DEPARTMENT OF HEALTH SERVICES
DIVISION OF COMMUNICABLE DISEASE CONTROL
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September 28, 2001

TO: All Local Health Officers
All Local Communicable Disease Controllers

SUBJECT: RECOMMENDATIONS ON THE INVESTIGATION AND CONTROL OF MENINGOCOCCAL DISEASE CASES/OUTBREAKS, ESPECIALLY IN SCHOOL SETTINGS

This past school year was extraordinary in terms of media attention and public anxiety about possible transmission of infection from meningococcal disease cases that occurred in many areas of the state. The anxiety is understandable, as few other diseases can strike a perfectly healthy child on one day and cause death just a day or two later.

The statewide incidence of disease, however, was NOT remarkable by historical standards. The last major upsurge in California was in 1987-1989 when an average of >600 cases per year was reported. But, since 1996, the number of cases reported statewide has consistently been under 450/year and we project 350-370 cases for year 2001. California's incidence rates these past few years have been comparable to the national incidence rate of approximately 1 per 100,000/year.

However, what was remarkable this past school year was that we witnessed:

- 5 school clusters (one, each, at high schools in Truckee, Folsom, Santa Rosa, Livermore, and Los Angeles)
- deaths in some of these students
- intense media publicity surrounding every meningococcal case that occurred, even sporadic ones.

By contrast, in the past two decades there had been only two previous school clusters, one in 1988 at a middle school in Santa Clara County and one in 1993 at a high school in San Luis Obispo. The 5 school clusters this past school year were NOT due to the same meningococcal strain, and we would like to dispel any notion that there was one particularly virulent strain circulating or that there was an epidemic. There was neither.

Mass chemoprophylaxis campaigns were conducted for some of the clusters this past school year. These consumed enormous resources from both local health departments (LHDs) and school administrations to accomplish the logistics, carry out the campaigns, provide media interaction, and participate in school assemblies and "town hall" meetings to answer questions from the anxious public, much of all that happening concurrently!

After assisting several LHDs this past season, we thought it would be helpful to provide some recommendations and written materials that LHDs might use in managing meningococcal cases in school and other institutional settings that may come up in their jurisdictions. These include a Meningococcal Disease Case and Outbreak "Quicksheet" which provides details on the step-by-step identification of cases, how to confirm the diagnosis, how to identify close contacts who merit chemoprophylaxis, the choice of antimicrobial agents and their relative indications and contraindications, and when to consider mass chemoprophylaxis (and vaccination) in school settings. We also enclose an updated Q&A Fact Sheet on this disease and information on meningococcal vaccine for two audiences: (1) for parents of schoolchildren and (2) for LHDs.

Especially because of the level of public anxiety that accompanies each case of meningococcal disease, we recommend that printed information be quickly and widely distributed in school settings, even after a single case has occurred. The fact that a case has occurred will almost certainly become public knowledge, anyway, so it would be good to be in control of, and to help prepare, the information to be disseminated to be sure that it is accurate. With the assistance of LHDs in preparing these notices, we believe that school management should be able to provide information that states that:

- A case has occurred (no identifiers on the case, of course, but perhaps the age or grade level, etc., could be given)
- The chance that another case will occur is very small
- Chemoprophylaxis is being given to all those who had close contact (directly via oral secretions, or indirectly by shared drinks, etc.)
- For all others, chemoprophylaxis is <u>not</u> indicated and may actually do some harm
- There are signs and symptoms of meningococcal disease to watch for: fever, headache, stiff neck, and/or bleeding under the skin (LHDs might consider appending the Q&A Fact Sheet to the take-home notice that is to be distributed)
- If any of these signs/symptoms should develop, seek immediate medical consultation
- Treatment of the disease is usually successful, especially if begun early
- People should confer with their physician, as needed.

For this purpose, we enclose a sample letter that can be adapted for use by LHDs, working with schools, for distribution to parents/students.

If 2 or more cases occur in a school setting, it is important to review the relatedness of those cases. We wish to emphasize that nearly all of the school-wide, mass chemoprophylaxis campaigns conducted last season <u>could have been obviated</u>—

because direct links between cases were ultimately identified—had the effort to identify social links between cases been maximized before, not after, a mass campaign was carried out. We've come to appreciate how some parents may not know their teenagers' social contacts: they may know about their kids' scheduled, after-school activities (clubs, sports teams, etc.), but it will take interviewing the case and especially his/her best friends (if the case can't provide much history), to learn about certain social activities, such as attendance at "rave" and other parties where intimate contacts tend to occur and, in fact, did take place in last season's outbreaks. (There, students kissed and shared drinks, cigarettes, and other objects that went from mouth to mouth). These types of contacts were ultimately identified in last school year's clusters, but only after the mass chemoprophylaxis campaigns had already begun.

We suspect that some of the school clusters last year would not have happened had "ring containment" chemoprophylaxis been extended beyond the usual household and other easily recognizable close contacts, to include such contacts in party-type settings. If the meningococcal cases in a school setting can be found to have had a social link, then only that particular social group (as well as the usual contacts, such as household members) would need chemoprophylaxis, not the entire school body.

At the risk of being repetitious, we cannot emphasize, enough, that the energy that LHDs put out at the "front end" of these investigations can obviate the work expended later. When links are not vigorously sought and, therefore, not found, then there may be no alternative than to conduct mass chemoprophylaxis (and possibly mass vaccination, too).

We hope this information will prove helpful. If there should be any questions or you need further clarification on anything, please call Jon Rosenberg, M.D. or S. Benson Werner, M.D., at (510) 540-2566; and, for questions on meningococcal vaccine issues, please call Loring Dales, M.D., at (510) 540-2065.

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Enclosures: See following page

(1) Meningococcal Disease Case and Outbreak "Quicksheet"
(2) Q&A Fact Sheet on Meningococcal Disease
(3) Vaccine information, 2 pieces: one for LHDs on the role of meningococcal vaccine in school settings where there are cases/outbreaks, and another for parents who are considering meningococcal vaccination as a routine immunization for their children
(4) Sample letter to parents/students in a school/institutional setting where there has been a meningococcal disease case
(5) CD Brief articles on meningococcal disease and mass chemoprophylaxis with ciprofloxacin, dated 2/14/01 and 3/04/01, respectively

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MENINGOCOCCAL DISEASE Case and Outbreak 'Quicksheet'

Infectious agent: The bacterial agent *Neisseria meningitidis*

Mode of transmission: a) direct contact with oral secretions
b) indirect contact with a colonized, but usually asymptomatic, individual via shared drinks, cigarettes, lipstick, toothbrushes, etc.

CASE DEFINITION and CLASSIFICATION (for purposes of public health reporting)

Clinical Case Definition: ☐ meningitis and/or
☐ meningococcemia

Case Classification:

Confirmed -meets clinical case definition and there is
☐ isolation of *N. meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, rarely, from joint, pleural, or pericardial fluid, etc.

Probable -meets clinical case definition and there is
☐ serum or CSF positive for *N. meningitidis* by polymerase chain reaction (PCR)
or ☐ positive antigen test in CSF. Note: positive antigen test results from urine or serum are NOT reliable for laboratory diagnosis of meningococcal disease.
or ☐ clinical purpura fulminans in the absence of a positive blood culture

CLINICAL FEATURES

Incubation: 2-10 days, commonly 3-4 days
Disease: acute onset of fever, headache, and stiff neck (in those with meningitis) or petecchial rash or purpura in those with bloodstream infection (meningococcemia)

LABORATORY TESTING AND CONFIRMATION

- ☐ See "Case Classification" above, re confirmatory laboratory testing
- ☐ Note that if antibiotic was used prior to specimen collection, culture may not be positive. In that event, PCR can be done (at State lab) and gram stain (at the clinical laboratory) may be helpful in diagnosis

RECOMMENDED CHEMOPROPHYLAXIS OF CONTACTS

Agent*	Children	Adults
Rifampin, oral	< 1 month: 5 mg/kg q12h for 2 days ≥ 1 month: 10 mg/kg q12h for 2 days	600 mg q12h for 2 days (Not to be used in pregnant women. May reduce effectiveness of oral contraceptives. Will stain body secretions and so could permanently stain contact lenses, etc).
Ceftriaxone, injection	125 mg IM for children under 15 years of age, one dose	250 mg IM, one dose
Ciprofloxacin, oral	See detailed note in CD Brief, issue of 3/04/01 (week #10). Though ciprofloxacin has not yet been approved by FDA for use in children under 18 years because of concern for arthropathy noted in juvenile animals, this has not been observed in humans. CDHS supports its use in high school students (≥ 14 years) in mass chemoprophylaxis, if there is capacity to treat the rare case of anaphylactic reaction that can occur (see CD Brief, issue of 2/14/01, week #7). A great advantage of ciprofloxacin over rifampin is that students can be observed taking the one dose necessary to confer protection. (See attached CD Briefs).	500 mg, po, once (Not to be used in pregnant or lactating women).

Agent*	Children	Adults
Sulfadiazine, oral (Use **only IF**: the organism has been shown to be sensitive. Note, also, that this drug is in rare supply).	125 mg/kg/day divided into 4 equal doses, on each of 2 consecutive days	1.0 gm q 12 hrs for 4 doses

*****There is one study indicating success in eliminating carriage of *N. meningitidis* (in 93% of colonized nursing students) with one 500 mg oral dose of azithromycin. No national body has yet recommended its use for chemoprophylaxis; it merits consideration and further study.

CASE INVESTIGATION OF MENINGOCOCCAL DISEASE AND FOLLOW-UP

This is a reportable disease. Both confirmed and probable cases must be reported to CDHS on Meningococcal Disease Case Report Form, DHS #8469.

1. Investigation:
   - ❑ Upon notification of a suspect case, complete the Meningococcal Disease Case Report Form by conducting interview with the meningococcal case or household members (and, sometimes, best friends of teenage cases).

   Help:
   - ❑ If there is more than 1 case in the same social/institutional/school setting, confer with CDHS/DISB (510/540-2566) to discuss management and follow-up.

   Patient data:
   - ❑ Confirm patient information (at a minimum: name, age, address, phone number, school affiliation, onset date).

   Medical data:
   - ❑ Confirm clinical signs and symptoms: fever (how high), stiff neck(?), petechiae or purpura(?)
   - ❑ Collect pertinent medical information: where hospitalized, doctor's name and phone number, type of antibiotic therapy, when started, ever had meningococcal vaccine, when?

   Laboratory data:
   - ❑ Collect all laboratory data that support diagnosis of meningococcal disease. Please send all *N. meningitidis* isolates from normally sterile body sites to the State's Microbial Diseases Laboratory (MDL) for serogrouping (and subtyping, as necessary). See "Note from the State's Microbial Diseases Laboratory," at the end of this Quicksheet.

   Contacts:
   - ❑ Determine ALL contacts at potential risk. Do this ASAP to arrange prompt chemoprophylaxis. Health Canada (Canada's equivalent of our CDC) and UK's Communicable Disease Surveillance Centre recommend prophylaxis of contacts as far back as 7 days before onset of illness in the case, whereas CDC and ACIP have never made recommendations on this. The common practice, today, however, is to prophylaxe contacts who had meaningful exposure to a case on the day of onset and thereafter, until patient isolation and treatment. The consensus is that cases are more infectious around the time of onset than in preceding days.
   - ❑ If possible, and if case can give history, confer with case about his/her close contacts
   - ❑ Household contacts are at risk and may know of others at risk
   - ❑ If case attends day care center (DCC), all contacts there should properly be considered at risk
   - ❑ If patient is a teenager/college student, confer with case's best friends about sports exposures (particularly shared water bottles), social gatherings, and "rave" parties (that parents/guardians might not know about) where the case might have attended and put others at risk by kissing, sharing drinks or cigarettes, etc.
   - ❑ Rarely, those who provided certain types of medical care (e.g., mouth-to-mouth resuscitation) may be at risk
   - ❑ After taking down all such information, prepare a list of ALL individuals deemed to be at genuine risk and who thus merit chemoprophylaxis. A sample "Contact Follow-Up Sheet" is attached for use or adaptation for local needs.
2. Chemoprophylaxis:
   - ❑ Provide or recommend appropriate chemoprophylaxis to all those on the above list, using the appropriate agents and schedules provided in the above table.

3. Notification
    - ❑ Send letter out immediately to all in any institutional setting (such as a school) where a case of meningococcal disease has occurred, to provide information that a case has occurred, that the chance of another case is remote, that chemoprophylaxis is unnecessary and inappropriate unless individuals have been contacted by public health authorities, but it is important to provide the intended audience with information on the signs and symptoms to look for, if they develop. If signs and symptoms do occur, advise immediate medical consultation.

MENINGOCOCCAL DISEASE OUTBREAK CONTROL RECOMMENDATIONS

- Definition: An "organization-based" outbreak (e.g., a school outbreak) is defined as the occurrence of 3 or more cases during ≤ 3 months in people who have a common affiliation but no close contact with each other, resulting in a primary contact rate of ≥ 10 per 100,000 persons. Note that co-primary cases (i.e., case patients who have onsets within 24 hours of each other) and secondary cases (who had close contact with a primary case-patient and then had onset of illness ≥ 24 hours after onset of illness in the primary case patient) should be excluded from calculations of a primary attack rate.

- Compare isolates, and subtype if possible, to see if isolates match.

- Mass chemoprophylaxis can be considered if case definition of ≥ 3 cases is met, though some might consider mass prophylaxis even when there are just 2 unassociated school cases. (If mass chemoprophylaxis is planned, review above table for chemoprophylaxis regimens and schedules). When mass chemoprophylaxis is embarked on, this should be accomplished ASAP, ideally in one day (to prevent "ping-ponging" of pharyngeal colonization). Chemoprophylaxis confers prompt protection, whereas immunization-induced immunity will take 7-10 days to develop.

- Immunization can be considered if the outbreak strain is one of the 4 components in the present vaccine formulation (A, C, Y, & W-135). The logistics in mounting a schoolwide vaccination program are formidable and not to be taken lightly. The caveats about this vaccine, namely, that vaccine-induced protection takes 7-10 days to develop, and that meningococcal vaccine boosters in the future may not be as effective as the initial immunization, etc., are detailed in another attachment.

- An immunization program may be appropriate where mass chemoprophylaxis has failed to reach more than ¾ of the population, or failed to prevent additional cases, or the outbreak appears to be spreading to other schools in the school system, portending a protracted outbreak with many more cases than if just one school were involved.

- Notification: It is important for LHDs to report to practicing physicians in the area, and to the media, why the mass campaign (schoolwide or other) is being launched, what is being done, and to whom. If at all possible, endeavor to disseminate this information BEFORE such a campaign is launched (or as soon thereafter as is possible), to avoid the crush of phone calls to practicing physicians (who might otherwise be "in the dark" as to what to say to callers); such notices should also reduce the crush of calls that would otherwise go to LHDs.

NOTE FROM THE STATE'S MICROBIAL DISEASES LABORATORY

Strains of *Neisseria meningitidis* recovered from normally sterile body sites (e.g., blood, CSF) should be serogrouped for epidemiologic reasons. The Microbial Diseases Laboratory (MDL) will group any invasive *N. meningitidis* isolates submitted by county public health laboratories and encourages use of this service. For further information regarding serogrouping and shipment of *N. meningitidis* strains, please contact the Special Pathogens Unit of the MDL at (510) 540-2255. In addition to culture confirmation (identification) and serogrouping of *N. meningitidis* isolates, the MDL offers on a selected basis a number of molecular techniques for identification, serogrouping, and subtyping of *N. meningitidis* isolates. These tests include PCR assays for species identification and serogrouping (serogroups B, C, W135, and Y), and pulsed-field gel electrophoresis (PFGE) and *por*A gene sequencing for molecular subtyping. Acceptable specimens include bacterial strains, 0.5 mls CSF (shipped frozen), 0.5 mls of blood (with anticoagulant, shipped refrigerated), or frozen brain tissue. For further information regarding molecular tests, please contact the Molecular Diagnostics Unit of the MDL at (510) 540-3158.

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Contact Follow-Up Sheet

For each contact to a meningococcal case that is identified, record the information itemized below. Besides household contacts, consider best friends and the information they can provide about contacts that the case may have had. Medical personnel who had contact with the case's oral secretions (e.g., through mouth-to-mouth resuscitation, etc.) should also be recorded.

NAME	AGE	SEX	TYPE OF CONTACT* (by # below)	DATE(S) OF CONTACT	PHONE NUMBER	ADDRESS	RECOMMENDED PROPHYLAXIS?	PROPHYLAXIS TAKEN? (SELF-REPORT)	OTHER ANTIBIOTICS USED?
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	
							Yes No	Yes No Unk If Yes, which_____	

*Type of contact:
(1) Household
(2) Shared food, drinks, cigarettes, lipstick, or other articles put in/on mouth
(3) Intimate social contact
(4) Day care center or preschool center contact
(5) Medical personnel
(6) Other, explain

California Department of Health Services
Division of Communicable Disease Control
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September 21, 2001

Q & A FACT SHEET
ON
MENINGOCOCCAL DISEASE

Meningococcal disease is one of the most feared infectious diseases in the United States. Although outbreaks are rare and even individual cases are uncommon, they frequently cause great concern when they occur. Reasons include the ability of this particular disease to affect previously healthy persons without warning and cause serious illness and sometimes death. But, actually, meningococcal infections are difficult to catch. The spread of the disease can be limited by diagnosing and treating cases of disease soon after the onset of symptoms and treating all those who have had close contact with an infected person. This Fact Sheet is intended to answer questions commonly asked by the public about meningococcal disease.

WHAT IS MENINGOCOCCAL DISEASE?

Meningococcal disease is caused by *Neisseria meningitidis* bacteria. The two most common types of meningococcal disease are: (1) meningitis, when the bacteria infect the fluid and the covering of a person's spinal cord and brain, and (2) infection of the bloodstream, called meningococcemia.

ARE THERE OTHER CAUSES OF MENINGITIS?

Meningitis is most often caused by viruses or bacteria. Knowing whether meningitis is caused by a virus or bacterium is important because the severity of illness and the treatment differ. Viral meningitis is generally less severe and resolves without specific treatment, while bacterial meningitis can be quite severe and may result in brain damage, hearing loss, or learning disability. For bacterial meningitis, it is also important to know which type of bacteria is causing the meningitis because antibiotics work better against some bacteria than others and can prevent some types from spreading and infecting other people. *Streptococcus pneumoniae* and *Neisseria meningitidis* are the leading causes of bacterial meningitis in the United States.

WHAT ARE THE SYMPTOMS OF MENINGOCOCCAL DISEASE?

Most people who have meningitis have stiff neck, headache, and high fever. These symptoms can develop over the course of several hours, or may take 1 to 2 days to develop. Other symptoms include nausea, vomiting, discomfort in looking at bright lights, confusion, and sleepiness. Newborns and infants may not have a stiff neck but appear slow or inactive, irritable, or simply stop acting normally. As the disease progresses, patients of any age may have seizures.

Patients with bloodstream infection often have a rash beginning as a smooth red area followed by small red blotches due to bleeding under the skin that don't blanch (turn paler) on pressure. Around 10%-15% of cases of meningococcal disease are fatal. Of patients who recover, 10% have permanent hearing loss or other serious after effects.

HOW IS MENINGOCOCCAL DISEASE DIAGNOSED?

Early diagnosis and treatment are very important. If you or a member of your family has symptoms suggesting meningitis or bloodstream infection described above, seek medical care immediately. Don't put it off. The diagnosis is usually made by growing bacteria from spinal fluid or blood. The spinal fluid is taken by performing a spinal tap, in which a needle is inserted into an area in the lower back where fluid in the spinal canal can easily be removed. Identification of the type of bacteria is important for selecting the best antibiotics for treatment.

ARE THERE DIFFERENT TYPES OF MENINGOCOCCAL BACTERIA?

Yes, there are. Two types (called serogroups) of meningococcal bacteria, serogroup B and serogroup C, cause most (80-90%) of the meningococcal infections in the U.S. and serogroup Y and W-135 make up most of the other cases. There are geographic differences in the types causing disease; in California, serogroup B, for which there is currently no vaccine available, is the most common. Serogroup A, which rarely causes disease in the United States, is the most common cause of epidemics in Africa and Asia. Within each serogroup there are many subtypes, called strains. Only one strain of one serogroup will be responsible for an outbreak. Special testing, done in public health laboratories, can identify the particular strain.

HOW COMMON IS MENINGOCOCCAL DISEASE?

Meningococcal disease is uncommon. In the U.S. each year, there are 1-2 cases for every 100,000 people, with 300 to 400 occurring in California. It is most common in children under five years old, but can also affect teenagers and older persons (over 60 years old). It is more common between late winter and early spring. Most of the cases occur one at a time. Rarely, outbreaks occur.

WHAT IS AN OUTBREAK OF MENINGOCOCCAL DISEASE?

An outbreak of meningococcal disease is defined as the occurrence of 3 or more cases from the same serogroup (or strain if such typing is available) in less than 3 months in people who have a common affiliation but no close contact with each other, resulting in a rate of disease greater than 10 cases per 100,000, or 10 times the usual rate. By convention, persons with disease who had close contact with another case or who had onset within 24 hours of each other should not be included in this case count, for purposes of determining whether or not there is an outbreak. Five to ten outbreaks of meningococcal disease are recognized in the U.S. each year, including 1 or 2 outbreaks or clusters in California. Outbreaks tend to occur in schools or other institutions but can also occur in communities, particularly among persons in close contact with each other.

IS IT EASY TO GET MENINGOCOCCAL DISEASE?

No, it is not. The bacteria are passed only by direct and very close contact with someone who is infected or is carrying the bacteria. Many people (as many as 2 in 10) carry the bacteria in the back of the nose and throat at any given time, especially in winter. While most of these people are healthy and do not themselves develop disease, they may pass the bacteria on to others. Why only a very small number of those who have the bacteria in their nose and throat develop disease, while others remain healthy, is not understood. Factors that affect an individual's immune system's ability to fight off the infection are important. People at increased risk of developing meningococcal disease are those living

in crowded living quarters (such as prisons and barracks), those who have had recent infections of the respiratory system (especially influenza), those with chronic illnesses, and those exposed to cigarette smoke. Drinking in bars has also been identified as a risk factor. Disease usually develops within two weeks after exposure.

The bacteria are transmitted from person-to-person in secretions from the nose and throat. They can live outside the body for only a few minutes, so that if the organisms are coughed onto a desk or toy, for example, they will soon die off and persons touching those objects later will not become infected. Also, the organisms cannot pass through normal skin but can enter the body through the mucous membranes of the nose or mouth or possibly the eyes. They are not spread by casual contact or by simply breathing the air near a person with disease or carrying the bacteria. They are not carried by animals or in the water or soil.

AM I OR MY CHILD AT INCREASED RISK FOR MENINGOCOCCAL DISEASE?

You are at increased risk if you are a close contact of somebody with meningococcal disease. Close contact means living with or having intimate contact with such an individual. People in the same household and persons attending or working in the same day-care setting as an individual with disease are considered close contacts. Intimate contact means direct exposure to the secretions from the nose and throat of an infected person; examples are kissing, sharing cigarettes, lipstick, lip balm, or drinks such as soda cans or water bottles, or mouth-to-mouth resuscitation. Being at increased risk means that your risk of developing meningococcal disease is significantly greater than that of other people in your community, and you should receive a recommended antibiotic to prevent the disease. If you have simply been in the same school, or shared transportation, or had social contact but did not have close contact with someone who recently had meningococcal disease, you are not at increased risk compared to others in your community.

You can also get the bacteria from close contact with a well person who is carrying the bacteria. In fact, most people who develop disease have not had contact with cases: cases rarely know a case that occurred earlier. Rather, his or her exposure was from someone who was a healthy carrier and there is no way to know who that person was.

WHAT CAN I DO TO KEEP FROM GETTING MENINGOCCOCAL DISEASE?

If you did any of the following with a patient who did develop meningococcal disease:

- lived in the same house;
- worked (adult) or played (child) in the same day-care setting with a child patient;
- were directly exposed to secretions from their mouth or nose, either directly (by kissing, etc.) or indirectly (by sharing a drink, etc.);

you should be treated with a recommended antibiotic. A number of different antibiotics are available for this purpose. They will eliminate the bacteria from the throats of most persons, therefore decreasing the risk of disease. They will usually prevent illness if given within 10 days after exposure to a case, but may not be effective if the bacteria have already started to invade your body from your throat. For this reason, you should be observed carefully for the development of illness even if given preventive antibiotic treatment. All of the antibiotics that can be used for prevention can have side effects. Besides the concern over side effects, it is also important that only those at increased risk of meningococcal disease receive antibiotics, since the meningococcal bacteria can develop resistance to the antibiotics

when they are overused, and then those antibiotics would no longer be effective when you really need them.

IS THERE ANYTHING ELSE WE CAN DO?

Yes. As a general recommendation, you and your children should wash hands frequently and avoid sharing drinks from the same container used by others (for example water bottles used in sports or shared soda cans) and avoid sharing of eating utensils or other materials that make mouth contact.

WHAT ABOUT VACCINATION?

Meningococcal vaccination is not recommended for routine immunization. The meningococcal vaccine currently licensed for use in the U.S., whose trade name is Menomune®, protects against four of the five major meningococcal serogroups: A, C, Y, and W-135. It is about 85-100% effective against those four but lasts a relatively short period of time, from 3-10 years. It does not protect against serogroup B disease that causes, on average, about 40-45% of meningococcal disease cases in California. Thus, overall this vaccine reduces one's risk of meningococcal disease by about half. The vaccine does not protect (or protects very poorly) infants and children under age 2 years, the age at which meningococcal disease is most common. The vaccine is given in a 1-dose schedule, and it takes about 7-10 days after receiving the vaccine for a person to develop protection. Thus, for persons just exposed to meningococcal disease, vaccine will not protect quickly enough; for immediate protection these persons need to take antibiotics. In children immunized at age 2-4 years, protection from the vaccine does not last long, dropping to a level of less than 10% protection after 3 years. For children immunized at age 5 years and older, protection lasts considerably longer but a booster dose is recommended every 3-5 years if one wants to continue protection. On the other hand, there is some evidence suggesting that booster doses of this vaccine do not protect as well as the first dose does.

Meningococcal vaccination is recommended only for certain persons at higher-than-average risk for meningococcal disease: persons with certain immune system problems, travelers to countries where meningococcal disease is common, and laboratory workers exposed to the meningococcal bacteria that may get suspended in the air. It should be considered for college freshmen that will live in on-campus housing. These persons should discuss the need for meningococcal vaccination with their physicians.

WHERE CAN I GET MORE INFORMATION?

Your doctor or health care provider should be your first source of information about your health and the steps you should take to protect yourself. We are making every effort to ensure that they have all the information available to do so.

Your local health department is available to answer additional question you might have.

Additional information is available at the Division of Communicable Disease Control of the California Department of Health Services (http://www.dhs.ca.gov/ps/dcdc/html/publicat.htm) or CDC (http://www.cdc.gov/ncidod/dbmd/diseaseinfo/meningococcal_g.htm) web sites.

CONSIDERATION OF MENINGOCOCCAL VACCINE IN ELEMENTARY AND SECONDARY SCHOOL SETTINGS

➢ INFORMATION FOR LOCAL HEALTH DEPARTMENTS ➢

Vaccine Description

The currently licensed quadrivalent polysaccharide vaccine (containing serogroup A, C, Y & W-135 antigens) is marketed by Aventis Pasteur, Inc. (1/800/VACCINE). Brand name is Menomune®. Licensed for use in persons aged 2 years and older. The manufacturer's list price is approximately $56/dose.

While this vaccine can be administered to anyone aged 2 years and older, the USPHS Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics (AAP) recommend this vaccine ONLY for persons in certain higher risk groups or situations. The ACIP and AAP do not regard school enrollment, per se, as a high risk situation and thus do NOT recommend meningococcal vaccine for schoolchildren unless some special circumstance exists (e.g., pupil has a certain type of immune system deficiency). Therefore, private and public health care plans generally do not cover the cost of routine meningococcal immunization for school-aged beneficiaries, in the absence of a special high-risk situation.

Routine Meningococcal Immunization

- Three national advisory groups - the American Academy of Pediatrics (AAP), the U.S. Public Health Services Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP) – provide standard recommendations for immunizations of infants and children in this country.
- None of these advisory groups recommends that all children, or all schoolchildren, should be routinely immunized with the meningococcal vaccine currently available in the U.S., though this vaccine is licensed for use in anybody aged 2 years and older. The reasons why these groups do not recommend that all children receive this vaccine include:
  1. the rarity of meningococcal disease,
  2. failure of the vaccine to protect the age group at highest risk (infants and children under age 2 years),
  3. failure of the vaccine to protect against meningococcal serogroup B, which causes 40-45% of cases,
  4. short duration of protection that the vaccine provides to young children, and
  5. protection from booster doses of the vaccine may not be as good as that produced by the initial dose.
- The AAP, ACIP and AAFP do recommend routine meningococcal vaccine for certain persons at higher than average risk for meningococcal disease:
  1. persons with certain immune system problems,
  2. travelers to countries where meningococcal disease is common, and
  3. laboratory workers exposed to the meningococcal bacteria that may get suspended in the air.
  4. The AAP and ACIP also indicate that meningococcal immunization should be considered for college freshman who will live in on-campus housing

Vaccine Role in Managing School Meningococcal Disease Episodes

The role for Menomune® in these situations is very limited for several reasons:

- It does not protect against *Neisseria meningitidis* serogroup B, which has been responsible for 30-50% or more of school meningococcal disease episodes.
- It does not eliminate nasopharyngeal carriage, so that its use does not halt transmission of the organism in the population at risk.
- There is suggestive evidence that booster doses of this vaccine are not as effective as initial immunization (Richmond P: *JID*:2000;181:761-4), so that immunization is perhaps best reserved for situations where there is relative certainty that increased risk currently exists.

- Immunization takes 7-10 days to confer protection, and since a few days are almost always needed to develop and implement an emergency immunization campaign, two weeks can elapse between the time an outbreak control immunization is decided upon and when protection of the majority of the population targeted is achieved.

The last of these limitations – related to time lapse until protection of the group targeted can be achieved – is particularly important. A review of school-based meningococcal disease clusters in the U.S. (Zangwill KM: *JAMA* 1997;277:389-95) found that such clusters are quite small and of short duration. Two-thirds of school meningococcal disease clusters known, or presumed, to have been due to the same *N. meningitidis* strain were comprised of just two cases, ¼ of three cases, and the remainder (just under 10%) of 4 cases. Further, almost ¾ of subsequent cases occurred within 2 weeks after onset of the index case, with none of the school clusters/outbreaks lasting over a month.

Protocol for Vaccine Usage Consideration in School Meningococcal Disease Episodes

The USPHS Advisory Committee on Immunization Practices (ACIP) has published a guide for vaccine use consideration in these situations (*MMWR* 2000;46/No.RR-5). Protocol summary:

- Ascertain if all confirmed and probable cases in the school are known to have been, or may possibly have been, due to same vaccine-preventable meningococcal serogroup - A, C, Y or W-135. If subtyping (by electrophoresis or PCR) has been done on specimens from cases, ascertain if all appear to be of same subtype.
- Count the index case (exclude any co-primary cases – i.e., those with onset within +/- 24 hours of the index case) and all subsequent cases whose onset was within 3 months of the index case's onset and whose ONLY link to the index case and/or each other is attendance at and/or working at the same school. That is, exclude subsequent cases for which personal contact or subgroup epidemiologic linkages (e.g., shared social or sports activity, etc.) with one or more of the other cases at the school are identified.
- If 3 or more cases meeting the above criteria are identified at the school, an immunization program should be considered. Determine the target population for immunization; e.g., entire student body at the school, entire student body plus faculty/staff, etc., and initiate immunization ASAP.

The obvious problem with this protocol and the reason the ACIP only recommends that an immunization program "… should be considered" relates to the timing limitations described earlier. Given the observations that less than 10 percent of multi-case outbreaks in a school exceed a total of 3 cases and that 2 weeks will likely elapse between the decision to launch an immunization program and achievement of vaccine-induced protection for the risk group targeted, the chance that the immunization program will prevent additional cases at the school is very small. Thus, ACIP indicates that consideration can also be given to an immunization program after only two cases meeting the criteria outlined above are identified. However, in most such instances chemoprophylaxis will be preferred to immunization because it confers more rapid protection and because it can dampen or halt transmission of the causal organism in the school.

For all of the above reasons, immunization programs are rarely used in school meningococcal disease cluster/outbreak situations. An immunization program may be appropriate where mass chemoprophylaxis has failed to reach more than ¾ of the population, or failed to prevent additional cases, or the outbreak appears to be spreading to other schools in the school system, portending a protracted outbreak with many more cases than if just one school were involved.

LGD/ 9/14/01

MENINGOCOCCAL IMMUNIZATION FOR CHILDREN

⮜ INFORMATION FOR PARENTS ⮞

Meningococcal Disease and Meningitis

- Meningitis is an inflammation of the lining of the brain and spinal cord. When caused by a virus, meningitis is usually (though not always) rather mild. When caused by bacteria, meningitis is severe and can result in death or permanent brain or nerve damage. Traditionally the most common causes of bacterial meningitis in babies and children have been the bacterial species *Hemophilus influenzae*, *Streptococcus pneumoniae*, and *Neisseria meningitidis*.
- Meningococcal disease is a serious illness caused by the bacterium *Neisseria meningitidis*. Bacteremia (blood poisoning) and meningitis are the most common forms of meningococcal disease.
- At least five different serogroups of the meningococcal bacterium *Neisseria meningitidis* are known to cause meningococcal disease. In the United States, serogroups B and C each cause about 40-45% of cases; serogroups Y and W-135 cause nearly all of the remaining 10-20%. Serogroup A meningococcal disease is rare in the U.S. but is a common form of this disease in Africa and Asia.
- Overall in the U.S., meningococcal disease strikes about one in every 100,000 persons per year. The disease is most common in infants under age 1 year, and it is more common in children under age 3 years than in older children, teenagers and adults.

Meningococcal Vaccine

- The meningococcal vaccine currently licensed for use in the U.S., whose trade name is Menomune®, protects against four of the five most common meningococcal serogroups (A, C, Y, and W-135) with an effectiveness somewhere between 85% and 90%. It does not protect against serogroup B disease. Thus, overall, for persons aged 2 years and older this vaccine can reduce risk of meningococcal disease (including meningococcal meningitis) by about half.
- The vaccine does not prevent meningitis due to viruses or other bacteria.
- The vaccine does not protect (or protects very poorly) infants and children under age 2-3 years, the age at which meningococcal disease risk is highest.
- The vaccine is given in a 1-dose schedule, and it takes about 7-10 days after receiving the vaccine for a person to develop protection. Thus, for persons just exposed to meningococcal disease or likely to be exposed within the next week or so, vaccine will not protect quickly enough; for immediate protection these persons need to take antibiotics.
- In children immunized at age 2-4 years, protection from the vaccine does not last long, dropping to a level of less than 10% protection after 3 years. For children immunized at age 5 years and older, protection lasts considerably longer, though a booster dose is recommended every 3-5 years if one wants to continue protection.
- There is some evidence that booster doses of this vaccine may not protect as well as the first dose protects.
- Safety: the most common reactions to this vaccine are temporary pain and redness at the site of injection and low-grade fever. Severe reactions are very rare.

Routine Meningococcal Immunization

- Three national advisory groups - the American Academy of Pediatrics (AAP), the U.S. Public Health Services Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP) – provide standard recommendations for immunizations of infants and children in this country.
- None of these advisory groups recommends that all children, or all schoolchildren, should be routinely immunized with the meningococcal vaccine currently available in the U.S., though this vaccine is licensed for use in anybody aged 2 years and older. The reasons why these groups do not recommend that all children receive this vaccine include:

    1. the rarity of meningococcal disease,
    2. failure of the vaccine to protect the age group at highest risk (infants and children under age 2 years),
    3. failure of the vaccine to protect against meningococcal serogroup B, which causes 40-45% of cases,
    4. short duration of protection that the vaccine provides to young children, and
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- The AAP, ACIP and AAFP do recommend routine meningococcal vaccine for certain persons at higher than average risk for meningococcal disease:
  1. persons with certain immune system problems,
  2. travelers to countries where meningococcal disease is common, and
  3. laboratory workers exposed to the meningococcal bacteria that may get suspended in the air.
  4. The AAP and ACIP also indicate that meningococcal immunization should be considered for college freshman who will live in on-campus housing.

County of _____
Department of Health

Date_____

Dear Parents and Students,

This letter is to provide you with information on a case of meningococcal disease that occurred at_____ High School. This disease, caused by the bacterium *Neisseria meningitidis*, generally occurs in 2 forms: (1) meningitis (which is an inflammation of the tissues covering the brain) and/or (2) bloodstream infection that leads to bleeding under the skin. A ___-year-old student in the _____ grade became ill on _____(date)_____and was diagnosed with meningococcal infection (type B/C/other?). The student is currently hospitalized and is under treatment (or died, or is recovering).

The _____ County Department of Health is identifying/has identified persons who had close contact with this student and who should have antibiotic prophylaxis. Close contacts are those living in the same household or those who had shared oral secretions, as by kissing or sharing foods, drinks, water bottles, cigarettes, lipstick, etc. For all other persons, including those who had casual contact as would occur in most school-related activities, the risk of infection is extraordinary low and approaches that in the population at large (one case.100,000 population/year). For them, antibiotic prophylaxis is NOT indicated and is not advised.

Although the risk of disease to other students is quite low, parents are advised to be alert for signs of meningococcal disease. These include, but are not limited to: fever headache, stiff neck, and/or rash that does not blanch on pressure (suggesting bleeding under the skin). If any of these signs or symptoms should develop, the student should be taken immediately to a physician or emergency room to be evaluated for possible meningococcal disease. Antibiotic treatment of the disease is usually successful, especially if it is started early.

To reduce the spread and the risk of this communicable disease, we recommend that Students avoid intimate contact and NOT share foods, drinks, lipstick/balm, and Cigarettes, etc. If you have any questions, please telephone_____at _____.

Sincerely,

COMMUNICABLE DISEASE CONTROL
DIVISION OF

CALIFORNIA
CD BRIEF

This weekly report of surveillance and laboratory activities from the Division of Communicable Disease Control of the California Department of Health Services contains information on investigations in progress and/or diagnoses that may not yet be confirmed. This communication is intended for the use of local health departments, should be considered privileged, and **not distributed** further.

Report of meeting of 2/14/01 (week 7)

Mass chemoprophylaxis to prevent meningococcal disease at Folsom High School*

Just as Truckee High School had done in mid-December 2000 (see **CD Brief** #2 for 2001), a schoolwide chemoprophylaxis campaign was conducted last week at Folsom High School in Sacramento County following the identification of another meningococcal case in that school's population. On Wednesday, February 7, a Folsom High School student died of meningococcal disease. Another student from that school died in early January, and a third student was suspected to have had this disease in January, at the time of the first case, but the diagnosis was never confirmed by culture. That person recovered.

Both students who died had serogroup B *Neisseria meningitidis.* This particular serogroup causes nearly 50% of meningococcal disease in this country but is NOT covered by the current vaccine formulation against meningococci.

Because of this new case, the Sacramento County Department of Health and Human Services took prompt measures to prevent illness in students and staff at the high school by endeavoring to eradicate infection in those who might have been exposed recently, and might possibly be in the incubation phase of disease. This was done by encouraging ALL to be treated, ALL at the same time, to avoid "ping-ponging" of meningococci between people who might be colonized but take their prophylaxis at different times. The local health department provided ciprofloxacin ("Cipro") free-of-charge to the entire school population, and the drug was made available from the local health department's (LHD's) own in-house supply. The estimated cost was about $1/dose.

Accordingly, on Friday, February 9, a total of 2590 doses of ciprofloxacin were given in single 500 mg. oral doses at Folsom High School, and at Folsom Lake and Kinney campuses. All students, staff, and volunteers at these facilities were offered the medication. Parents gave informed consent for their teenage students, either by returning signed forms which their youngsters took home, or they gave permission by witnessed telephone contact the day of the mass prophylaxis. The mass chemoprophylaxis effort was skillfully orchestrated with the help of the school administration, school nurse, volunteers, parents, and representatives of the LHD. EMTs from the local fire department were on hand to help with any emergencies. The students were brought to the multipurpose room by their teachers. Every one who had parental consent and had no medical contraindications was given one pill of Cipro to take. Altogether, at least 90 % of the student body took prophylaxis.

Eight individuals experienced adverse reactions immediately, or in the first few hours, after taking the antibiotic. Five students and 3 adults received attention for probable or possible medication-related problems. Four of the 8 had allergic reactions. One of these had laryngeal edema, periorbital edema, and some difficulty breathing. That student was given epinephrine on site, sent to a hospital emergency room where Benadryl and corticosteroids were administered, was observed for a while, and then released. Two others experienced only hives. A fourth had facial edema and laryngeal spasm, was seen and treated at an emergency room, and was also released. The other three individuals reported a variety of symptoms, including gastrointestinal upset, which may not have been related to the medication. None of those with allergic reactions reported KNOWN past exposure to quinolones but that doesn't

necessarily mean that they couldn't have had intentional exposure to this antibiotic for a variety of conditions that they/their parents could not recall. None of the 8 required hospitalization, and all did well.

The local health department will continue to monitor the situation of meningococcal disease in Sacramento County. As of February 14, there have been 9 lab-confirmed or probable cases of meningococcal disease reported to the LHD in 2001. The two deaths at Folsom High School are among the 9.

A future issue of **CD Brief** will discuss ciprofloxacin, its off-label use in children both prophylactically (as for meningococcal disease) and therapeutically (for a variety of conditions), and its good safety record despite concerns about possible arthropathies that have been reported in animal studies.

∗ Reported by Glennah Trochet, M.D. (Health Officer) and Pam Bradley, P.H.N., of the Sacramento County Department of Health and Human Services

Influenza update – Week 6 (02/04/01-02/10/01)

Inpatient data (Kaiser-specific):

Northern California (17 sites): Overall influenza admission rate was at 7% for week 6, similar to 6% for week 5. However, South San Francisco was at 11% for week 6.

Southern California (4 sites): Overall influenza admission rate was at 6% for week 6, from 8% for week 5.

Pharmacy data (Kaiser-specific):

Northern California Kaiser outpatient pharmacies reported a total of 119 influenza antiviral prescriptions filled for week 6, a 30% decrease from week 5.

Southern California had a total of 189 influenza antiviral prescriptions filled for week 6, a 39% decrease from week 5.

CDC California sentinel physicians:

Outpatient influenza-like illness (ILI) visits were at 5% for week 6, similar to 6% for week 5.

Non-CDC sentinel physicians:

Outpatient ILI visits were at 9% for week 6, from 11% for week 5.

Viral isolation/detection:

With 14 of 18 sites reporting for week 6, a total of 60 influenza detections were reported. Twenty were type A: 5 from Fresno, 4 from Alameda, 2 each from Orange, Sacramento, San Mateo, and Solano, and 1 each from Contra Costa, San Benito, and San Luis Obispo Counties. Forty were type B: 21 from Orange, 8 from San Diego, 3 each from Los Angeles and Sacramento, and 2 each from Alameda and Santa Clara, and 1 from San Luis Obispo County.

In addition, 305 RSV detections were reported: 101 from Alameda, 44 from Los Angeles, 39 from Sacramento, 24 from Fresno, 18 from Santa Clara, 15 from San Bernardino, 10 from San Mateo, 8 from Contra Costa, 6 from Placer, 5 each from San Diego, Sonoma, and an unknown county, 4 from Orange, 3 each from Marin, San Luis Obispo, Solano, and Tulare, 2 each from San Francisco and San Joaquin, and 1 each from Calaveras, Kern, Madera, Merced, and Ventura Counties.

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COMMUNICABLE DISEASE CONTROL
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Report of meeting of 3/04/01 (week 10)

Prophylaxis of children with ciprofloxacin to prevent meningococcal disease

It may surprise many to learn that ciprofloxacin is not approved by the Food and Drug Administration (FDA) for use in children under the age of 18, except as treatment or prophylaxis following exposure to inhalation anthrax. The language of the package insert reads: "Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established. Ciprofloxacin causes arthropathy in juvenile animals." The warning goes on to say: "Ciprofloxacin and other quinolones have been shown to cause arthropathy in immature animals of most species tested. Damage of weight bearing joints was observed in juvenile dogs and rats. In young beagles, 100 mg/kg ciprofloxacin, given daily for 4 weeks, caused degenerative articular changes of the knee joint. At 30 mg/kg, the effect on the joint was minimal. In a subsequent study in beagles, removal of weight bearing from the joint reduced the lesions but did not totally prevent them."

While the American Academy of Pediatrics Red Book 2000 does not recommend ciprofloxacin for meningococcal chemoprophylaxis for persons younger than 18 years of age, it also states "This drug appears to be well tolerated in children, does not appear to cause arthropathy, and is effective as an oral agent for treating a number of diseases that would otherwise require parenteral therapy." [1]

If therapeutic dosing does not appear to cause arthropathy in children, then it would stand to reason that one-dose therapy, as used in prophylaxis, would be even less of a risk. Ciprofloxacin was used recently for mass prophylaxis in two high schools in Northern California following multiple cases of invasive meningococcal disease for whom no obvious epidemiological connections could be established during the short window of opportunity to arrange prophylaxis (see CD Brief issues 01-2 and 01-7). Both schools obtained informed consent from parents, beforehand. In one school, over 700 doses were administered and, in the other, over 2,000. To date, none of the arthropathies reported in animals have been reported from either school. However, 4 cases of allergic reactions, including anaphylaxis (laryngeal edema) in 2, were reported. The package insert for ciprofloxacin states that the drug has been associated with hypersensitivity, even following a single dose, with rash reported in about 1%. However, in a report of 3200 college students who received ciprofloxacin for prophylaxis of meningococcal disease, 3 cases of anaphylactoid reaction (combinations of tight throat, facial swelling, and/or rash) occurred, for a rate of 1:1000,[2] comparable to that in our series.

Ciprofloxacin has several advantages over other alternatives for prophylaxis for meningococcal disease,

particularly when used in large population groups where high rates of simultaneous compliance are necessary. It is administered in a single dose oral dose in contrast to rifampin, which is administered every 12 hours for 2 days, and to ceftriaxone, which is administered intramuscularly. Ciprofloxacin is relatively inexpensive, costing approximately $1 per dose, and is usually accessible to public health departments which use it commonly to treat gonococcal infections. When ciprofloxacin was used in the above high schools, supervising attendants noted attempts by some students to avoid taking the medication. Such direct observation would usually not be feasible with subsequent doses of rifampin. The United Kingdom guidelines for the control of meningococcal disease note "Ciprofloxacin is useful when large numbers of contacts need prophylaxis, such as in the management of outbreaks in colleges or military camps."[3] It is also noted that "there is evidence of its safety in children." Rifampin can interfere with the efficacy of oral contraceptives, some antiseizure and anticoagulation medications, and can stain soft contact lenses. Neither rifampin nor ciprofloxacin is recommended for use in pregnant women. Rapid emergence of rifampin-resistant strains of *N. meningitidis* following prophylaxis has been observed; this has not been studied, to date, for ciprofloxacin.

Since ciprofloxacin appears so useful for prophylaxis of meningococcal disease, we are taking this opportunity to review, below, the evidence of its safety in children. It should be noted that ciprofloxacin is also not FDA-approved for meningococcal prophylaxis in adults and, so, such use constitutes an off-label use; but the issue in adults does not revolve around safety such as arthropathy. As cited by CDC, "Ciprofloxacin in various dosage regimens is >90% effective in eradicating nasopharyngeal carriage. A single 500-mg oral dose of ciprofloxacin is a reasonable alternative to the multidose rifampin regimen. Ciprofloxacin levels in nasal secretions far exceed the MIC_{90} for *N. meningitidis* following oral dosing. Ciprofloxacin is not generally recommended for persons <18 years of age or for pregnant and lactating women because the drug causes cartilage damage in immature laboratory animals. However, a recent international consensus report has concluded that ciprofloxacin can be used for chemoprophylaxis of children when no acceptable alternative therapy is available." [4]

Ciprofloxacin has been used extensively in children for the <u>treatment</u> of pulmonary infection in cystic fibrosis, as well as for salmonellosis and shigellosis. Other uses in children include chronic suppurative otitis media, meningitis, septicemia, and urinary tract infection. It is estimated that the number of prescriptions of ciprofloxacin filled in the US for children 1 year of age or younger rose from about 6,000 in 1992 to 12,000 in 1996; among children 6-12 years old, the number rose from 10,000 to 35,000 during the same period.[5] A retrospective study conducted by the Boston Collaborative Drug Surveillance Program[6] reviewed the records of over 1700 patients $\leq$17 years who received at least 1 dose of ciprofloxacin. There were no cases of newly diagnosed acute arthritis that were likely ciprofloxacin-induced. Hampel et al.[7] described the safety findings in 1795 children who received 2030 treatment courses of intravenous or oral ciprofloxacin as part of surveillance for the compassionate use of ciprofloxacin worldwide. Arthralgia occurred during 31 ciprofloxacin treatment courses (1.5%) and the majority of events were of mild to moderate severity and resolved without intervention. Other studies, including some prospective, of children receiving ciprofloxacin in Israel,[8] India,[9,10] and the Slovak Republic and Viet Nam[11] have found no evidence that ciprofloxacin caused a delayed arthropathy or any permanent joint damage. In 1993, The International Society of Chemotherapy commissioned a review of the use of fluoroquinolones in children in numerous settings. In regard to safety, it was concluded: "Results indicate that prolonged therapy with the fluoroquinolones is effective and well-tolerated with no significant evidence of arthropathy, bone abnormalities, or other serious adverse events." [12]

In summary, DISB supports the use of ciprofloxacin for mass prophylaxis in high school settings when such a

step is indicated and there is capacity to treat rare anaphylactic reactions that may occur. The advantages in this situation, especially where those students receiving the drug are 14-18 years of age and are thus nearly adults, outweigh the risks. We have yet had to confront the situation of using it in settings where younger children are involved. We are not, at this point, recommending its use for prophylaxis of individual children following direct contact with a case of invasive meningococcal disease as in household settings but clinicians may choose to do so, especially after reviewing the references cited in this note.

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Varicella outbreak

The Immunization Branch is working with San Diego County Health Department to investigate an outbreak of varicella infections at an elementary school (K-5). Currently, at least 25 children have been identified with varicella; about 50% of these children may have been vaccinated against varicella.
In clinical trials, varicella vaccine produces seroconversion in greater than 95% of healthy children, and attack rates of illness among exposed persons decrease by 80% or more. Illness in vaccinated children and adults appears to be much milder than natural infection. One factor that may lower vaccine effectiveness is a breech of storage and handling requirements. Varivax must be kept at -20°C (+4°F) or colder during shipment, stored at -15°C (+5°F) or colder, and used within 30 minutes of reconstitution. Since this is the only routine childhood vaccine that requires freezing, many providers and facilities are not accustomed to checking and maintaining the cold chain, which could explain some of the apparent vaccine failures.

We have already witnessed a dramatic drop in the incidence of varicella in association with increasing immunization rates. The Immunization Program at the Centers for Disease Control and Prevention is currently developing guidelines that recommend the investigation of varicella outbreaks with more than 5 cases when

some of the ill persons reportedly had prior immunization. Goals of our current investigation are to determine if the outbreak was caused by a vaccine strain (rather than wild virus), vaccine efficacy, and the impact of the vaccine on reducing clinical severity.

Continued measles activity in California

Two more cases of measles have been reported, one in Riverside County and one in San Mateo County. The Riverside County case is a 3-year-old boy with rash onset on 2/20/01. This child was U.S. born, but had no documentation of MMR vaccination. The source of infection is not known. The case had no history of international travel or visitors, although he visited Universal Studios in L.A. County during his exposure period. This case is not linked to the recent measles cases in Japanese tourists, since his likely exposure period ended before their visit to Southern California. The San Mateo County case is a 30-year-old woman who recently traveled to the U.S. from Australia, with rash onset on 3/1/01. She was not infectious on the flight. Before she left Australia, she was in contact with her brother, a known measles case, and part of an ongoing outbreak of measles in Australia. County public health departments are following up contacts to both cases. As yet, there have been no additional cases.

Between January 1 and March 1, 2001, a total of 11 measles cases have been reported in California. For the same period in 2000, there were only 3 cases reported, and 19 reported for the year in total. Nine of the 11 cases reported in 2001 were international imports, eight of them from Asian countries (Japan, Korea, Philippines). In addition, an outbreak of three cases, reported in December 2000, began with an imported case from the Philippines. Measles imported by international travelers continues to be a source of disease in California, especially from countries where measles is endemic (Japan and Philippines) or occurring in outbreak form (Korea and Australia).

Drug recall

WYETH-AYERST Laboratories has voluntarily recalled a tuberculosis medication, Trecator SC 250 mg Tablets (Ethionamide Tablets, USP). Please examine your Trecator SC 250 mg Tablets inventory immediately. If you have Lot number 3990893 on hand, cease distribution immediately and contact Universal Solutions, Inc. at 1-800-777-6565 and choose Option #1 for Customer Service.

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