Meningococcal Disease!

PROTOCOL CHECKLIST

☐ Enter available information into Merlin upon receipt of initial report
☐ Review background on disease, case definition, and laboratory testing (see page 2)
☐ Contact provider
☐ Contact reporting laboratory and request that isolate be sent to the Bureau of Public Health Laboratories for serogrouping
☐ Interview patient, family, or guardian (see page 5)
  ☐ Review disease facts
    ☐ Modes of transmission
    ☐ Incubation period
    ☐ Symptoms/types of infection
  ☐ Ask about relevant risk factors as detailed on the Merlin extended data screen
  ☐ Determine if patient was hospitalized for reported illness
  ☐ Document pertinent clinical symptoms and type of infection
  ☐ Determine *N. meningitidis* vaccination history (see page 8)
    ☐ Include the age or year received
  ☐ Identify possibly exposed close contact* who may have been exposed to the patient’s respiratory droplets.
  ☐ Determine whether patient or symptomatic contact has exposures in sensitive situation (i.e., daycare, college dormitory, military, other congregate living settings, health care workers, etc.)
    ☐ Recommend exclusion for patient and symptomatic contacts
  ☐ Recommend and ensure access to prophylaxis for close contacts as appropriate (see page 7)
  ☐ Provide education on prevention through vaccination and prophylaxis as indicated
  ☐ Address patient family’s questions or concerns
☐ Follow-up on special situations, including exposed contacts or patients in sensitive situations (see page 7)
☐ Enter additional data obtained from interview into Merlin
Meningococcal Disease

1. DISEASE REPORTING

A. Purpose of reporting and surveillance

1. To identify persons who have been exposed by close contact to the index patient, in order to recommend antibiotic prophylaxis (chemoprophylaxis) and to inform possible exposed persons about signs and symptoms of illness.

2. Under rare circumstances, during a community outbreak, to recommend mass prophylaxis through immunization or antibiotics in a defined population or community.

B. Legal reporting requirements

Laboratories and physicians are required to report to county health departments (CHD) immediately by phone upon initial suspicion or laboratory test order.

C. County health department investigation responsibilities

1. Begin investigation on the same day as notification, 24/7.

2. Contact the submitting laboratory as soon as possible after a patient is reported and request that the N. meningitidis isolate be submitted to Florida Department of Health (DOH), Bureau of Public Health Laboratories (BPHL)-Jacksonville for confirmation and serogrouping.

3. Identify close contacts of patient with meningococcal disease and recommend antibiotic prophylaxis as appropriate as soon as possible, ideally within 24 hours.

4. Work with medical providers, BPHL, and the Bureau of Epidemiology to seek additional laboratory testing at the Centers for Disease Control and Prevention to confirm suspected cases.

5. In some circumstances, public health investigations and actions are necessary for illnesses that have a high clinical suspicion of meningococcal disease, but do not meet reporting case definition. For consultation on such circumstances, contact the Bureau of Epidemiology 24/7 at 850-245-4401.

6. Report all confirmed, probable, or suspected patients with meningococcal disease in Merlin (MENINGOCOCCAL DISEASE, CODE 03630).
   a. An extended data screen is available in Merlin to report additional clinical and risk factor data.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Neisseria meningitidis is one of the leading causes of bacterial meningitis in the United States. Meningococcal disease incidence is highest in late winter to early spring. Incidence of meningococcal disease peaks among persons in three age groups: infants and children aged <5 years (particularly infants 0-5 months), adolescents and young adults aged 16 through 21
years, and adults aged ≥65 years. In the United States, approximately 98% of cases of meningococcal disease are sporadic; however, outbreaks of meningococcal disease do occur.

A. Etiologic agent

*Neisseria meningitidis* is a gram-negative diplococcal bacterium. Approximately 800-1,500 cases of meningococcal disease occur annually in the United States, a rate of 0.3-0.5/100,000 population. Serogroups A, B, C, Y, and W cause almost all invasive disease worldwide; however, serogroups B, C and Y are the major causes of meningococcal disease in the United States. However, the proportion of cases caused by each serogroup varies by age group. National data indicates that approximately >50% of disease among infants younger than 1 year of age is caused by serogroup B *N. meningitidis*. Serogroups C, Y, or W, cause 75% of all cases of meningococcal disease among persons aged ≥11 years. Serogroup A is rare in the United States. Since 2009, Serogroup W is the most common serogroup identified in Miami-Dade, Broward, and Palm Beach counties.

B. Description of illness

Invasive meningococcal disease most commonly presents as meningitis, meningococcemia, or both.

Meningitis is the most common presentation of invasive meningococcal disease. In older children, adolescents, and adults, sudden-onset headache, fever, vomiting, myalgias, photophobia, irritability, decreased ability to concentrate, agitation, drowsiness, and meningeal signs (neck stiffness, Kernig’s or Brudzinski’s sign), cloudy CSF, with or without a rash are seen.

Symptoms of meningococcemia (blood infection) include acute onset of fever, malaise, myalgia, weakness, cold extremities and skin pallor, headache and/or drowsiness, often accompanied by hypotension and shock, which may lead to organ failure and death. A petechial or purpuric rash, a classic sign of meningococcal septicemia, is seen in 40% to 80% of cases of meningococcemia but may be difficult to detect initially. A maculopapular blanching rash can also be an early sign in the disease, can progress to a petechial or purpuric rash, or can persist in some cases.

Less common clinical presentations include pneumonia, arthritis, and epiglottitis, pericarditis, conjunctivitis, sinusitis, otitis, or urethritis. Infections with *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and other bacteria can be clinically indistinguishable from meningococcal disease.

Up to 12% of infections are fatal, even with appropriate antibiotic treatment, and mortality in adolescents approaches 25% nationwide. Sequelae associated with meningococcal disease occur in 10-20% of survivors and include hearing loss, neurologic disability, digit or limb amputations, and skin scarring.

C. Reservoirs

Humans are the only reservoir.

Asymptomatic colonization of the upper respiratory tract provides the source from which the organism is spread among a population. *N. meningitidis* organisms are carried in the
nasopharynx of about 5–10% of the healthy population. Carrier rates of up to 25% have been documented in some groups in the absence of any reported infections of meningococcal disease. However, less than 1% of those colonized develop invasive disease. Therefore, colonization is common, but invasive disease is rare.

D. Modes of transmission

Transmission occurs through respiratory droplets or by direct contact with nasopharyngeal secretions from a colonized person – symptomatic or otherwise. Close contacts* of a patient are at increased risk of becoming colonized/infected and developing illness. The attack rate for household contacts of patients is 500–800 times that for the general population. Risk of disease in close contacts is highest during the 10-day period following exposure.

E. Incubation period

The incubation period is usually 3 to 4 days, but may range from 2 to 10 days.

F. Period of communicability

Persons can transmit the organism to others as long as meningococci are present in nasal or pharyngeal secretions. Patients with invasive disease should be considered infectious from 7 days prior to disease onset until 24 hours after initiation of treatment with appropriate antibiotics. Contacts exposed to the patient >8 days before his/her onset of illness are not at increased risk of disease.

G. Treatment

Penicillin G, administered intravenously every 4 to 6 hours, is the therapy of choice for invasive disease once the diagnosis is definitively established. Third generation cephalosporins are also used. Empiric therapy with cefotaxime or ceftriaxone is recommended at the time the patient presents because meningococcemia and meningococcal meningitis cannot be distinguished clinically from disease caused by other bacterial pathogens. Depending on the antibiotic used, therapy for invasive disease may not eradicate the organism from the nasopharynx, and chemoprophylaxis may also be required.

H. Prophylaxis

Rifampin, ciprofloxacin, and ceftriaxone are all appropriate drugs for chemoprophylaxis (see Table 1). They are 90–95% effective in reducing nasopharyngeal carriage of N. meningitidis.

I. Meningococcal disease in Florida

During 2005–2014, 354 infections of meningococcal disease were reported in Florida. Of those reported infections, 94% were able to be serogrouped. Of these, 34.5% were serogroup W, 26.1% were serogroup B, 19.5% were serogroup Y, 18.0% were serogroup C, and none were serogroup A. In general, the annual incidence of meningococcal disease has decreased in the past decade, although from 2009-2013 disease rates in southeast FL increased as a result of the spread of serogroup W.
3. CASE AND DEFINITIONS

A. Clinical description

Meningococcal disease manifests most commonly as meningitis and/or meningococcemia that may progress rapidly to purpura fulminans, shock, and death. Other manifestations might be observed.

B. Clinical criteria for case classification

Clinical purpura fulminans in the absence of a positive blood culture.

C. Laboratory criteria for diagnosis

Confirmatory:
- Isolation of *Neisseria meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid) or from purpuric lesions
  - OR
- Detection of *N. meningitidis*-specific nucleic acid in a specimen obtained from a normally sterile site (e.g., blood or CSF) using a polymerase chain reaction (PCR).

Presumptive:
- Detection of *N. meningitidis* antigen in formalin-fixed tissue by immunohistochemistry (IHC)
  - OR
- Detection of *N. meningitidis* antigen in CSF by latex agglutination.

Supportive:
- Gram-negative diplococci, not yet identified, from a normally sterile site (e.g., blood or CSF).

D. Case classifications

**Confirmed:**
A person with confirmatory laboratory evidence.

**Probable:**
A person with presumptive laboratory evidence.

**Suspect:**
- Clinical purpura fulminans in the absence of a positive blood culture
  - OR
- A person with supportive laboratory evidence.

**Comment**
Positive antigen test results from urine or serum samples are unreliable for diagnosing meningococcal disease. Sputum cultures are not considered confirmatory as sputum is not obtained from a normally sterile site.

*Isolates of N. meningitidis must be sent to BPHL for determination of serogroup.*
4. LABORATORY SERVICES

A. Criteria for diagnosis

Meningococcal disease is most commonly diagnosed by isolation of *N. meningitidis* from blood or cerebral spinal fluid (CSF). After administration of any antibiotics, sensitivity of bacterial culture can be low. In this situation, a Gram stain of CSF, assays to detect bacterial antigen in CSF, and polymerase chain reaction (PCR) tests for *N. meningitidis* DNA can be helpful. For illness for which there is a high clinical suspicion for meningococcal disease and cultures are negative, *N. meningitidis*-specific PCR of blood and CSF is recommended. Isolates are required to be sent to the BPHL according to 64D-3.

B. Services available at BPHL

1. BPHL provides isolate confirmation and serogrouping for *N. meningitidis*. Clinical laboratories should be contacted for each reported patient to assure that all *N. meningitidis* isolates recovered from normally sterile sites are forwarded to the BPHL. All submissions should be accompanied by a Clinical Lab Submission Form: www.floridahealth.gov/programs-and-services/public-health-laboratories/forms-publications/_documents/DH1847--rev-5-13.pdf.

2. For *N. meningitidis* PCR orders, BPHL will forward specimens to the Centers for Disease Control and Prevention. Results will not routinely be available in time for clinical or public health decision making.

3. Packaging and shipping: Contact BPHL for training dates. The BPHL conducts approximately 20, face-to-face trainings per year all over Florida, free of charge. DOH employees must register for the classes in the DOH online training system called, TRAIN. For shipping guidance, please contact BPHL.


5. ROUTINE CASE INVESTIGATION

A. Contact the physician or hospital

1. Confirm that an invasive meningococcal disease infection has been diagnosed in the reported patient.

2. Obtain the following:
   a. Date of onset
   b. Signs and symptoms
   c. Type of infection (i.e., meningitis, sepsisemia)
   d. Predisposing conditions
   e. Tests performed
   f. Treatment
   g. Prophylaxis of family or other close contacts* (e.g., health care workers) at the facility
   h. Request medical records

3. Determine if the patient or proxy is aware of the meningococcal disease diagnosis.
4. Obtain as much demographic information as possible, including contact information (home, cell, and work numbers). Ask how and where the patient, or proxy, can be contacted.

5. Notify the physician that you will be contacting the patient, or proxy, as DOH follows up on all reports of meningococcal disease infections in FL to identify contacts and prevent further infections. It may also be appropriate, at this point, to determine if the physician has any concerns about the CHD contacting the patient, or proxy.

6. Review the clinical history, physical exam findings and laboratory results.

7. Conduct a public health investigation for all confirmed, probable, and suspect patients.

8. In some circumstances, public health investigations and actions are necessary for illnesses that have a high clinical suspicion of meningococcal disease, but do not meet reporting case definition. For consultation on such circumstances, contact the Bureau of Epidemiology 24/7 at 850-245-4401.

B. Interview the patient

1. Contact the patient or proxy, as soon as possible, to complete an interview even if this means visiting or calling them at the hospital.

2. The extended data screen in Merlin needs to be completed and can help guide the interview.

3. Items to cover during the interview:
   a. All activities in the seven days prior to symptom onset, (e.g., school, work, daycare, sports, parties, etc.)
   b. Identify all persons living in the household during the seven days prior to symptom onset.
   c. Obtain information about the patient’s high risk settings, (e.g., daycare, long term care facility etc.)
   d. Symptoms and onset date of symptoms
   e. Exposure to other ill persons with similar symptoms
   f. Identify all persons who had close contact* with the patient that could have resulted in exposure
   g. Travel history (If travel was outside FL or the country, notify the Bureau of Epidemiology.)
   h. Hospitalization history
   i. Pregnancy status
   j. Immunization status
   k. Other risk factors defined on the extended data screen (e.g., drug use, sexual history, etc.).

C. Environmental evaluation

Generally, no environmental evaluation is necessary, although in outbreak settings, an investigation may be warranted to identify environmental factors (e.g., disinfection practices, ventilation patterns, etc.) that may favor droplet transmission.
D. Merlin data entry

Create a case in Merlin under disease code MENINGOCOCCAL DISEASE-03630. Enter the data collected into Merlin, being sure to include all required fields on the Basic Data screen, Extended Data screen, complete the Case Symptoms screen, and attach all relevant labs. Please attach ALL labs received via electronic laboratory reporting (ELR) to the case.

6. CONTROLLING FURTHER SPREAD

A. Infection control recommendations

In addition to standard precautions, hospitalized patients should be cared for using droplet precautions until at least 24 hours after initiation of effective antibiotic treatment.

B. Case management

Some of the antibiotics commonly used for treatment do not reliably eradicate nasopharyngeal colonization. Unless ceftriaxone or ciprofloxacin (which are effective against colonization) was used, it is recommended that the patient also be given chemoprophylaxis to eliminate carriage before hospital discharge.

C. Contact management

1. Identify all persons who had close contact* with the patient that could have resulted in exposure, and events (e.g., parties, sporting event, resuscitation) where close contact could have occurred during the 7 days prior to patient’s onset until 24 hours after initiation of appropriate antibiotics. Obtain the name, address, and telephone number of exposed persons. Date of birth, weight, and any history of allergies will also be needed if chemoprophylaxis is to be provided.

2. Persons who had close contact* with the patient, during the 7 days prior to onset until 24 hours after initiation of appropriate antibiotics, should be offered prophylaxis. Since close contacts are at highest risk of becoming ill immediately after patient’s onset of symptoms, prophylaxis should be initiated as soon as possible, ideally less than 24 hours after identification of the index patient. Chemoprophylaxis is not recommended for persons who have had only brief or casual contact with the patient. Close contacts exposed most recently should be prioritized for chemoprophylaxis since the incubation period is usually less than 4 days. Chemoprophylaxis given more than 2 weeks after exposure has little value.

3. Symptomatic contacts experiencing fever, rash, lethargy, irritability, headache, stiff neck, confusion, light sensitivity, vomiting, or rash should be referred to a health care provider immediately for evaluation.
Table 1. Recommended Chemoprophylaxis Against Meningococcal Disease

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Duration</th>
<th>Efficacy (%)</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 month</td>
<td>5mg/kg, orally, every 12 hours</td>
<td>2 days</td>
<td></td>
<td>May decrease efficacy of some seizure and anticoagulant medications</td>
</tr>
<tr>
<td>≥1 month</td>
<td>10mg/kg orally, every 12 hours (not to exceed 600 mg)</td>
<td>2 days</td>
<td>90-95</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15 years</td>
<td>125mg, IM</td>
<td>Single</td>
<td>90-95</td>
<td>To decrease pain at injection site, dilute with 1% lidocaine</td>
</tr>
<tr>
<td>≥15 years</td>
<td>250mg IM</td>
<td>Single</td>
<td>90-95</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 month</td>
<td>20mg/kg, orally (not to exceed 500 mg)</td>
<td>Single</td>
<td>90-95</td>
<td>Not recommended routinely for people younger than 18</td>
</tr>
<tr>
<td>Azithromycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10mg/kg (not to exceed 500 mg)</td>
<td>Single</td>
<td>90</td>
<td>Not recommended routinely</td>
</tr>
</tbody>
</table>

Source: 2015 Report of the Committee on Infectious Diseases, American Academy of Pediatrics

a. Rifampin, ciprofloxacin, and ceftriaxone are all appropriate drugs for chemoprophylaxis (see Table 1). They are 90–95% effective in reducing nasopharyngeal carriage of *N. meningitidis*.
b. Rifampin is the drug of choice for most children. Rifampin is not recommended for pregnant women. Those taking rifampin should be informed that the following side effects can occur: gastrointestinal upset, orange discoloration of urine and tears, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives.
c. Ciprofloxacin is typically used for chemoprophylaxis of persons 18 years and older. Ciprofloxacin is not recommended for pregnant women.
d. Ceftriaxone can be used for children and adults (including pregnant women) to eradicate nasopharyngeal carriage if rifampin is contraindicated.

D. Immunization

Meningococcal disease vaccination is recommended for 11-12 year olds and those with specific risk factors. Detailed vaccine recommendations are found here: [www.cdc.gov/vaccines/vpd-vac/mening/who-vaccinate.htm](http://www.cdc.gov/vaccines/vpd-vac/mening/who-vaccinate.htm).

There are three kinds of meningococcal vaccine available for use in targeted groups in the United States:
1. Meningococcal conjugate vaccines (Menactra®, MenHibrix® and Menveo®)
2. Meningococcal polysaccharide vaccine (Menomune®)
3. Serogroup B meningococcal vaccines (Bexsero® and Trumenba®)

Vaccination of expanded at risk groups may be useful when a significant outbreak of disease due to serogroup A, B, C, Y, or W is continuing in a defined population (e.g., a school, institution, or community)(see Section 7 Managing Special Situations). Vaccination is not recommended to protect contacts of sporadic patients, unless persons have an existing indication for vaccination.
E. Education

1. Exposed

Potentially exposed persons should be instructed to watch for symptoms (fever, rash, lethargy, irritability, headache, loss of appetite, stiff neck, or vomiting) regardless of whether or not prophylaxis is recommended, and instructed to seek medical care immediately should such symptoms develop.

2. All

In addition to routinely recommended immunization, persons should practice respiratory hygiene and good health behaviors to stop the spread of respiratory pathogens.

Persons can keep many pathogens to themselves by:

- Covering the nose and mouth with a tissue when sneezing, coughing or blowing the nose
- Throwing out used tissues in the trash as soon as possible
- Staying home if coughing or febrile
- Seeing a doctor as soon as possible if coughing and febrile and following the doctors’ instructions
- If requested, using face masks provided in doctors’ offices or clinic waiting rooms
- Not sharing things like cigarettes, towels, lipstick, toys, or anything else that might be contaminated with germs
- Not sharing food, utensils or beverage containers with others
- Avoiding close contact with ill persons
- Practicing good handwashing procedures:
  - Using warm water and soap or alcohol-based hand sanitizers to wash hands
  - Always washing hands after sneezing, blowing the nose, or coughing, or after touching used tissues or handkerchiefs
  - Washing hands often when sick
  - Washing hands before eating, or touching eyes, nose or mouth
  - Washing hands after contact with a sick person

*Examples of close contact with meningococcal case patients include:

1. Direct face-to-face contact with a symptomatic case patient during the contagious period. This includes household and immediate family members, boyfriends/girlfriends, and child care contacts (those who spend many hours together or sleep under the same roof) or who are at increased risk for contact with respiratory secretions of the case patient.

2. An obvious exposure that involves direct contact with respiratory, oral, or nasal secretions from a case patient during the contagious period (e.g., a cough or sneeze in the face, sharing eating utensils, sharing water bottles, kissing, mouth-to-mouth resuscitation, or performing intubation or nasotracheal suctioning without appropriate use of droplet precautions).

3. Close proximity for a prolonged period of time with a case patient during the contagious period (e.g., sitting next to an infected individual for 8 hours or more
on an airplane). Risk of droplet exposure increases with longer duration and closer proximity of contact.

4. Health care workers are not at increased risk and prophylaxis is not recommended unless they have had direct contact with the case patient’s nasopharyngeal secretions (e.g., performing intubation or nasotracheal suctioning without appropriate use of droplet precautions).

Close contacts may also be identified among persons in the following groups:

1. Non-household close friends or other social contacts
2. Some passengers during shared transportation, depends on length of exposure
3. Some contacts at community activities or at the place of employment
4. Some health care workers caring for a case patient without wearing a mask
5. Children attending an after-school care group or play group on the same days as the case patient

Note: Close contact does not include activities such as walking by a person or briefly sitting across a waiting room or office.

7. MANAGING SPECIAL SITUATIONS

A. Case attends a child care facility

If a child with invasive meningococcal disease has attended any such facility during the week before onset then, within 24 hours of the initial report, the CHD should:

1. Interview the operator and inspect the written attendance records to identify other possibly infected patients among staff or attendees during the previous month.

2. Notify the parents of children who are in the same classroom as the patient (preferably in writing) of the occurrence of meningococcal disease in an attendee. The notice should advise parents to seek chemoprophylaxis for their children without delay if their child attended on any of the same days that the patient was present while likely infectious.

3. Advise parents to watch their children carefully for a 10-day period (after the index patient was last present in the child care center at the same time as their child while likely contagious) for signs of illness, especially high fever, and to seek medical care immediately if illness should occur.

4. Instruct the child care operator to notify the CHD immediately if another person becomes ill with symptoms of meningococcal disease.

5. Recommend chemoprophylaxis to all staff in the ill child’s classroom.
6. Children and staff in other rooms are usually not at elevated risk, and therefore in most instances do not need chemoprophylaxis. However, it should be determined if children from other classrooms have risk of direct exposure to the index child’s respiratory droplets (e.g., shared drinks, utensils, etc.) or spend time together in one room at the beginning and/or end of the day.

7. It may be helpful to provide a fact sheet on meningococcal disease to all persons associated with the child care center when a meningococcal infection has occurred in a staff member or attendee, or even the parent of an attendee.

B. Outbreak situations

In certain meningococcal disease outbreaks, vaccination is recommended to help stop the disease from spreading. Outbreaks can occur in communities, schools, colleges, prisons, and other populations. An outbreak occurs when there are multiple cases of the same serogroup in a community or institution over a short period of time. Depending on the size of the institution and specific circumstances, having just two cases of the same serogroup may be considered an outbreak. For suspected outbreaks, please consult the Bureau of Epidemiology 24/7 at 850-245-4401.

For more information on outbreak situations, please see: www.cdc.gov/meningococcal/outbreaks/index.html.

8. IMPORTANT LINKS

A. Meningococcal Disease, Florida Department of Health

B. Meningococcal Disease Vaccination Recommendations, CDC
   www.cdc.gov/vaccines/vpd-vac/mening/who-vaccinate.htm

C. Red Book, American Academy of Pediatrics
   aapredbook.aappublications.org/

D. Epidemiology and Prevention of Vaccine-Preventable Diseases
   www.cdc.gov/vaccines/pubs/pinkbook/index.html

E. Meningitis, CDC
   www.cdc.gov/meningitis/index.html

F. Manual for the Surveillance of Vaccine-Preventable Diseases, Chapter 8-Meningococcal Disease, CDC
   www.cdc.gov/vaccines/pubs/surv-manual/chpt08-mening.html