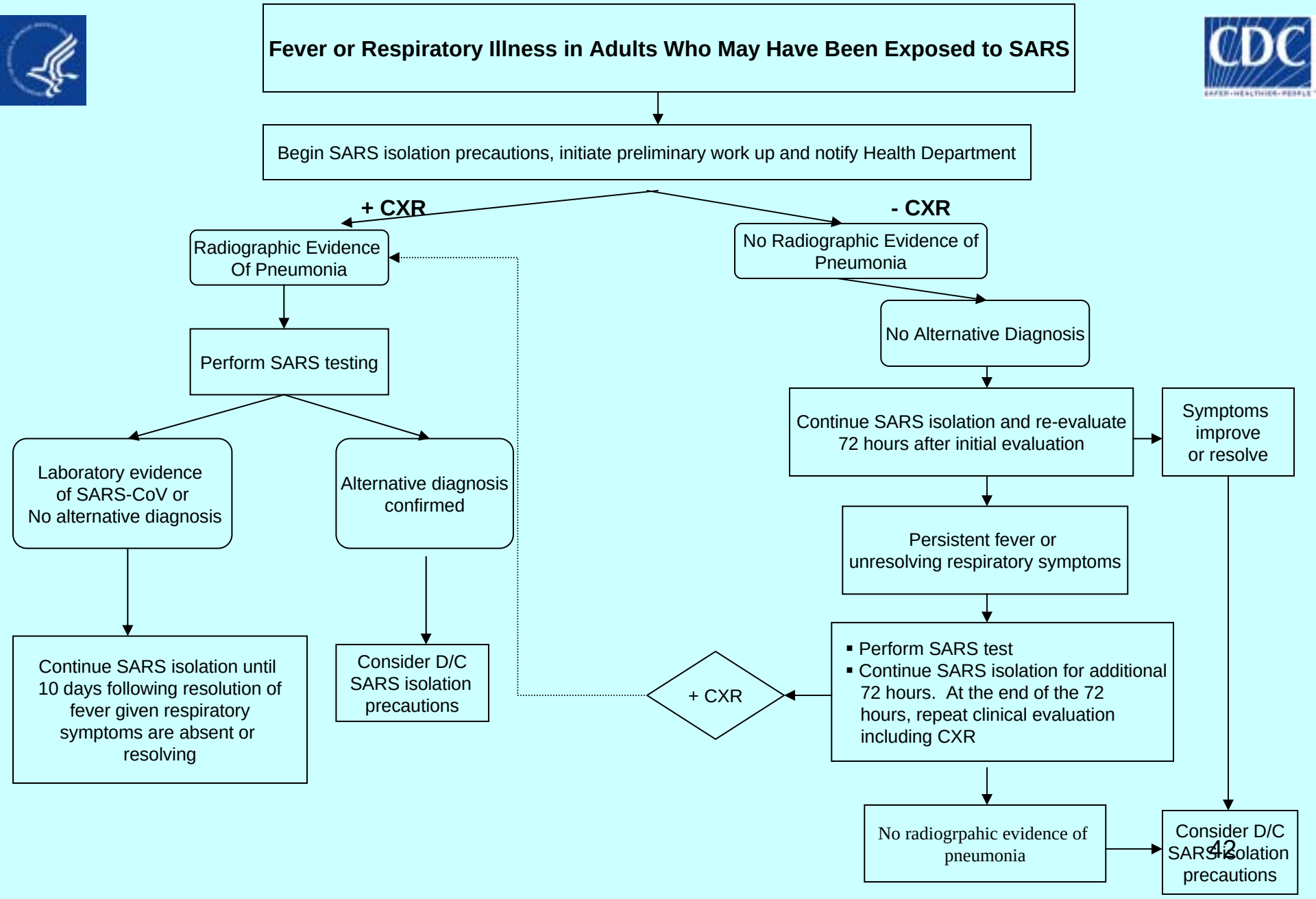

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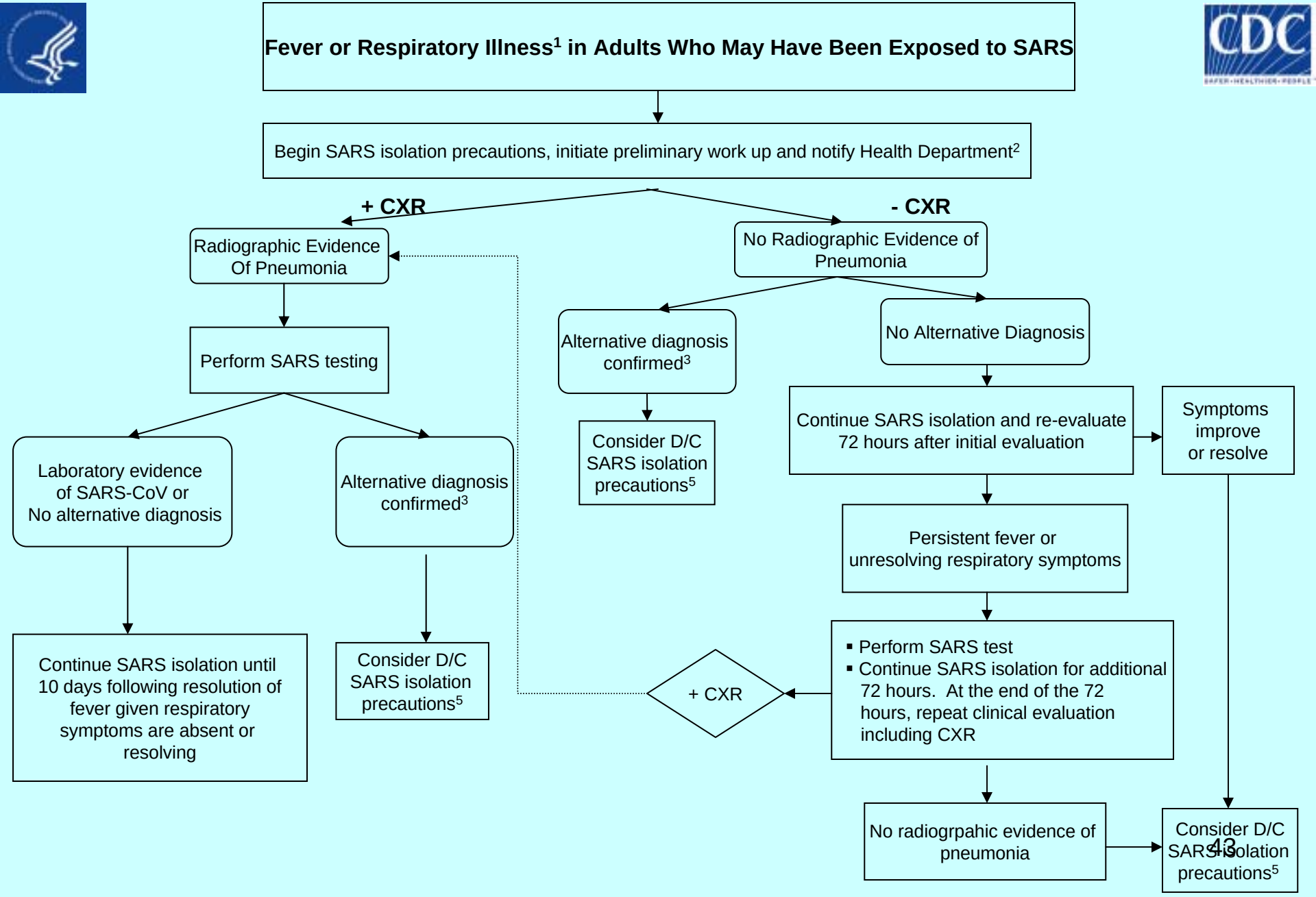

# Additional Considerations

- **Community outbreaks**
- **Nosocomial SARS**
- **Elderly and underlying chronic illness**
- **Pediatrics**

# Importance of Communication with Public Health Authorities

- clinicians must have frequent updates regarding location of SARS activity
- mechanisms for rapid communication between clinicians and public health agencies must be in place
- communication important in rapid identification of emerging areas of SARS activity

# Treatment of Patients with SARS

- **No proven effective therapy**
  - **Optimize supportive care**
- **Treat for other potential causes of community-acquired pneumonia of unknown etiology**

# Treatment of Patients with SARS

- **Potential therapies requiring further investigation**
  - **Cystine proteinase inhibitors**
  - **Interferons**
  - **Immunomodulatory agents**
    - **Corticosteriods**
    - **SARS-CoV specific immune globolin**
    - **Others?**

# Summary

- Early recognition of patients with SARS is critical to successful control of future outbreaks.
- Clinical features alone cannot reliably distinguish SARS from other respiratory illnesses
- Currently available SARS CoV tests unlikely to be helpful in early clinical decision making
- Epidemiologic features are the key to early recognition and clinical decision making
  - Importance of rapid communication between clinicians and public health authorities
- The approach to early recognition will vary depending upon the level of SARS activity in the surrounding community and the world