Clinical Management of Chronic Hepatitis B
Revised 2004

Scope

This guideline is for general practitioners, internists, and pediatricians. It recommends a diagnostic work-up for patients with chronic active hepatitis B and referral for treatment to physicians with expertise in hepatitis.

The goal is to:
• Prevent the spread of the virus to other persons
• Improve the patient’s quality of life
• Cure the disease where possible

**Recommendation 1:** Patient counselling

Counsel patients to prevent spread. See the attached patient guide.

**Recommendation 2:** Confirmation of chronic active hepatitis B

Confirm active hepatitis B by positive surface antigen (HBsAg).

Confirm chronic hepatitis by an elevated ALT (alanine amino transferase) monthly for three consecutive months.

Confirm chronic hepatitis B with a repeat positive HBsAg six months later.

Note: In adults, less than five per cent of acute hepatitis B infections will result in chronic disease. Chronic carriers may occasionally clear surface HBsAg spontaneously without treatment. If given hepatitis B immune globulin (HBIG) and vaccinated at birth, less than 10 per cent of children of carrier mothers will develop chronic disease. If not given HBIG or vaccinated at birth, 90 per cent will develop chronic disease.

**Recommendation 3:** Indications for referral for treatment (adults only)

Patients who meet the following criteria should be considered for referral to a physician with expertise in hepatitis treatment.

• Patients whose liver enzymes are elevated – ALT more than 1.3 times the upper limit of normal, monthly for three consecutive months.

• Patients with end-stage liver disease (e.g. cirrhosis) who may present with normal ALT levels.

Treatment of patients with chronic hepatitis B is complex and referral to a specialist is recommended.
Patients not meeting the above criteria should be monitored (see Recommendation 6).

Children: refer to Recommendation 10.

**RECOMMENDATION 4:** Relative contraindications to treatment

While all cases should be considered on an individual basis, the following factors are relative contraindications to treatment. If in doubt seek consultation with a specialist.

Relative contraindications to treat with interferon:

- non-compliant patient or psychosocially unstable
- ongoing drug or alcohol abuse; however, individual situations should be considered
- significant disease, such as heart disease, uncontrolled diabetes mellitus, active psychosis, severe depression, auto-immune disease, active bacterial infection (e.g. osteomyelitis)
- decompensated liver disease
- myelosuppression, e.g. thrombocytopenia (platelet count less than 80 x 10^9/L), neutropenia (neutrophil count less than 1 x 10^9/L)

Relative contraindications to treat with lamivudine:

- Although there are few contraindications, treatment is complex and specialist consultation is recommended.

**RECOMMENDATION 5:** Treatment of adult patients

Treatment should be given by a physician with expertise in hepatitis.

Notes: As ALT, serology and nucleic acid tests are imperfect markers, a liver biopsy is strongly indicated before treatment is initiated.

Treatment with interferon for 16 weeks will lead to an antiviral response in 25 to 30 per cent of individuals. Treatment with lamivudine for a year or more will lead to an antiviral response in 15 to 40 per cent of individuals. Prolonged therapy increases the risk of antiviral resistance.

What constitutes a hepatitis B antiviral response is complicated because of viral variability in patients and variability in the interpretation of the different available tests, e.g. ALT, HBsAg, HBeAg, HBV DNA.

Treatment protocols for chronic hepatitis B are constantly evolving. A recent document on the management of viral hepatitis is available at: http://www.hepatology.ca/cm/FileLib/ViralHepatitisCanadianConsensus2004.pdf

**RECOMMENDATION 6:** Monitoring untreated patients

If the ALT is normal or less than 1.3 times the upper limit of normal, repeat the ALT at three, six, and 12 months.

If the ALT remains normal or less than 1.3 times the upper limit of normal after one year of monitoring, repeat the ALT annually.

If the ALT is more than 1.3 times the upper limit of normal for three consecutive months, specialist referral is strongly recommended.
**RECOMMENDATION 7:** Monitoring treated patients

The physician with expertise in hepatitis who is actively treating the patient will individualize monitoring depending on the patient’s needs.

**RECOMMENDATION 8:** Determining if the patient is “cured”

Cure is achievable in only a small percentage of patients, but disease progression can be modified. The treating specialist will determine the length of treatment (see Recommendation 5).

The chance of clearing HBsAg with treatment is low, but disease progression can be modified by achieving a “sero-conversion”. A sero-conversion means achieving the following:

In patients who are initially HBeAg positive:
- A negative HBeAg
- A negative HBV DNA
- A positive HBeAb (positive anti-HBe), although this is not always possible

In patients who are initially HBeAg negative:
- A negative HBV DNA
- A positive HBeAb (positive anti-HBe)

Patients should have the above test results on three occasions over a three-month interval. Many patients treated with lamivudine achieve sero-conversion by 12 months of treatment, but treatment of 24 to 36 months may result in a higher patient response rate.

The occurrence of a HBV viral resistance mutation (usually at the YMDD locus) during treatment with lamivudine is high:
- 14 per cent by 12 months of treatment
- 30 per cent by 24 months of treatment
- 50 per cent by 36 months of treatment

A mutation is suggested if the ALT and AST become significantly elevated after an initial fall from the pre-treatment level. Prolonged treatment after development of the YMDD mutant is still controversial, but improvement in liver pathology with decreased fibrosis may occur if treatment is continued.

**RECOMMENDATION 9:** Screening for hepatocellular carcinoma (HCC)

HCC may occur in the absence of cirrhosis. The presence of cirrhosis will increase the risk of HCC further. Although the cost benefit of screening has yet to be proven, screening is suggested in all patients age 30 or older with one or more of the following risk factors:

- Infection at birth (perinatal/vertical transmission)
- Male gender
- Duration of infection for multiple decades
- Family history of HCC
- Co-infection with hepatitis C
- Groups at high risk, e.g. Asian, refugee populations

The most important risk factor is chronic infection for multiple decades. In addition, all patients with active disease (elevated AST, ALT) including cirrhosis are at risk.
Suggested screening consists of an abdominal ultrasound and serum alpha-fetoprotein at approximately six-month intervals.

**RECOMMENDATION 10: Infants and children**

Diagnostic testing for infants and children is complex and treatment guidelines are controversial. All pediatric patients should be referred to a pediatric specialist with expertise in viral hepatitis.

All infants born to hepatitis B virus (HBV) carrier mothers (i.e. HBsAg positive) should have received HBIG and the full course of HBV vaccination (0, 1, and 6 months). Vaccine failure in the neonate is rare, but does occur (less than 10 per cent) and is probably related to transplacental transmission before birth.

Follow-up testing should be performed at approximately three months after the HBV vaccination series is completed, as follows:

- HBsAg to detect vaccine failures
- anti-HBc (total) to detect previous infection
- anti-HBs to confirm vaccine effectiveness or failure

**RECOMMENDATION 11: Needlestick injuries**

**Hepatitis B**

Verify the immune status in the needlestick recipient and consider HBIG and a hepatitis B vaccine booster as appropriate. The risk of transmission is about 25 per cent. The risk of chronic infection after a needlestick injury, however, is almost zero in immunized populations.

**HIV**

Refer to the web site of the BC Centre for Excellence in HIV/AIDS at www.cfenet.ubc.ca/guide/page/sectg/tbsq.html

For further information see the Centres for Disease Control and Prevention (US) web site at www.cdc.gov/ncidod/hip/Blood/exp_blood.htm

**Rationale**

**Burden of Disease**

In British Columbia, approximately 40,000 persons are chronically infected with hepatitis B and another 40,000 persons are chronically infected with hepatitis C. Without treatment about 15 to 30 per cent of chronic hepatitis B and C carriers will develop cirrhosis and end-stage liver disease, hepatocellular cancer, or require liver transplantation over the next 2 to 4 decades. Approximately 100 individuals die of end-stage liver disease in B.C. per year (about three-quarters are due to hepatitis). The cost of end-stage liver disease, including lost income, is estimated at $1,000,000 per person and the cost of liver transplantation is $100,000 to $200,000 per person.

**Outcomes**

Interferon or lamivudine treatment can convert 25 to 35 per cent of HBe antigen positive patients to positive anti-HBe (positive HBeAb) and decrease the long-term risk of cirrhosis.\(^1\)\(^-\)\(^6\) Prolonged treatment with lamivudine for up to four years increases the probability of response, but also increases the risk of antiviral resistance 30 to 50 per cent. This undesirable outcome may alter lamivudine’s treatment effectiveness. For HBV, unlike HCV, complete ‘cure’ is not yet possible for most patients.
Evidence
Most data are based on randomized controlled trials. However, long-term follow-up has been limited to interferon treated patients. Data on lamivudine treated patients suggest similar improvements in outcome, but the duration of therapy and the importance of antiviral resistance remain unclear. Also the test methodologies to assess HBV antiviral effectiveness are not well standardized.

Benefits, harms, and costs
Given the long-term risks of HBV-associated liver complications, the relatively well-tolerated regimens of lamivudine favour its use over interferon, which is associated with a high rate of side effects. Therapy is approximately $1800/year per patient treated. However, questions remain regarding how long to treat, what are the risks, what are the implications of antiviral resistance, and how to measure the treatment response.

Guideline benefits and risks
Both HBV and HCV diagnosis and therapy are rapidly evolving and there is critical need to provide information to practitioners to assist in diagnosis, care and follow-up. Untreated chronic HBV and HCV place patients at risk of poor outcome due to hepatic damage. Given the medical complexity of hepatitis and the variation in knowledge and practice, guidelines are necessary for accurate diagnosis and follow-up. This guideline is expected to improve case-finding and support evidence-based clinical interventions.

References
Sponsors

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

Funding for this guideline was provided in full or part through the Primary Health Care Transition Fund.

Effective Date: October 1, 2004

This guideline is based on scientific evidence current as of the effective date.

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• to recommend actions that are sufficient and efficient, neither excessive nor deficient
• to permit exceptions when justified by clinical circumstances.
### Clinical Management of Chronic Hepatitis B

<table>
<thead>
<tr>
<th>Summary</th>
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1. **Patient counselling:**
   - Counsel to prevent spread.

2. **Confirmation of chronic active hepatitis B:**
   - Do HBsAg.
   - If +, repeat at 6 months.
   - If HBsAg remains +, do ALT.
   - If ALT > 1.3 times upper normal limit, do ALT monthly for 3 consecutive months.

3. **Indications for referral for treatment (adults):**
   - If ALT > 1.3 times upper limit for 3 consecutive months.

4. **Relative contraindications to treatment:**
   - Non-compliant patient, drug or alcohol abuse, significant disease, etc.

5. **Treatment of adult patients:**
   - The physician with expertise in hepatitis treats with interferon or lamivudine.

6. **Monitoring untreated patients:**
   - Repeat ALT at 3, 6, 12 months, then annually.

7. **Monitoring treated patients:**
   - Individualized depending on patient’s needs.

8. **Determining if the patient is “cured”:**
   - Only a small percentage of patients are cured, but disease progression can be modified by sero-conversion.

9. **Screening for HCC:**
   - Screen patients age 30 or over with one or more risk factors.

10. **Infants and children:**
    - Refer to a pediatric specialist with expertise in viral hepatitis.

11. **Needlestick injuries:**
    - The risk of transmission is about 25 per cent, but the risk of chronic infection is almost zero in immunized persons.
What is hepatitis B?
Hepatitis B is a liver disease caused by infection with a virus. In adults, less than five per cent of new infections will go on to long-lasting (chronic) liver disease. Treatment of chronic disease can lessen damage to the liver.

How is hepatitis B spread?
• Having sex with an infected person
• Contact with the blood of an infected person
• Injection drug use. If using drugs, do not share or re-use needles.
• To a baby during delivery by an infected woman
• Transfusion of blood products (rare). Inform your doctor if you have ever received blood or are a donor

What will help me get better?
• Don’t use alcohol – it accelerates liver damage in patients with hepatitis B
• Eat well to help your liver heal
• Get vaccinated for hepatitis A if you have no prior infection or immunity
• The value of herbal remedies remains unknown

How can I protect others from getting infected?
• Don’t let others come in contact with your blood, e.g. a bloody nose or cut
• Don’t share needles or other equipment for intravenous drug use, tattooing or body piercing
• Don’t share spoons or straws for intranasal cocaine use
• Don’t share anything that might have blood on it, like a razor or toothbrush
• Ask your sexual partner(s) to be tested for hepatitis B immunity (you have a high risk of spreading the virus to them)
• Ask your sexual partner(s) to get vaccinated, if they are not immune to hepatitis B
• Tell your other health care providers, e.g. dentist or laboratory technician that you are infected with hepatitis B
• Use condoms 100 per cent of the time, unless your partner is immune

You cannot spread hepatitis B by:
• Coughing, kissing or hugging
• Sharing eating utensils or drinking glasses

If you are a mother carrying hepatitis B:
• Be sure that your baby is vaccinated at birth, at one month, and at six months.
• Breastfeeding is safe for babies who have been vaccinated and who have received hepatitis B immune globulin (HBIG) at birth

For updated information:
• Visit the BC Centre for Disease Control Web site: www.bccdc.org/topic.php?item=59
Scope

Objective: To improve the identification of patients with acute coronary syndromes (ACS): acute myocardial infarction and unstable angina. To reduce the number of patients with ACS sent home in error after initial evaluation. This guideline does not address chronic stable angina.

Target Population: Adults presenting with chest pain in physicians’ offices, walk-in clinics and emergency departments.

Recommendation 1: Selection of patients who may have ACS

Patients presenting with prolonged (more than 10 minutes) acute chest pain suggestive of ACS (see Table 1) should be evaluated by a history and physical examination. If a patient presents in a physician’s office or walk-in clinic and no alternative cause can be found, the patient should be sent to the Emergency Department for further evaluation and observation. A patient who is suspected of having an acute coronary syndrome should not be sent to a laboratory for an ECG or measurement of cardiac markers.

Recommendation 2: Initial evaluation in emergency department

Patients with chest pain suggestive of acute coronary syndromes (ACS) should be evaluated with a history, physical examination, an electrocardiogram (ECG) and cardiac markers*, preferably troponin.

*The term cardiac markers refers to proteins such as troponin I and T, creatinine kinase MB (CK-MB) and myoglobin, which are released into the blood after heart muscle necrosis. Emergency rooms should have troponin tests available.

Recommendation 3: Management of high-risk patients

Patients with ST segment elevation and/or definite elevation of cardiac markers should be treated immediately with the intent of opening the infarct-related artery and maintaining perfusion. Patients with a compatible history and a clearly abnormal ECG (without ST elevation), moderately elevated cardiac markers or hemodynamic compromise should be treated for acute myocardial ischemia.

Recommendation 4: Management of patients without high-risk features

Patients with a compatible history, but without high-risk features should have an ECG and cardiac markers, preferably troponin, performed at 6 or more hours after onset of pain.

Patients with elevated cardiac markers or abnormal ECG at 6 hours should be admitted and treated for acute myocardial ischemia.
Patients without elevated cardiac markers at 6 or more hours and normal ECG should be considered low or intermediate risk according to the accompanying table.

Intermediate risk patients where clinical suspicion remains high but tests at 6 hours are negative should have a stress test (with or without a radionuclide scan) prior to discharge.

Low-risk patients without an obvious alternative explanation for the chest pain should have urgent out-patient physician follow-up, advice to return if the pain recurs and arrangements for an out-patient stress test (with or without radionuclide scan).

Table 1:

Features of persistent chest pain that suggest ACS:

- Cardiac chest “pain” is usually described by the patient as an unpleasant sensation in the chest: “pressing”, “squeezing”, “constricting”, “bursting”, “burning”, “a band around the chest”, “a weight in the centre of the chest”, or a “vise tightening around the chest”. Clenching the fist in front of the sternum (Levine’s sign) is a strong indication of an ischemic origin of the pain.
- It is important to note that the sensation is often not described as being severe. The discomfort may radiate or be completely isolated to the neck, jaw, teeth, epigastrium, shoulder or arms (most commonly the left). It is frequently associated with shortness of breath, diaphoresis, weakness, nausea and vomiting, and occasionally associated with gas, belching and “indigestion”.
- The discomfort may be partially or fully relieved by nitro-glycerine, but may not respond to nitro-glycerine at all. There may or may not be a prodrome of the discomfort precipitated by exercise, cold weather, or emotional stress; relieved by rest or nitro-glycerine.
- Chest discomfort that lasts for more than 10 minutes or occurs at rest suggests unstable angina; chest discomfort that lasts for more than 20 minutes suggests acute myocardial infarction. An acute coronary syndrome may present with acute shortness of breath with or without evidence of chest pain.

Features of chest pain that do not suggest ACS:

- Pain or discomfort that is localised to the skin or chest wall and can be reproduced by localised pressure
- Pain that is localised to a small area of the chest (<3 cm in diameter), or pain that radiates to the right lower chest.
- Pain that is sharp, stabbing or knifelike and aggravated by deep breathing, or rotating the chest. Pain that is worse in the supine position and relieved by sitting up or leaning forward is suggestive of pericarditis.
- Pain that lasts for less than 15 seconds is rarely ischemic in origin.
- Dissection of the aorta often causes pain in the back in addition to the front of the chest.
### Table 2: Risk Stratification

#### High Risk ACS

Prolonged chest pain either > 20 minutes or ongoing, with one or more of the following high-risk features:

- Acute myocardial infarction within the past 4 weeks
- Pain with ST abnormalities on the ECG
- ECG: Transient ST-segment elevation or depression > 0.5mm
  - Sustained ST-segment depression > 0.5 mm
  - T-wave inversion >1 mm in > 5 leads
  - Deep (e.g. > 5 mm) T-wave inversion
  - Recurrent myocardial ischemia with ECG ST-segment shift with or without pain
- Positive cardiac markers:
  - Troponin level/CK-MB index-clearly positive with compatible history
- Hemodynamic compromise with ongoing chest pain: heart failure/hypotension

**30-day rate of death or myocardial infarction: 12-30%**

#### Intermediate Risk ACS

No high risk features, but one or more of:

- Ongoing chest pain
- Crescendo angina preceding rest pain
- Borderline positive troponin at 6-12 hours post onset of pain
  (A positive level will depend on the particular method used by your laboratory).
- Previous intervention: percutaneous transluminal coronary angioplasty/coronary artery bypass surgery
- Known coronary disease, two or more risk factors for coronary artery disease (CAD)
- Increased baseline risk: e.g. diabetes, elderly

**30 day rate of death or myocardial infarction: 4-8%**

#### Low Risk ACS

No high-or intermediate-risk features:

- Chest pain: single episode at rest (resolved), crescendo exertional angina
- ECG: normal or non-specific abnormalities or unchanged from previous

**30-day rate of death or myocardial infarction: <2%.**
Figure 1  Evaluation of Acute Chest Pain

- **Chest Pain > 10 min at rest** (possible ACS, no alternative cause)
  - Discharge if clear non-serious cause
  - Admit to emergency dept for further evaluation

- **Possible ACS**
  - Test: ECG, cardiac markers
  - ECG abnormalities other than ST elevation, ongoing pain, positive cardiac markers, or hemodynamic abnormalities
    - ACS Confirmed
    - ST elevation / LBBB Positive cardiac markers
    - Manage as Acute MI – Evaluate for reperfusion
  - Normal ECG and cardiac markers
    - Possible ACS
      - Observe and follow-up at ≥ 6 hrs from onset of pain
      - No recurrent pain, negative repeat ECG & markers
        - Stress test intermediate risk: before discharge low risk: within 72 hrs
        - Negative
          - Inform patient of warning symptoms - follow up at 30 days by family physician
        - Positive
          - Manage as Acute Ischemia
  - Possible ACS
    - ECG abnormalities other than ST elevation, ongoing pain, positive cardiac markers, or hemodynamic abnormalities
      - ACS Confirmed
      - Recurrent ischemic pain, positive ECG or cardiac markers
        - ACS confirmed
      - Negative
        - Inform patient of warning symptoms - follow up at 30 days by family physician
    - Manage as Acute MI – Evaluate for reperfusion

- **Recurrent chest pain** re-evaluate as at beginning of algorithm
- **ST elevation / LBBB Positive cardiac markers**
  - Manage as Acute MI – Evaluate for reperfusion
- **Normal ECG and cardiac markers**
  - Possible ACS
    - Observe and follow-up at ≥ 6 hrs from onset of pain
    - No recurrent pain, negative repeat ECG & markers
      - Stress test intermediate risk: before discharge low risk: within 72 hrs
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      - Negative
        - Inform patient of warning symptoms - follow up at 30 days by family physician
    - Manage as Acute MI – Evaluate for reperfusion
Rationale

The diagnosis of acute coronary syndromes (ACS) among patients with chest pain is easily missed because no single objective test reliably identifies ACS in these patients. Inappropriate discharge can lead to preventable acute myocardial infarction (AMI) or sudden death. A recent Canada-US study showed that 57-99% of patients presenting to an emergency department with chest pain were admitted for further investigation. In the participating Canadian hospitals only 13-51% of admitted patients ultimately proved to have an acute coronary syndrome. Some US centres have established chest pain evaluation units (CPEUs) to limit unnecessary coronary care unit (CCU) admissions. These CPEUs apply 9-12 hour step-wise AMI rule out protocols using observation, serial ECGs and cardiac markers, provocative tests and cardiac imaging. The CPEUs have reported reduced costs and improvements in the identification of ACS compared with facilities that admit all patients to the CCU. Chest pain units are not established in British Columbia partly because their true cost-effectiveness is unknown.

Clinical variables associated with ACS include gender, age, family history, previous angina or AMI, pain characteristics, syncope, response to nitro-glycerine, diaphoresis, nausea and vomiting, blood pressure, rales, jugular venous distensions, heart sounds, descriptive gestures and arrhythmias. Many of the above are strong predictors of ACS but their clinical utility in individual patients is uncertain. Women, in particular, often do not complain of typical chest pain and present with atypical symptoms.

ECG abnormalities are strong positive predictors but as many as 82% of patients with ACS-related chest pain have normal or near normal ECGs.

Cardiac markers including CK-MB, myoglobin and troponins are released during AMI. The sensitivity of CK-MB assays and troponins improves with serial testing but never reaches levels high enough at the initial assessment to rely on markers alone to rule out AMI or unstable angina.

Stress tests may be dangerous in high risk patients, require skilled interpretation and have limited availability outside major centres.

In a recent ongoing evaluation in two Vancouver hospitals, 4.5% of patients with an AMI and 6.8% of patients with unstable angina were discharged with a non-ACS diagnosis. Most clinicians consider these rates too high. The need for a clinical decision tool is urgent and there is great potential for improvements in detecting ACS.

Diagnostic uncertainty leaves physicians with a difficult decision: to discharge and risk missing a potentially lethal diagnosis, or to admit for an expensive investigation. The most difficult cases of ACS to identify are those with chest pain but negative ECGs and cardiac enzymes. The American Heart Association (AHA) has recently published a guideline for the management of patients with unstable angina and non-ST elevation myocardial infarction (NSTEMI). The algorithm from the AHA guideline has been adapted (see Figure 1) to help BC physicians manage patients who present with chest pain in the ambulatory setting. A table of risk features is also provided (Table 1) to aid in diagnosis. This table is adapted from work by Fitchett et al, who modified the AHA/ACC guideline for the Canadian setting. The objective of this guideline is to reduce the rate of missed cases of myocardial infarction and unstable angina sent home in error.
References:


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Funding for this guideline was provided in full or part through the Primary Health Care Transition Fund.

Effective Date: November 1, 2003

This guideline is based on scientific evidence available at the time of the effective date.

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Guideline for
The Diagnosis and Treatment of
Acute Otitis Media in Children

This clinical practice guideline (CPG) was developed by an Alberta Clinical Practice Guideline working group. Note: This guideline does not apply to the following patients:
• less than 6 weeks old
• premature infants who are hospitalized
• craniofacial abnormalities such as cleft palate
• immunocompromised or severe underlying systemic disease
• complications of AOM (e.g., sepsis, mastoiditis).

GOALS
♦ To increase the accuracy of the diagnosis of acute otitis media.
♦ To optimize the management of acute otitis media.
♦ To reduce antibiotic use for the treatment of myringitis and OME.

PREVENTION
♦ Handwashing.
♦ Breast feeding.
♦ Avoidance of environmental tobacco smoke.
♦ Avoidance of feeding in a supine, flat position.

DIAGNOSIS
Acute Otitis Media (AOM)
♦ Symptoms: pain, fever, irritability.
♦ On direct otoscopy the only specific sign of AOM is a bulging, inflamed eardrum.
♦ In the absence of bulging, the eardrum must demonstrate acute inflammation and decreased mobility on pneumatoscopy.
♦ Routine cultures of ear drainage offer no diagnostic advantage in identifying potential pathogens.

DEFINITIONS
♦ Acute otitis media (AOM): inflammation and pus in the middle ear accompanied by symptoms and signs of ear infection.
♦ Myringitis (“red eardrum”): inflammation of the tympanic membrane alone or in association with otitis externa.
♦ Otitis media with effusion (OME): also known as Serous Otitis Media: fluid in the middle ear without symptoms or signs of acute inflammation of the ear.
♦ Chronic suppurative otitis media - persistent inflammatory process associated with perforated tympanic membrane and draining exudate for more than 6 weeks.

ISSUES
♦ It is critical to differentiate between i) AOM, ii) myringitis, and iii) OME.
♦ The overuse of antibiotics in ill defined ear infections has led to increasing antimicrobial resistance.
♦ In children aged 2 years or older, the need for antibiotics in AOM is controversial.
♦ Antibiotics may reduce the risk of complications in AOM; however, the incidence of these complications is low.
♦ Evidence indicates that 5 days of antibiotic therapy is sufficient for first line treatment of uncomplicated AOM in the majority of patients.

PRACTICE POINT

Diagnosis of Myringitis
♦ Normal mobility on pneumatoscopy with redness which may be peripheral.
♦ Antibiotics are not indicated.
Note: Inflammation only at the superior pole may progress to AOM; consider follow-up.

Diagnosis of Otitis Media with Effusion (OME)
♦ Lack of acute inflammation despite visible fluid or reduced mobility on pneumatoscopy.
♦ Antibiotics are not indicated.

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.
MANAGEMENT

General

♦ Pain/fever should be controlled with systemic analgesics (acetaminophen, ibuprofen).

♦ Decongestants/antihistamines are not beneficial in the treatment of AOM itself.*

   *Note: Some experts believe that antihistamines and/or decongestants may be of benefit when allergies play a role in the etiology.

♦ Topical corticosteroid/antibiotic preparations are not recommended.

Antibiotic Therapy

♦ Myringitis
   • Antibiotics are not indicated.

♦ Otitis Media with Effusion
   • Antibiotics are not indicated.

♦ Acute Otitis Media

   Children less than 24 months old:
   • Treat with antibiotics (See Table 1).

   Children aged 2 years or older:
   • Most cases of AOM resolve with symptomatic treatment alone and do not require antibiotics.
   • Treat symptomatically for 48-72 hours from symptom onset if pain/fever is manageable with systemic analgesics, providing adequate follow-up can be assured.
   • If symptoms worsen or fail to respond to symptomatic treatment with systemic analgesics after 48-72 hours, treat with antibiotics (See Table 1. See Background for further information on dosage and duration.)

Follow-Up

♦ If the patient remains symptomatic at 48 to 72 hours (following treatment with analgescs or first line antibiotics), or is deteriorating, follow-up is recommended.
   • Reassess patient for:
     - acute complications of AOM (e.g., mastoiditis, meningitis, facial paralysis);
     - other diagnoses;
     - compliance with medications.
   • Non-responders (See Table 2).
   • A follow-up exam at completion of treatment is not required if the patient is asymptomatic.

   Note: Up to 50% of children will have an effusion 1 month post AOM. Further antibiotic therapy not required.

♦ Follow-up 3 months post AOM episode is recommended to assess for persistent OME, which may lead to hearing loss.

   Note: Up to 10% of children will have an effusion 3 months post AOM.
   • Perform hearing evaluation if effusion present at 3 months post AOM.
   • Refer to an ENT specialist if hearing loss.

♦ Given the increasing incidence of resistant organisms, diagnostic tympanocentesis should be considered where there has been failure of 2 consecutive courses of antibiotics (first line followed by second line agent) with persistent symptoms.

Antibiotics NOT Recommended in AOM

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Activity against Penicillin</th>
<th>Activity against Haemophilus/Moraxella</th>
<th>Activity against S. pneumoniae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalaxin</td>
<td>poor</td>
<td>no activity</td>
<td>resistant</td>
</tr>
<tr>
<td>Cefaclor1,2</td>
<td>no activity</td>
<td>marginal activity</td>
<td>resistant</td>
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<td>Cefixime</td>
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<td>resistant</td>
<td>resistant</td>
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<tr>
<td>Ceftriazone</td>
<td>routine use</td>
<td>potential for increased resistance</td>
<td>may be an option</td>
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<tr>
<td>Erythromycin</td>
<td>poor</td>
<td>against Haemophilus/Moraxella</td>
<td></td>
</tr>
<tr>
<td>Quinolones</td>
<td>not recommended in patients &lt;16 years old, broad spectrum, potential to induce resistance.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>no activity</td>
<td>against Haemophilus/Moraxella</td>
<td></td>
</tr>
</tbody>
</table>
RECURRENT AOM

Management

♦ If recurrences are more than 6 weeks apart, treat with first line agents (See Table 1).

Note: Use high dose amoxicillin (90 mg/kg/day PO divided BID or TID for 10 days)

♦ If recurrences are less than 6 weeks apart, treat with second line agents (See Table 2).

Frequent Recurrences of AOM

♦ Observation over time is reasonable because of a decreasing incidence of AOM with advancing age.

♦ Consider ENT referral for tympanostomy tubes if:
  • OME for ≥ 3 months with bilateral hearing loss ≥ 20 dB.
  • ≥ 3 episodes in 6 months
  • ≥ 4 episodes in 12 months
  • Retracted tympanic membrane.

Antibiotic Prophylaxis

♦ With increasing antibiotic resistance, antibiotic prophylaxis is not recommended. On average, antibiotic prophylaxis decreases AOM by ~1 episode per year.

BACKGROUND

Introduction

Acute otitis media is the most frequently diagnosed bacterial infection in pediatric patients. It has been suggested that otitis media is overdiagnosed in North America, as it is said that 84% of children have at least 1 episode of AOM by 3 years of age. In the United Kingdom, the incidence is approximately 70%.

Epidemiology and Risk Factors

Acute otitis media is a disease of infancy and childhood, with a peak incidence between 6 and 9 months. Studies indicate that by 1 year of age, more than 60% of children have had 1 episode of AOM, and 17% of children have had at least 3 episodes of AOM. After the age of 6, less than 40% of children develop AOM and only 30% have 3 or more episodes.

The earlier the age of onset of AOM, the greater the recurrence rates. Studies indicate that 60% of children who had their first episode of AOM before the age of 6 months have 2 or more recurrences in 2 years.

Persistent effusion is seen after AOM in 50% of children 1 month post AOM, 20% at 2 months and 10% at 3 months. The earlier the onset of AOM, the greater the likelihood of persistent effusion. Persistent fluid in the middle ear is associated with conductive hearing loss, and can hinder language development and school performance.

Environmental tobacco smoke may be an important risk factor for middle ear disease.

Daycare attendance has been associated with an increased incidence of AOM. This is likely due to an increased incidence of respiratory tract infections in group daycare settings. The incidence of myringotomy and tympanostomy tubes is also greater in this population of children.

Male sex is associated with an increased incidence of AOM. The Boston study showed that breastfeeding for a period as short as even 3 months decreased the incidence of AOM in the first year of life.

First nations children appear to be more prone to develop chronic suppurative otitis media which can be very resistant to treatment. It is unclear whether genetic or environmental factors play the most significant role.

There is a seasonal aggregation of AOM with a peak in the fall and winter. The incidence may be related to an increased rate of viral upper respiratory tract infections at those times.

Etiology

Reliable microbiological diagnosis of AOM requires culture of tympanocentesis fluid through an intact drum.

The major bacterial pathogens causing AOM have not changed significantly over the last 2 decades and are similar for infants, children and adults.
**Table 1: 1st Line Agents in the Treatment of AOM**

<table>
<thead>
<tr>
<th>Recommended Therapy and Dose</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard Dose</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>5 days*</td>
<td>♦ Amoxicillin retains best coverage of oral β-lactam agents against <em>S. pneumoniae</em> (including intermediate strains).</td>
</tr>
</tbody>
</table>
| High Dose                    | 5 days*  | ♦ Higher dose (90 mg/kg/day) recommended if:  
  • recent (<3 months) antibiotic exposure and/or daycare centre attendance.  
  or  
  • recurrent AOM: 6 weeks to 3 months apart. Note: less than 6 weeks is considered failure of therapy. |

| **β-lactam allergy**         |          |          |
| Azithromycin                 | 1st day  then 4 days | ♦ Compared to cefuroxime, cefprozil has a better taste but inferior coverage of *Haemophilus spp* and penicillin intermediate *S. pneumoniae*. |
| Clarithromycin               | 5 days*  |          |

| **Non Type I beta-lactam allergy/anaphylaxis** | Duration | Comments |
| Cefuroxime axetil            | 5 days*  |          |
| Cefprozil                    | 5 days*  |          |

*R Note on Duration*  
Use 10 days if: <24 months old; perforated eardrum; recurrent AOM

---

**Table 2: 2nd Line Agents in the Treatment of AOM**

<table>
<thead>
<tr>
<th>Recommended Therapy and Dose</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Failure of Amoxicillin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin - clavulanate</td>
<td>10 days</td>
<td>♦ Amoxicillin - clavulanate will provide coverage for penicillin intermediate <em>S. pneumoniae</em> and β-lactamase producing organisms</td>
</tr>
<tr>
<td>or</td>
<td></td>
<td>Use amoxicillin-clavulanate 7:1 formulation</td>
</tr>
</tbody>
</table>

| Cefuroxime axetil            | 10 days  | ♦ Provides best coverage of all oral cephalosporins against penicillin intermediate strains of *S. pneumoniae* and provides good coverage of *Haemophilus/Moraxella/S. aureus*.  
  ♦ Due to poor taste of suspension recommend tablets if possible (can crush tablets and put in palatable fluid). |
| or                           |          |          |

| Cefprozil                    | 10 days  | ♦ Compared to cefuroxime, cefprozil has a better taste but inferior coverage of *Haemophilus spp* and penicillin intermediate *S. pneumoniae*. |
| or                           |          |          |

| **β-lactam allergy**         |          |          |
| Azithromycin                 | 1st day  then 4 days | ♦ Macrolides have been shown to be less efficacious than amoxicillin-clavulanate. |
| Clarithromycin               | 10 days  |          |
The most frequent causative agent of AOM is Streptococcus pneumoniae (40%), followed by nontypeable Haemophilis influenzae (25%), Moraxella catarrhalis (10%), Group A Streptococcus (2%) and Staphylococcus aureus (2%). Up to 15% of middle ear fluid cultures reveal 2 organisms and findings from the left and right ear may differ. About 20-30% have no bacterial pathogens identified and presumably are viral in etiology.

The emergence of bacterial strains that are increasingly resistant to antimicrobial agents is a growing concern in Canada and worldwide. Inappropriate use of antibiotics for viral upper respiratory tract infections has been a major contributor to antimicrobial resistance. Currently, 25% of Haemophilus influenzae and 90% of Moraxella catarrhalis produce β-lactamase enzymes which will inactivate penicillin and amino penicillins. Recently, there has been a dramatic increase of multiple antibiotic resistant Streptococcus pneumoniae. Currently, 8% of Streptococcus pneumoniae isolates in Alberta demonstrate in vitro resistance to penicillin, with 1.4% of these isolates exhibiting high level resistance (MIC ≥ 2 mg/mL). In Alberta, resistance to macrolides for S. pneumoniae is approximately 9%.

**Diagnosis**

The diagnosis of AOM requires the presence of inflammation and pus in the middle ear, and acute onset of symptoms and signs of ear infection, i.e., earache, fever, irritability, poor feeding or vomiting, often associated with cough and rhinitis. This differentiates AOM from:

- **Myringitis** - inflammation of the tympanic membrane. This is usually associated with viral infections of the upper respiratory tract and may also be seen temporarily in the crying child.

- **OME** - fluid in the middle ear without signs or symptoms of acute inflammation of the eardrum.

- **Chronic suppurative otitis media** - persistent inflammatory process associated with perforated tympanic membrane and draining exudate for more than 6 weeks. Many cases actually represent Otitis Externa that has been inappropriately treated. It is difficult to see a perforation in a chronically draining ear, especially if the external canals are inflamed. In these cases, mastoid x-rays and perhaps even a CT scan of the external canal, middle ear, and mastoid cells, becomes quite important for diagnosis.

Earache is a significant symptom predicting AOM but may also be a symptom of teething, wax in the ear canal, and migraine. A small number of children will have AOM without earache, but will generally have purulent rhinitis, irritability, night restlessness and sometimes fever.

The diagnosis of AOM is made by history and direct visualization of the tympanic membrane (the wax may have to be removed). On direct otoscopy, the only specific sign is a bulging eardrum. In the absence of a bulging eardrum but with clinical suspicion of AOM, pneumatic otoscopy is necessary to differentiate AOM from myringitis. In children where this is difficult, corroboration with clinical symptoms is essential. Younger children usually need to be restrained. Visualization of the tympanic membrane may still be difficult because of the narrow diameter of the ear canal which may also be tortuous.

Early AOM may be diagnosed by inflammation which is seen along the handle of malleus, and in the superior pole of the tympanic membrane. At this stage, the rest of the tympanic membrane usually still has good mobility with insufflation by the pneumatic otoscope. With these findings, the child should be followed closely.

Other less common diagnostic methods include tympanometry and acoustic reflectometry. These methods must still be used in conjunction with compatible history.

Diagnosis may be difficult in a younger child but it is important to accurately do so. A first episode of AOM before 6 months of age is likely to lead to recurrence of AOM, and subsequently, significant periods of OME with diminished hearing, leading to delayed speech development and impaired cognitive functioning.

In the child who is younger than 2 months of age, there is a significant risk of bacteremia associated with AOM.
Management of AOM

Antibiotic therapy is recommended for AOM in children under 24 months. Some studies have suggested that routine use of antibiotics, especially in children 2 years and older, is not indicated because of the high rate of spontaneous resolution. A meta-analysis of 5400 children with AOM indicated that antibiotic therapy enhanced acute symptom relief by 13.7% despite a spontaneous recovery in 81% of cases. Spontaneous resolution is organism specific: S. pneumoniae 10%; H. influenzae 50%; M. catarrhalis 75%. A randomized trial in the United Kingdom in 2001 compared providing immediate antibacterial therapy with delaying antibacterial agents for 72 hours in children aged 6 months to 10 years. Seventy six percent of children in the delayed group never required antibiotics and 70% were symptomatically better at 72 hours. This compared to an 86% “symptom improved” rate in the treatment group. Immediate use of antibiotics was associated with one day shorter illness but no difference in school absence or pain scores. Some experts recommend watchful waiting for 48 to 72 hours before initiating antibiotic therapy if symptoms are manageable with analgesics. This approach may be appropriate in patients over 2 years of age if good follow-up can be assured. Some groups recommend against this approach if the child presents with bilateral AOM. Regardless of whether or not antibiotics are given, the management of pain, especially during the first 24 hours, should be addressed. Acetaminophen and ibuprofen provide effective analgesia for mild to moderate pain, are readily available, and are recommended as the mainstay of pain management for acute otitis media.

The goals of antibiotic treatment of AOM are to:

♦ Produce a clinical cure.
♦ Prevent complications.
♦ Eradicate bacteria from the middle ear.

All of these goals can be achieved in most children. The most important factor is not to prescribe antibiotics for inappropriate diagnosis of AOM. Since S. pneumoniae has the lowest spontaneous resolution rate and is associated with more serious complications, it is essential to ensure optimal coverage for this organism.

Amoxicillin at doses of 40 mg/kg/day given TID should be considered as the first line oral therapy for low risk children (no previous exposure to antibiotics in the last 3 months and not attending daycare centres). Amoxicillin at doses of 90 mg/kg/day divided BID or TID should be considered as the first line oral therapy for AOM in high risk children (those who have received antibiotics in the past 3 months and/or who are attending daycare centres).

Amoxicillin is the current antibiotic of choice for AOM for the following reasons:

♦ Adequate coverage for organisms involved in AOM.
♦ Best activity of all oral b-lactam agents against penicillin intermediate S. pneumoniae.
♦ Excellent middle ear concentrations.
♦ Relatively few adverse effects.
♦ Lower potential to induce resistance.
♦ No other antibiotic agent has been proven superior to amoxicillin in clinical trials.

The choice of an agent remains uncertain in cases where amoxicillin treatment fails. There are many reasons why treatment appears to fail. These include incorrect diagnosis, poor compliance, inadequate antibiotic dosage or frequency, persistence of pus in an undrained middle ear, viral infection or presence of resistant bacteria. If the patient fails standard dose amoxicillin therapy, potential pathogens include viruses, b-lactamase producing organisms (Haemophilus, Moraxella) or penicillin resistant S. pneumoniae. In these cases it is recommended to use high dose amoxicillin-clavulanate (90mg/kg/day divided BID using the 7:1 formulation) to provide coverage for these bacterial pathogens (see Table 2). If the child is not responding or is deteriorating on the recommended regimens, consultation with a specialist and consideration of tympanocentesis for culture and susceptibility is recommended to rule out high level resistant S. pneumoniae.

In penicillin allergic patients, trimethoprim/sulfamethoxazole (TMP/SMX) and erythromycin-sulfisoxazole have been recommended as alternatives to amoxicillin. However, because of increased resistance, these agents are no longer recommended. The newer macrolides can be used (NB: erythromycin is not adequate for the management of AOM as it has poor activity against Haemophilus spp and Moraxella catarrhalis), or a second-generation cephalosporin (cefuroxime axetil, cefprozil) can be used in those patients who are not allergic to cephalosporins nor anaphylactic to penicillins. Resistance to macrolides continues to increase and the routine use of these...
agents in AOM in patients who are not beta-lactam allergic is not recommended.\textsuperscript{9,36}

The standard duration of antibiotic therapy for AOM has been 10 days. A number of well designed, randomized studies have compared shorter courses of antibiotic therapy (3 to 7 days) with traditional 10 day courses. Based on these studies,\textsuperscript{29} reduced duration of therapy from 10 days to 5 days appears to have equivalent efficacy for uncomplicated AOM. Reduced duration of therapy has several advantages including reduced potential to promote antibacterial resistance, reduced adverse effects, increased compliance, and reduced cost. Longer courses of antibiotics have been associated with resistant S. pneumoniae.\textsuperscript{38} The results favouring 10-day therapy have been most significant in children less than 2 years old. Thus children less than 2 years of age or those who present with perforation of the tympanic membrane should receive 10 days of antibiotic therapy.\textsuperscript{39}

Steroids are not recommended for the treatment of otitis media with effusion because of limited scientific evidence that this treatment is effective. Tonsillectomy has not been found to be effective in the management of otitis media with effusion. Adenoidectomy, however, may be useful in chronic/recurrent otitis media.

Treatment of AOM with antihistamines or decongestants is not recommended. A Cochrane review of 2569 cases found that there was no benefit in outcome in patients taking antihistamines or decongestants alone and that there was an increase in adverse effects associated with these drugs.\textsuperscript{40}

**Follow-up**

Normally the symptoms of AOM should resolve within 72 hours of initiating antibiotic treatment. However, middle ear effusion may persist for up to 1 month in 50% of patients and up to 3 months in 10% of patients despite bacteriological cure. \textbf{Therefore, persistence of middle ear fluid after a full course of antibiotic therapy for AOM is not an indication for continued therapy or institution of treatment with a second line antibiotic.}\textsuperscript{18}

**Recurrence**

Recurrent otitis media is defined as 3 or more episodes of acute otitis media over the preceding 6 months, or four or more episodes in the last year. Under these circumstances, prevention of further attacks is desirable. Modification of risk factors, when possible, may be of benefit.

Elimination of smoking from the environment and avoidance of pacifiers have been shown to help reduce recurrence of otitis media.\textsuperscript{5} As the child grows older, the incidence of recurrence declines. If recurrences persist, consultation with a specialist is recommended.

**Antibiotic Prophylaxis**

Antibiotic prophylaxis has only minimal effects on recurrent otitis media, decreasing recurrences by approximately one episode per year.\textsuperscript{40} Given the high risk of developing antibiotic resistance associated with prolonged use of antibiotics, antibiotic prophylaxis is no longer recommended in the management of recurrent otitis media.

**Referral**

Referral to ENT for consideration of myringotomy and tympanostomy tubes is recommended if:
- OME for \( \geq 3 \) months with bilateral hearing loss \( \geq 20 \) dB.
- \( \geq 3 \) episodes in 6 months
- \( \geq 4 \) episodes in 12 months
- Retracted tympanic membrane (need to rule out significant pathology such as cholesteatoma)\textsuperscript{40}.

**FUTURE DIRECTIONS**

Vaccines have been highly successful in preventing many childhood diseases but until now have not been helpful in preventing AOM. The currently licensed 23 valent polysaccharide pneumococcal vaccine is not immunogenic in young children. A new conjugated pneumococcal vaccine is undergoing clinical trials in younger children and may have a role in the prevention of AOM in the future.

**Primary References**

AOM must be diagnosed by:
- bulging, inflamed eardrum
- or
- acute inflammation and decreased mobility on pneumatoscopy

- Child has received antibiotics in the last 3 months?
  and/or
- Child attends daycare centre?
  and/or
- Child has recurrent disease (> 6 weeks from last episode)?

Duration of antibiotic therapy:
- 5 days
- 10 days if:
  - < 24 months old
  - perforated eardrum
  - recurrent AOM
  - failure of 1st line agents


19. Hiekkinen T, Ruuskamen O. Signs and symptoms predicting acute otitis media [see comments]. Archives of Pediatric and Adolescent Medicine, 1995; 149: 26-29.


SELECTED READINGS


Toward Optimized Practice (TOP) Program

Arising out of the 2003 Master Agreement, TOP succeeds the former Alberta Clinical Practice Guidelines program, and maintains and distributes Alberta CPGs. TOP is a health quality improvement initiative that fits within the broader health system focus on quality and complements other strategies such as Primary Care Initiative and the Physician Office System Program.

The TOP program supports physician practices, and the teams they work with, by fostering the use of evidence-based best practices and quality initiatives in medical care in Alberta. The program offers a variety of tools and out-reach services to help physicians and their colleagues meet the challenge of keeping practices current in an environment of continually emerging evidence.

TO Provide Feedback

The Alberta CPG Working Group for Antibiotics is a multi-disciplinary team composed of family physicians, infectious diseases specialists, internal medicine, pediatricians, microbiologist, hospital and community pharmacists, epidemiologist, consumers, and Alberta Health and Wellness representative. The team encourages your feedback. If you have difficulty applying this guideline, if you find the recommendations problematic, or if you need more information on this guideline, please contact:

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Website: www.topalbertadoctors.org
Guideline for Treatment of Gastroesophageal Reflux Disease (GERD) in Adults

This guideline has been adapted from the Canadian Consensus Conference on the Management of Patients with Gastroesophageal Reflux Disease.¹

GOALS

To position health care professionals in Alberta to optimize the management of Gastroesophageal Reflux Disease (GERD) in Adults.

DEFINITION

GERD is defined as a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications.²

EXCLUSIONS

The recommendations contained in this guideline do not apply to:

• Pregnant or lactating women
• Patients under the age of 18 years

RECOMMENDATIONS

Investigation

♦ Diagnosis of GERD can usually be established on the basis of a careful history and physical examination. Further investigation is generally not required.³

♦ Patients with GERD symptoms and alarm features (Table 1) require prompt investigation: endoscopy is preferred.¹

♦ GERD is not caused by H. pylori infection and eradication of H. pylori is not known to effect the disease or its management.⁴

Table 1

Alarm Features for GERD
• Dysphagia (solid food, progressive)
• Odynophagia (painful swallowing)
• Bleeding/anemia
• Weight loss

Other Indications for Further Investigation
• Potentially cardiac chest discomfort
• Respiratory symptoms secondary to reflux
• Consider if failure to respond to 8 weeks of medical therapy (some may take 16 weeks to respond)¹

Management of Uncomplicated GERD (see Algorithm)

The Role of lifestyle modification:

♦ Lifestyle modification has limited effectiveness for GERD¹ and is usually ineffective in severe GERD symptoms.⁵

♦ Emphasize strategies that have added health benefits (Table 2)

Table 2

Lifestyle Modification
• Weight control
• Reduction of alcohol, tobacco and caffeine intake
• Avoid lying down within 2 hours of eating
• Elevation of the head of the bed
• Avoidance of foods that trigger symptoms:
  - spices
  - peppermint
  - chocolate
  - citrus juices

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.
RECOMMENDATIONS cont.

♦ Over-the-counter antacid or H2RA’s can be recommended if they have not already been tried. These treatments are useful for mild or infrequent symptoms.!

♦ If symptoms are relieved by lifestyle modification and/or over-the-counter medication; continue as necessary.

♦ If patient fails to respond to lifestyle modification and/or over-the-counter medication add antisecretory therapy as a therapeutic trial:

1. Proton pump inhibitor (PPI) once daily for 4-8 weeks

♦ If symptoms are not resolved by treatment or if symptoms recur consider:

1. Extending therapy to 16 weeks after careful review to determine diagnostic accuracy; or
2. Consider BID PPI for 4 weeks; or
3. If previous treatment did not use PPI then, PPI is recommended for 4-8 weeks

♦ Follow-up at 2 to 4 weeks to review the diagnosis and reassess management.

♦ Failure to respond to 16 weeks of PPI therapy warrants a careful reassessment of diagnosis and usually further investigation preferably by endoscopy.

♦ Patients whose symptoms require ongoing use of acid suppression medication for many years should have an endoscopy by 10 years into their condition to search for Barrett’s esophagitis.!

BACKGROUND

Introduction

Evidence indicates that up to 36% of otherwise healthy persons suffer from heartburn at least once a month, and that 7% experience uncomplicated GERD and symptoms of heartburn as often as once a day. It has been estimated that approximately 2% of the adult population suffers from complicated GERD, associated with macroscopic or histologic damage to the esophagus. The incidence of GERD increases after the age of 40, and it is not uncommon for patients experiencing symptoms to wait years before seeking medical treatment.23

GERD is believed to be caused by a combination of conditions that increase the presence of gastric content in the esophagus. These conditions include transient lower esophageal sphincter relaxation, decreased lower esophageal sphincter tone, impaired esophageal clearance, delayed gastric emptying, and decreased salivation.

Lifestyle factors can also cause increased risk of reflux. Smoking, large meals, fatty foods, caffeine, pregnancy, obesity, body position, drugs, and hormones may all exacerbate GERD. Hiatus hernia frequently accompanies GERD and may contribute to prolonged gastric content exposure time following reflux. Patients with GERD do not necessarily have a hiatus hernia and, conversely, those with hiatus hernia do not invariably have GERD. The excessive reflux experienced by patients with GERD overwhelms their intrinsic mucosal defense mechanisms, resulting in symptoms and sometimes damage.

The most common symptom of GERD is heartburn. Besides the discomfort of heartburn, reflux may result in regurgitation. This is a sense of sour fluid rising effortlessly into the throat or mouth. There can be other symptoms such as odynophagia (pain on swallowing) and dysphagia (difficult swallowing). The reflux may also cause pulmonary symptoms such as coughing, wheezing, asthma, or aspiration pneumonia. Oral symptoms may also occur such as tooth enamel decay, gingivitis, halitosis, and water-brash (excessive reflex salivation); throat symptoms such as a soreness, laryngitis, hoarseness, and a globus sensation. Only a minority of patients with diagnostic GERD symptoms will have reflux esophagitis.!

Investigation of GERD

The patient who presents with typical uncomplicated GERD symptoms (heartburn and/or regurgitation), should be diagnosed by history
and generally does not require other investigations. If a therapeutic trial results in resolution of symptoms, therapy can be prescribed as necessary. If symptoms are not resolved, or there are alarm symptoms investigation and/or referral is recommended. Endoscopy is highly sensitive in identifying cancer, strictures, ulcers and erosions. Endoscopy will also demonstrate the presence of Barrett’s epithelium (where normal epithelium is replaced by abnormal metaplastic columnar cells).

Barrett’s epithelial changes are a consequence of prolonged and severe acid reflux in about 2-4% of cases of persistent reflux. As 0.5% of patients diagnosed with Barrett’s develop adenocarcinoma of the esophagus each year, patients with biopsy proven Barrett’s epithelium require ongoing surveillance.

For patients with persistent and recurrent symptoms, the physician should engage in thoughtful discussion regarding the risks and benefits of further investigation.

Barium studies of the esophagus are widely available and well tolerated (with little morbidity). However, barium studies have significant limitations in the evaluation of GERD. While a barium examination of the esophagus will detect strictures it is very insensitive in its ability to detect pathological reflux or mucosal damage, and it cannot detect the presence of Barrett’s epithelial changes (which requires obtaining a biopsy specimen and histologic confirmation).

Esophageal manometry can be used to evaluate peristalsis and to assess the function of the lower esophageal sphincter. Therefore, it may be useful in patients who have atypical chest pain or are to undergo anti-reflux surgery.

Ambulatory esophageal pH monitoring is reserved for the investigation of complicated GERD and provides a quantitative determination of the amount of time the esophageal pH is low, indicating persistent acid presence above the sphincter. Ambulatory pH monitoring is most useful in patients with atypical reflux symptoms such as chest pain, asthma, cough or hoarseness. In these patients it may be the only diagnostic test that can provide objective evidence of the problem.

Ambulatory esophageal pH monitoring is also useful in evaluating patients with an incomplete response to medical therapy to document that their GERD-like symptoms are indeed reflux related.

**Therapy for GERD**

Lifestyle modifications such as elevating the head of the bed can be helpful. Patients should also be advised to avoid bedtime snacks, eat low fat foods, quit smoking, and reduce alcohol consumption. These strategies may have other health benefits in addition to any improvement in GERD. Patients whose symptoms are not completely controlled by lifestyle modification may be advised to use over-the-counter medications including antacids or antisecretory agents. Response to medication should be reassessed periodically.

If the patient reports troublesome symptoms occurring 3 or more times in a week that are not controlled by over-the-counter therapy and lifestyle modification, therapy may be initiated with a regular dose of a PPI once a day for 4 weeks. Numerous trials have shown that short term treatment with acid suppression agents can effectively relieve the symptoms of uncomplicated GERD.

Patients whose symptoms are resolved after a course of therapy need no further investigation or therapy. Therapy may be repeated if symptoms recur. For those few patients who fail therapy with a PPI for 8 weeks, a trial of twice-daily PPI for 4 weeks may be tried. Subsequent treatment failures may require further investigation and referral.
REFERENCES


Additional references


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To Provide Feedback

The Alberta CPG Working Group for Dyspepsia is a multidisciplinary team composed of family physicians, general practitioners, gastroenterologists, pediatric gastroenterologists, a pathologist, radiologist, radiation oncologist, an infectious disease specialist, and representatives from the public and the Alberta Pharmaceutical Association. The team encourages your feedback. If you have difficulty applying this guideline, if you find the recommendations problematic, or if you need more information on this guideline, please contact:

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GERD - July 2000
Reviewed November 2001
Reviewed 2004
Reviewed 2006
Algorithm:
Management of Uncomplicated GERD

Recommend lifestyle modification and/or over-the-counter medication (if not yet tried and failed)

Assess response in 2 - 4 weeks

Response

- Discontinue medication
- Continue over-the-counter medications and lifestyle modification

Response

As a therapeutic trial:
- PPI once daily for 4 weeks
- Full dose H₂ receptor antagonist BID for 4 weeks

No response

Re-treat:
- If previous H₂RA, PPI is recommended for 4 weeks
  - Follow-up at 4 weeks
- If previous PPI given consider double dose PPI for 4 weeks
  - Follow-up at 4 weeks

If failure
- Reassess for alarm symptoms
- Reassess working diagnosis
- Complicated GERD
- Further investigation and/or referral suggested for recurrent or persistent symptoms