

## APPENDIX D

### CLINICAL EVALUATION

#### A. EVALUATION OF LIVER FUNCTION TESTS

##### References

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##### Introduction

The liver, as the primary site of metabolism of chemicals, is a potential site of damage from many chemicals used in the workplace. The most common workplace chemicals known to cause liver injury are the organic solvents. Many of the halogenated hydrocarbon solvents, the nitrogen-containing chemicals and the alcohol solvents can damage the liver. The more toxic chemicals, such as carbon tetrachloride, have been removed from the workplace because of liver damage, but may still be found in older specialized processes or in research facilities. Workplace exposures to the alcohol solvents, primarily ethyl and methyl alcohol, are infrequent causes of abnormal liver tests, but may cause abnormal findings if combined with non-workplace exposure or ingestion. Ethyl alcohol can also interact with the metabolism of numerous chemicals that affect the liver. In addition to hepatotoxic chemicals, many viral infections and some bacterial infections encountered primarily in the health care industry can cause acute and chronic liver abnormalities. Hepatitis B virus is a known cause of both acute and chronic liver disease. Workplace exposures to chemicals and infectious agents are also documented causes of liver cancer.

To screen for possible hepatotoxic effects from exposure to workplace chemicals, a "liver profile" or a battery of "liver function tests" are frequently measured. A typical "liver function tests" profile, includes: aspartate aminotransferase (AST, formerly called SGOT or serum glutamic-oxaloacetic transaminase); alanine aminotransferase (ALT, formerly called SGPT or serum glutamic-pyruvic transaminase); alkaline phosphatase (AP); and bilirubin. Occasionally other serum constituents, such as (-

glutamyl trans-peptidase (GGT), total bilirubin and fractionation into direct- and indirect-acting components, lactate dehydrogenase (LDH), total protein, and albumin, are also included. Each of these tests has a different specificity and sensitivity for different forms of liver damage. Those tests which reflect the specific type of liver damage should be used to minimize the possibility of abnormal results unrelated to occupational exposure.

The laboratory usually determines the normal ranges for liver tests, therefore normal ranges will vary by laboratory and type of analysis. Some tests are reported in International Units (IU) of activity, whereas others are reported in grams or milligrams per volume. Subtle changes in liver structure and activity may not be measured by these commonly used tests. Both early, mild changes and late, chronic changes can be missed with the routine panels. To measure for these types of changes, additional testing may be required and while rarely used for screening in our occupational health programs, may be useful for specific exposures.

Tests for the function and integrity of the liver can be divided into three general categories:

1. Tests that detect damage to the hepatocyte, or liver cell;
2. Tests of the liver's capacity to transport organic anions and metabolize chemicals;
3. Tests of the liver's biosynthetic capacity.

#### **Tests that Detect Damage to the Hepatocyte**

Injury to the liver from chemical toxicants has classically been divided into two major categories based upon the pattern of changes in liver enzyme activity.

**Hepatocellular Injury.** Hepatocellular injury is due to the toxicant's effect on all or part of the hepatocyte, including the cell membrane. The aminotransferases, AST and ALT, are the most commonly measured enzymes that detect hepatocellular injury. Elevated serum activity levels can be found whenever there is damage to cells rich in these enzymes, or whenever there are changes in cell permeability resulting in an increased rate of entrance of ALT or AST into the blood. Neither AST or ALT is specific for liver injury. AST is also elevated in injury to cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, and white and red blood cells. ALT, while found predominantly in the liver, is also found in many other tissues. Serum AST activity, and possibly ALT, may be elevated after physical exercise; exercise is thought to be a cause of elevated aminotransferases in runners. Presently, there are no commonly available tests to differentiate the source of elevated aminotransferases, e.g. whether the AST is from liver or muscle cells. AST and ALT are typically elevated in all types of liver disorders, including congestion of the liver due to heart failure and cancer with metastasis to the liver.

Two other commonly measured enzymes, (-glutamyl transpeptidase (GGT) and lactic dehydrogenase (LDH), can be elevated in hepatocellular injury. The GGT, while very sensitive for biliary tract disease, is not very specific for the liver. GGT elevations can be found with disorders of the pancreas, heart, kidney or lung. Isolated GGT elevations have been associated with ethyl alcohol ingestion and exposure to other substances which induce microsomal enzymes, a common group of metabolic enzymes in liver. Because of its lack of specificity, GGT is most useful in confirming the source of alkaline phosphatase elevation as described in the following section. LDH is not as sensitive as the aminotransferases for liver cell injury and is more useful as a marker for myocardial infarction and hemolysis.

**Cholestatic Injury.** Cholestatic injury, or cholestasis, is caused by changes in liver structure so that the normal secretion or flow of bile is disrupted. Alkaline phosphatase is the most commonly used screening test for cholestatic injury. In the non-pregnant adult, alkaline phosphatase originates in the liver, bone, and intestine, with the liver and bone being the primary sources. The different sources of alkaline phosphatase produce specific isoenzyme forms of the parent enzyme which can be differentiated with special procedures. Serum alkaline phosphatase normally increases in pregnancy and with active growth, therefore the usual normal levels of alkaline phosphatase do not apply to pregnant women or growing children. Serum alkaline phosphatase levels are generally slightly higher in men than women in the 15 - 50 year old age groups, but this difference usually disappears after age 60. Both sexes over age 60 generally have higher levels than younger age groups.

If serum alkaline phosphatase is elevated without other evidence of liver injury, it is often necessary to identify whether the liver or the bone is the source. Electrophoresis can be done to identify the specific isoenzyme of alkaline phosphatase. Heat or chemical inactivation of the enzyme have also been used because the bone isoenzyme is more heat sensitive than the other isoenzymes. The heat inactivation test may be easily disrupted with minor errors in technique and therefore the results may not always be reliable. A third method to confirm the hepatic source of elevated serum alkaline phosphatase, is to measure the serum activity of other enzymes known to increase in association with liver originating alkaline phosphatase. There are three such enzymes - serum leucine aminopeptidase, 5'-nucleotidase, and (-glutamyl transpeptidase. Each of these enzymes has specific indications and limitations in confirming the hepatic origin of alkaline phosphatase. Further information can be found in any internal medicine textbook.

### **Tests of the Liver's Capacity to Transport Organic Anions and Metabolize Chemicals**

The primary test in this category is serum bilirubin. A variety of clearance tests have also been developed to measure the

liver's capacity to remove and detoxify substances from the blood. These include dye, breath, caffeine clearance and serum bile acid tests.

Bilirubin is a breakdown product of heme-containing proteins. Approximately 80% of the bilirubin produced each day originates from the hemoglobin of senescent red blood cells. In the blood, the lipid-soluble bilirubin is bound to albumin and is transported to the liver where it is made water soluble through conjugation to a glucuronide. The conjugated bilirubin is then excreted into the bile and ultimately removed from the body through the feces. A small portion of bilirubin is re-absorbed in the gut as urobilinogen. The conjugated or water soluble bilirubin is the "direct-acting" bilirubin. The "indirect-acting" bilirubin correlates with the unconjugated fraction and is the difference between the total and the direct-acting bilirubin. Overall, bilirubin determinations are not sensitive indicators of hepatic function. Hyperbilirubinemia can be produced through a number of mechanisms, including intravascular hemolysis and bile duct blockage. Gilbert's syndrome, a congenital anomaly found in up to 5% of the population, is associated with increased serum levels of unconjugated bilirubin due to impaired hepatocellular uptake and/or conjugation.

Liver clearance tests and serum bile acids are not considered useful screening tests for the effects of common workplace toxicants. They may be useful for research on occupational liver disease. The dye clearance test currently used is the indocyanine green clearance which has been used in the evaluation of early hepatotoxicity in vinyl chloride exposed employees. This test, which requires intravenous administration of the dye, is generally reserved for research protocols. An older clearance test using sulfo-bromophthalein sodium is no longer used because of toxicity from the dye.

Breath clearance tests use radioactive labelled carbon-containing chemical compounds, which can be administered orally or intravenously, and are metabolized by the liver. Following metabolism, the labelled carbon atom appears in carbon dioxide exhaled from the lungs. The rate of labelled carbon dioxide clearance from the lungs correlates with the rate of chemical metabolism in the liver. Caffeine is also cleared and metabolized by the liver. Disappearance of caffeine from the serum or saliva after an oral dose has been used to quantify liver function.

Serum bile acid measurements may also be used to evaluate liver function. Bile acids are normally produced by hepatocytes and secreted into the bile. A small proportion of bile acids are reabsorbed in the intestine and removed from the blood by the liver. With liver dysfunction, serum bile acids may be elevated. Measurement of bile acids is useful in management of certain cholestatic liver disorders, mainly primary biliary cirrhosis and primary sclerosing cholangitis.

## **Tests of the Liver's Biosynthetic Capacity**

The liver produces the majority of serum proteins, including albumin, fibrinogen and coagulation factors. Albumin is quantitatively the most important serum protein; the serum level reflects the rate of synthesis, the rate of degradation, and the volume of fluid in the body. Serum albumin levels are generally normal in acute liver disorders. In chronic liver disorders, such as cirrhosis, serum albumin may be low because of decreased synthesis. If ascites is present, serum albumin may be decreased because of increased volume of distribution.

The liver produces many of the known coagulation factors and is also responsible for the clearance of some clotting factors from the blood. Measurement of the prothrombin time evaluates the function of five coagulation factors produced by the liver. Three of these factors also require vitamin K for synthesis of the active form. Therefore in addition to inadequate production of the coagulation proteins, vitamin K deficiency or inhibition may also produce an abnormal prolongation of prothrombin time. Correction of the prothrombin time after administration of parenteral vitamin K differentiates parenchymal liver disease from vitamin K deficiency. Although the prothrombin time is an insensitive indicator of liver disease and may remain normal even in severe chronic liver disease, this test has been found useful as a prognostic indicator in acute hepatocellular disease. Prolongation of the prothrombin time by 5-6 seconds above control may forecast the development of fulminant hepatic necrosis during acute viral hepatitis.

## **Significance and Evaluation of Abnormal Liver Function Tests**

In screening for possible effects of hepatotoxicants, it is important to select the liver function tests with the best combination of specificity and sensitivity. For routine screening of chemicals that are known or suspected to cause hepatocellular injury, the ALT is considered to be the aminotransferase most specific for the liver. To screen for possible cholestatic effects, the alkaline phosphatase, while not the most specific for the liver, is considered the most useful single indicator of cholestasis. Routine screening with "profiles" which also include AST, GGT, bilirubin, LDH and protein determinations, provide limited additional information.

When a liver function test is above the "normal range," the health care provider must decide if this finding is significant. The algorithms in chapter 4, figure (2), will help to evaluate workers with laboratory tests outside the published normal values. Very minor elevations (less than 1.5 times the upper limit of the normal range) may or may not be significant and may or may not warrant repeating the test. To make a decision on the significance of an abnormal test, the health care provider may find useful information through reviewing the individual's previous test results, reviewing the types and levels of exposures to

hepatotoxicants, reviewing test results in other similarly exposed employees, and performing a medical and occupational history and physical examination on the individual with the abnormal test. Since ingestion of ethyl alcohol and many drugs can affect liver function, it is important to obtain accurate information on the use of alcohol beverages and medications.

If, on review of the collected data, an abnormal liver test is thought to be significant and the abnormality persists on a second test, the health care provider may wish to obtain additional tests to confirm the hepatic origin of an abnormally elevated enzyme or order additional tests to help evaluate the extent of liver involvement. If the liver test abnormality could be due to workplace exposures, the tests results of co-workers should be reviewed and an industrial hygienist should be consulted so that all workplace exposures are reviewed. Specific types of liver disease, such as hepatitis A in a food service worker, may require extensive preventive medicine follow-up of co-workers and patrons of the food service.

During the evaluation of abnormal liver tests, some individuals may benefit from a two to four week trial of removal from exposure to known workplace hepatotoxicants or of abstinence from alcohol. If the abnormal tests return to normal after workplace removal, reassessment of occupational exposures and use of protective equipment is essential. If the abnormal liver test is found to be related to alcohol ingestion, the individual should receive appropriate counselling and referral. Individuals with persistent liver test abnormalities should be referred to their physician or a specialist for further evaluation.

## **B. EVALUATION OF ABNORMAL AUDIOGRAMS**

### **References**

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## **Introduction**

Noise is a common occupational exposure in Navy workplaces, and noise-induced hearing loss (NIHL) is one of the most common occupation-related disabilities. NIHL is a sensorineural hearing loss caused by long-term continuous exposure to noise in excess of 85 decibels (dB) or exposure to impact noise. The early, typical finding in NIHL is a decrease in the hearing threshold at 4000 hertz (Hz) or 4 kilohertz (kHz) on the audiogram. With continued, unprotected exposure to excessive noise, NIHL progresses (Figure 1). Other forms of occupational hearing loss include conductive hearing loss caused by explosions, trauma or burns, and sensorineural hearing loss caused by exposure to ototoxic substances or blunt head trauma.

All commands, shore and afloat, with noise exposures in excess of specified noise levels are required to have a Hearing Conservation Program as described in OPNAVINST 5100.23 and 5100.19 series respectively. Although the medical department is actively involved in many elements of the hearing conservation program, the occupational health clinic's primary role is in conducting and interpreting audiograms for noise-exposed personnel.

All personnel (civilian and active duty) require a baseline (preplacement or reference) audiogram on placement into a hearing conservation program. Following the baseline audiogram, testing is done periodically (annually, or more frequently, if indicated) and compared to the baseline to detect any changes or shifts in hearing threshold levels. Because of the importance of the baseline audiogram, it is imperative that this test be the highest quality possible. The individual should not have been exposed to noise for at least 14 hours prior to the baseline audiogram. The individual should also fully understand what is expected of him/her during the test, the audiometric equipment should be calibrated and properly functioning, and care should be taken to ensure that noise outside the audio booth does not interfere with testing. Shifts in hearing thresholds from the baseline audiogram may be temporary or permanent. The hearing conservation instruction outlines the procedures for determining a temporary threshold shift (TTS) or a permanent threshold shift (PTS). A threshold shift is considered "significant" if there is a change in hearing thresholds, as compared to the current reference audiogram, of 15 dB or greater in any frequency 1000 through 4000 Hz, or an average of 10 dB or more at 2000, 3000 and 4000 Hz in either ear.

**What is abnormal hearing?** Normal hearing, as measured by audiometry for the Navy's hearing conservation program, is detection of pure tones at the frequencies of 500, 1000, 2000,

the ear canal.

A person who has received otologic evaluation previously on the basis of the foregoing criteria should be re-evaluated if he/she develops ear pain, drainage, dizziness, disequilibrium, imbalance or severe persistent tinnitus, or shows significant change in hearing levels defined in the previous section.

B. In addition to the above recommendations, other sources also suggest referral to an audiologist or ear specialist for the following findings on audiogram:

1. Baseline audiogram - hearing loss equal to or exceeding 30, 40, or 50 dB at 3000, 4000, and 6000 Hz, respectively in one or both ears.

2. Any audiogram -

a. Unilateral or asymmetrical hearing loss, an average difference between ears of 40 dB or greater.

b. Any audiogram with a 40 dB or greater threshold at 500 Hz accompanied by a 25 dB or greater threshold at 1000 Hz.

c. Any audiogram with a 40 dB or greater difference between ears at any frequency.

It should be noted that these referral criteria are different than the criteria for referral to physician or audiologist based upon the development of a permanent threshold shift and the requirement for determining if a PTS is noise-related.

#### **Evaluation of Hearing Loss by the Occupational Health Physician.**

On evaluation of an individual with documented hearing loss, the occupational health physician has two primary concerns:

1. Attempting to identify the etiology of the hearing loss, specifically, is the hearing loss due to noise exposure (occupational or non-occupational), or any of a variety of medical conditions/exposures associated with hearing loss.

2. Ensuring an appropriate plan for follow-up. In attempting to identify the etiology of the hearing loss, the usual techniques of a thorough history, an appropriate physical examination, and review of all audiograms, usually provide enough information to determine if referral to an audiologist or ear specialist is required.

In the history it is important to inquire about changes in hearing, all sources of noise exposure, family history of hearing loss and exposure to ototoxic substances. The health care provider should complete a general review of systems, especially noting recent infections or subtle problems with the ears, balance and vertigo. On physical examination, blood pressure measurement, examination of the ears and selected neurologic system examinations

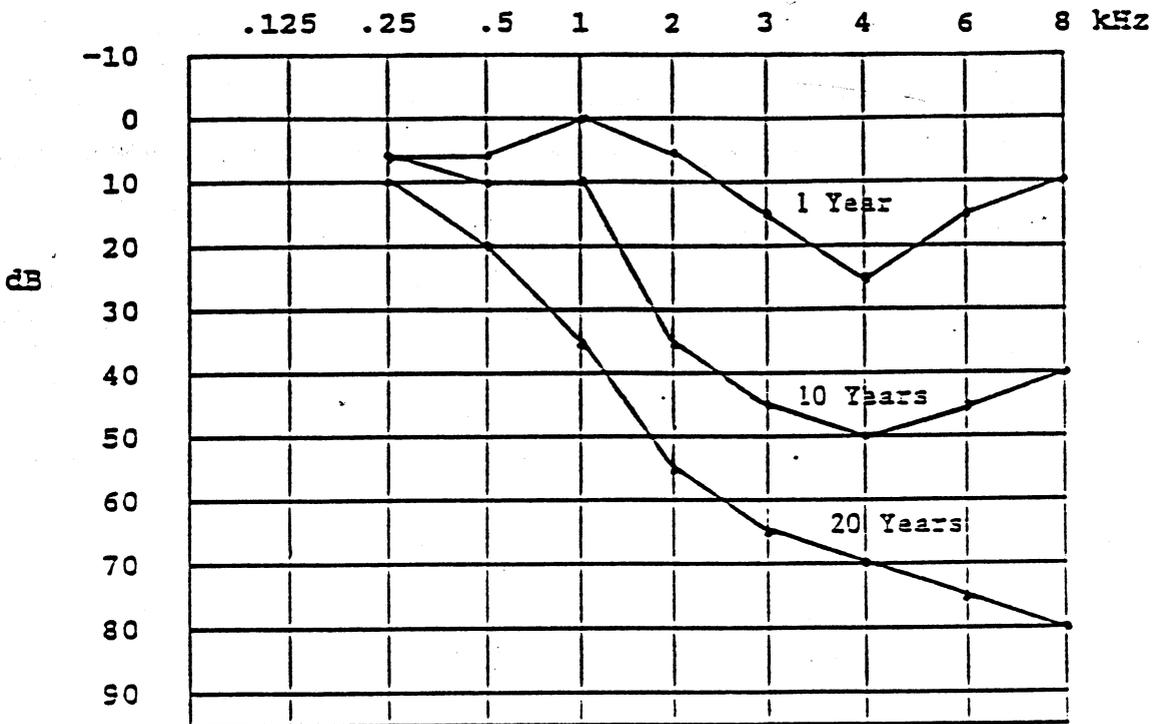


Figure 1. Progression of Noise-Induced Hearing Loss

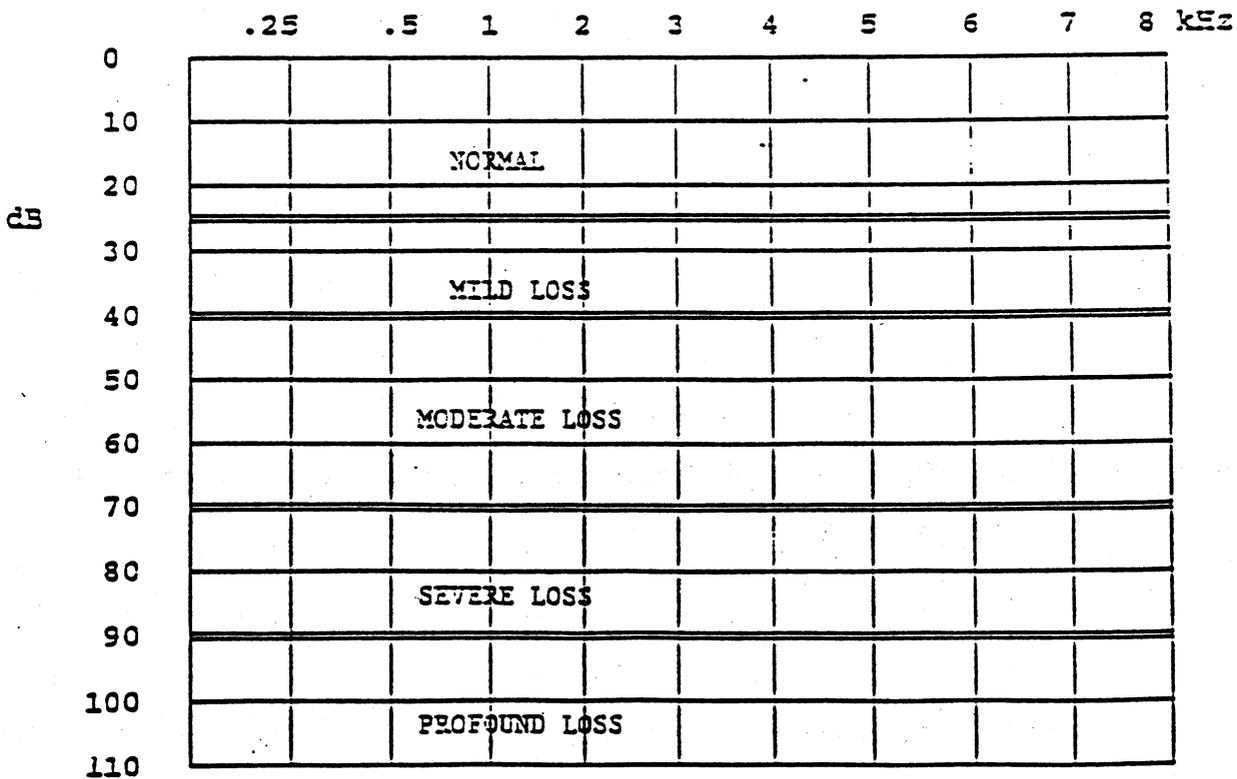


Figure 2. Classification of Abnormal Hearing

3000, 4000 and 6000 Hz at 20 decibels (dB) or less. (Some sources use hearing thresholds of  $\leq 25$  dB as normal hearing.) Classification systems for abnormal hearing or disability related to poor hearing are often based upon hearing thresholds in the normal speech perception frequencies of 500 - 3000 Hz. One classification of abnormal hearing, based upon speech perception threshold, is provided as Figure 2.

**When should an individual with abnormal hearing or a change in hearing be referred for further evaluation?**

A. The American Academy of Otolaryngology-Head and Neck Surgery has published the following suggested criteria for referral to an audiologist or ear specialist. This organization recommends that the original baseline audiogram, rather than a re-established baseline audiogram, should be used for comparison to identify individuals who will be referred for hearing loss.

Suggested Criteria for Referral to an Audiologist

1. Baseline audiogram
  - a. Average hearing level at 500, 1000, 2000, and 3000 Hz is greater than 25 dB in either ear.
  - b. The difference in average hearing level between the better and poorer ears of:
    - (1) more than 15 dB at 500, 1000, and 2000 Hz; or
    - (2) more than 30 dB at 3000, 4000, and 6000 Hz.
2. Periodic audiogram

Change for the worse in average hearing level, in either ear, compared to the baseline audiogram, of:

  - a. more than 15 dB at 500, 1000, or 2000 Hz; or
  - b. more than 20 dB at 3000, 4000 and 6000 Hz.
3. Any audiogram

Variable or inconsistent responses or unusual hearing loss curves.

Suggested Criteria for Referral to a Physician or Ear Specialist

1. History of ear pain, drainage, dizziness, severe persistent tinnitus, sudden, fluctuating or rapidly progressive hearing loss, or feeling of fullness or discomfort in one or both ears within the preceding 12 months.
2. Visible evidence of cerumen accumulation or a foreign body in

are usually appropriate. Minor problems, such as cerumen impaction or serous otitis, can often be treated and the individual can have his/her hearing retested.

If the hearing shift persists, the occupational health physician needs to determine the appropriate plan for follow-up. The required plan for follow-up will be based on the differential diagnosis of the hearing loss and may include referral to an audiologist or ear specialist. In some cases the plan may be education, re-fitting of hearing protection and a schedule for repeat hearing tests.

Noise-induced hearing loss is a preventable condition which can lead to significant disability. Whenever the diagnosis of NIHL is made, it is important that the individual is made aware of the diagnosis and is counselled on his/her hearing loss. The individual also needs to be made aware that continued, unprotected exposure to noise, whether occupational or non-occupational, may result in progressive hearing loss. He/she should be encouraged to use hearing protection regularly at work and when engaged in noisy recreational activities.

### **C. ASBESTOS MEDICAL SURVEILLANCE PROGRAM**

#### **References**

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#### **Introduction**

BUMED has tasked the Navy Environmental Health Center (NAVENVIRHLTHCEN) with centrally managing the Navy Asbestos Medical Surveillance Program (AMSP) ashore and afloat. These responsibilities include the following:

1. Providing professional and technical consultation on the medical aspects of occupational exposure to asbestos.

2. Maintaining and analyzing the central registry database containing information on personnel enrolled in the AMSP. This contains data from NAVMED 6260/5 (history and physical evaluation) and NAVMED 6260/7 (roentgenographic interpretation for pneumoconiosis).

3. Certifying equipment and technique of x-ray facilities to take AMSP chest films, and facilitating the forwarding of films for B-readings to NIOSH-certified B-readers.

### **Criteria for Enrollment in the AMSP**

The terms "asbestos current worker" program and "asbestos past worker" program used in this section refer to the medical surveillance programs in NEHC6260 TM96-1. Navy personnel may be placed in the AMSP if they meet any of the following criteria:

1. **"Asbestos current worker" program.** The criteria for enrollment are contained in the OPNAVINST 5100.23 series.

a. Military and civilian personnel who meet the exposure criteria defined in OPNAVINST 5100.23 series must be included in the AMSP and must remain in the program for "asbestos current worker" as long as the exposure criteria are met.

b. An individual enrolled in the "asbestos current worker" program must be removed from that program if he/she no longer meets the exposure criteria defined in OPNAVINST 5100.23 series. If he/she would like medical evaluation continued, he/she may be enrolled in the "asbestos past worker" program.

2. **"Asbestos past worker" program.** The Navy has developed a program for individuals with a history of past asbestos exposure in view of the long latent period between the first exposure to asbestos and the development of signs or symptoms of asbestos-related diseases. Placement in the AMSP on the basis of past asbestos exposure is a Navy specific program, i.e., not mandated by OSHA regulations. Enrollment in the program is voluntary, and individuals may request termination at any time. Military and civilian personnel with a history of asbestos exposure may be included in "asbestos past worker" program, based on professional evaluation, if any of the following criteria are met:

a. History of enrollment in the Navy AMSP; or

b. A history of participation, during past federal employment or military service, in any operation where visible airborne asbestos dust was present, including but not limited to rip-outs, for approximately 30 days or more in the past; or

c. The occupational health (OH) provider, with occupational medicine physician and industrial hygiene consultation, as needed, concludes that the individual had exposure to asbestos during past federal employment or military service that met the current OSHA criteria

for placement in the medical surveillance program, or its equivalent, for approximately 30 days or more in the past.

**Medical Records** Table I summarizes the medical records required for workers in the AMSP.

**TABLE I  
AMSP MEDICAL RECORDS**

<b>AMSP FORMS</b>	<b>ASBESTOS "CURRENT WORKER"</b>	<b>ASBESTOS "PAST WORKER"</b>
DD 2493-1	For <b>initial</b> exam. Complete entire form.	<b>Not required.</b>
DD 2493-2	For <b>periodic and termination</b> exam. Complete entire form.	<b>Not required.</b>
NAVMED 6260/5	For all exams. Complete entire form. Forward to NAVENVIRHLTHCEN.	For all exams. Complete entire form. Forward to NAVENVIRHLTHCEN.
NAVMED 6260/7	For all x-ray exams. Complete section 1 and forward with P/A chest film to the B-reader.	For all x-ray exams. Complete section 1 and forward with P/A chest film to the B-reader.
PHYSICIAN'S WRITTEN OPINION	For all exams. Provide employee and employer with a copy.	<b>Not required.</b>

<b>GENERAL MEDICAL FORMS</b>	<b>ASBESTOS "CURRENT WORKER"</b>	<b>ASBESTOS "PAST WORKER"</b>
OPNAV 5100/15 (paragraph 0803.2a.(1))	Include information and update with each AMSP evaluation.	Include information and update with each AMSP evaluation.
SF 600 INDUSTRIAL HYGIENE FORM	Include as available.	Include as available.
NAVMED 6150/20	Document as enrolled in AMSP based on <b>OSHA criteria.</b>	Document as enrolled in AMSP based on <b>past exposure</b>
SF 600 or SF 602	As needed. Use to document findings not recorded on other forms.	As needed. Use to document findings not recorded on other forms.

## Criteria for Removal from the AMSP

**"Current worker" program.** OPNAVINST 5100.23 series details the criteria for removal from the AMSP of personnel who are enrolled in the program on the basis of the OSHA criteria. As detailed in that series, documentation on the medical record and a letter to NAVENVIRHLTHCEN are required when the individual was inappropriately enrolled, or was enrolled because of potential exposure but was never actually exposed.

**"Past worker" program.** Removal of an individual from the program may be initiated by either the individual or the OH professional.

1. An individual enrolled in the AMSP on the basis of past exposure may be removed from the AMSP at any time that he/she declines further evaluation. In such a situation:

a. A physician's written opinion is not required, but if the staff decides to provide one to the individual, the individual's command should **not** be provided a copy since the relevant asbestos exposure did not occur during his/her current position.

b. A termination evaluation is not required, but is recommended in certain situations, such as cases with history of heavy asbestos exposures.

c. Document on the medical record the reason(s) for removal from the AMSP. No other documentation is required. NAVENVIRHLTHCEN does **not** need to be informed that the individual refuses further evaluation.

2. An individual enrolled in the AMSP on the basis of past exposure may be removed from the AMSP if, upon review of available information, the OH professional (with occupational medical physician consultation as needed) concludes that the individual did **not** meet any of the criteria for inclusion in the program and was therefore inappropriately enrolled. In such a situation:

a. A physician's written opinion is not required, but if the staff decides to provide one to the individual, the individual's command should **not** be provided a copy.

b. A termination evaluation is not required.

c. Document on the medical record the reason(s) for removal from the AMSP.

d. Forward the individual's name and social security number to NAVENVIR- HLTHCEN stating the reason(s) for removal from the AMSP.

## **Asbestosis**

The AMSP is directed primarily towards the early recognition of asbestosis. The following guidelines on asbestosis are adapted from those published by the American Thoracic Society (ATS):

Asbestosis is defined as interstitial fibrosis of the pulmonary parenchyma in which asbestos bodies or fibers may be demonstrated. When pathological findings are not available, as is generally the case, the diagnosis of asbestosis is a judgement based on consideration of all relevant clinical findings.

In making a diagnosis of asbestosis, there must be:

1. A reliable history of exposure, and
2. An appropriate time interval between exposure and detection (usually ten years or more).

In addition, the following are of recognized clinical value:

1. Chest roentgenographic evidence of type "s", "t", or "u", small irregular opacifications of a profusion of 1/1 or greater (ILO Classification of Pneumoconioses - 1980)
2. A restrictive pattern of lung impairment with a forced vital capacity below the lower limit of normal
3. A diffusing capacity below the lower limit of normal
4. Bilateral late or pan inspiratory crackles at the posterior lung bases not cleared by cough.

The chest roentgenographic findings are considered the single most important clinical criterion. When it is not met, considerable caution is warranted. The specificity of roentgenographic findings increases with increasing number of positive criteria. As in all clinical judgements, confounding variables, such as the presence of other clinical conditions that affect these criteria, should be evaluated.

## **Pleural Abnormalities**

Pleural abnormalities are often associated with parenchymal disease, but are different in epidemiology, clinical features, and prognosis. Exposure to asbestos may cause the following benign pleural abnormalities:

1. Pleural plaques. These are discrete, rounded lesions, usually bilateral, most often found on the posterolateral aspect of the lower parietal pleura or diaphragm. They are not believed to be pre-malignant lesions. Pleural plaques are well established

markers for asbestos exposure and are usually detected in asymptomatic individuals on routine chest roentgenography. The finding of pleural plaques on chest roentgenography is not, by itself, an indication to refer for further evaluation.

2. Pleural thickening. This is a focal or diffuse fibrosis of the visceral pleura with involvement from the apex to the base. Pleural thickening may impair pulmonary function and cause symptoms. Since many other disease processes can cause pleural fibrosis, the finding of diffuse pleural thickening on chest roentgenography is non-specific and is not necessarily related to asbestos exposure.

3. Pleural effusions. These are early manifestations of asbestos exposure and are characteristically unilateral sterile exudates. Other disease processes can cause pleural effusion and a careful evaluation for other causes, such as lung cancer or tuberculosis, should be undertaken before an effusion is attributed to asbestos exposure.

### Lung Cancer

Lung cancer risk is related to asbestos exposure in a linear, dose-related fashion. There is a synergistic effect of smoking and asbestos exposure on the development of lung cancer. Smoking significantly increases the risk of lung cancer. The latency period is seldom less than ten years and is usually over twenty years.

### Mesothelioma

Most malignant mesotheliomas of the pleural and peritoneal cavities are associated with exposure to asbestos. Cases may occur from transient exposure to asbestos. Cigarette smoking appears unrelated to the development of mesotheliomas. The latency period is usually greater than twenty years and is often as long as thirty or forty years after exposure.

### Other Malignancies

Some studies have associated asbestos exposure with excess cancers of the gastrointestinal tract and kidney. These studies are not considered conclusive.

### B-readings

Individuals with pulmonary signs and symptoms from acute illnesses should not be scheduled for an AMSP x-ray until the illness has cleared up, to avoid x-ray findings which may cloud the pneumoconioses findings.

NAVENVIRHLTHCEN contracts with NIOSH-certified B-readers to read all AMSP films using the ILO classification for pneumoconioses. All films must be read by the local radiologist before they are mailed for B-readings.

The B-reading is designed for epidemiological purposes, not for clinical evaluation. If the B-reading is significantly different from the reading of the local radiologist, the local radiologist should be asked to review the film. Because the local radiologist has access to information about the individual's history, physical examination and previous x-rays, and can take further x-rays if needed, his/her interpretation of the chest film is more important for clinical diagnosis than the B-reader's interpretation. Further action will depend on the clinical judgement of the examining physician. Referral to a pulmonary specialist may be indicated.

### **C-readings**

The technique used for taking AMSP films is different from those used for other purposes. Therefore, a medical facility can take AMSP x-rays only after its equipment and technique have been certified by NAVENVIRHLTHCEN. This is done by submitting films for C-readings.

Routine recertification is not required. Recertification is required when the x-ray equipment is changed or significantly modified. When NAVENVIRHLTHCEN identifies a problem with film quality, recertification may be required. The procedures for recertification of equipment and technique are the same as for the initial certification.

### **AMSP Certification of the Radiology Technique and Equipment**

The following procedures must be followed by medical facilities applying for AMSP certification:

1. Facilities must submit to NAVENVIRHLTHCEN six AMSP posterior/anterior (P/A) chest films for evaluation and B-reading interpretation. Table II describes the imaging systems and x-ray technique necessary to produce the optimum interpretation quality.
2. A NAVMED 6260/7 form and Table III form must be completed and forwarded to NAVENVIRHLTHCEN with each P/A chest film. The Table III form provides information on the imaging system, type of machine, technique, processing and Quality Assurance for the consulting radiologist.
3. NAVENVIRHLTHCEN forwards the submitted films and forms to a consulting radiologist (C-reader). If the C-reader determines that the films meet the ILO 1980 classification standards, the medical facility will be certified to take AMSP films. The C-reader's interpretation of readable films will be recorded on the NAVMED 6260/7 forms.

4. The C-reader's recommendations will be conveyed via NAVENVIRHLTHCEN letter to the submitting facility with the films and completed NAVMED 6260/7 forms. This letter will either notify the facility certifying its x-ray equipment and technique, or identify reasons for denying the certification. The letter providing certification includes detailed information for obtaining delivery orders and routinely sending chest films for B-readings under the NAVENVIRHLTHCEN centrally administered contract. A copy of this approval letter should be kept on file in the x-ray department.

Contact NAVENVIRHLTHCEN when questions arise concerning the certification status of a facility.

**Table II**  
**Imaging System and X-Ray Technique Recommendations**

<u>Parameter</u>	<u>Recommendation or Requirement</u>
Film	Medium or high speed
Screen	Medium or high speed
Grid	
Ratio	8:1 or 12:1
Lines/inch	100 - 103
Focal film distance	72 inches
Film size	14 inches X 17 inches
Film holder	Adjustable; cassette capable of being positioned vertically or horizontally
Projection	Posterior-anterior chest
Anode	Rotating
Focal spot size	Maximum 2 millimeters
Filtration	Minimum 2.5 millimeters aluminum
Time	a. Less than 1/20 second b. 1/10 second if single phase and less generator capacity than 300 milliamperes at 125 kilovolt peak or patient greater than 28 centimeters
Milliamperes	300 or greater
Kilovoltage	120 or greater

**Table III**  
**X-Ray Technique and Equipment Questionnaire**

1. Settings of chest film forwarded for evaluation:
  - a. Phototimer system used:
 

YES _____	NO _____
Milliamperes _____	Milliamperes _____
Backup Time _____	Time _____
Kilovolt Peak _____	Milliamperes-seconds (mAs) _____
	Kilovolt Peak _____
  - b. Focal Film Distance \_\_\_\_\_ Filtration \_\_\_\_\_
2. Type of equipment:
  - a. Manufacturer \_\_\_\_\_ Model \_\_\_\_\_
  - b. Generator type:
 

Single phase _____
Three phase _____
Other (specify) _____
  - c. Automatic collimation available: Yes \_\_\_\_\_ No \_\_\_\_\_
  - d. Films/intensifying screens used \_\_\_\_\_
  - e. Grid used: Ratio \_\_\_\_\_ Lines/inch \_\_\_\_\_
  - f. Maintenance provided by \_\_\_\_\_
3. Workload:
  - a. Radiographs:
 

Number of <u>all types</u> of films per week _____
Number of <u>chest</u> films per week _____
  - b. Retake rate: Percentage of films retaken \_\_\_\_\_
4. Darkroom:
  - a. Type of processing: Automatic \_\_\_\_\_ Manual \_\_\_\_\_
  - Manufacturer \_\_\_\_\_ Model \_\_\_\_\_
  - Type thermometer \_\_\_\_\_ Type timer \_\_\_\_\_
  - b. Maintenance:
 

Frequency for changing chemicals _____
Maintenance performed by: _____
Technician _____
Medical repair technician _____
Service contract _____

## B-reading protocol

MTFs certified to take AMSP x-rays must follow the procedures listed below to obtain B-readings:

1. Use SF-519A and **NAVMED 6260/7 Report Form** (Stock Number 0105-LF-009-9900) to order routine posterior/anterior (P/A) chest x-rays for individuals in the AMSP. Complete Section I of NAVMED 6260/7.

2. Do not ask the B-reader to make comparisons with old films. Do not forward other radiology reports, x-rays or related information. All additional x-rays and consultations are the responsibility of the examining physician, in consultation with the local radiologist as needed.

3. Follow the procedures below in preparing AMSP chest films for B-readings:

a. The local radiologist must read the films before they are forwarded to the B-reader. Use routine procedures established by the x-ray department to track films checked out of the department.

b. Forward only the P/A chest films and NAVMED 6260/7s to the B reader. You **must** always send both the original and copy of the NAVMED 6260/7 to the B-reader. **Do not send the films to NAVENVIRHLTHCEN.**

c. To obtain authorization for mailing AMSP chest films to the B reader, use the sample letter on the following page to request the DD 1155 (delivery order) from NAVENVIRHLTHCEN. The number of radiograph evaluations you request in the letter will be entered in block 19 of DD 1155. If the number of AMSP chest evaluations varies from the number on the DD 1155, contact NAVENVIRHLTHCEN to have the order modified **before you ship the films and DD 1155 to the B-reader.** Failure to comply could result in an unauthorized procurement with funding charged to your activity.

d. Each chest film must have an accompanying NAVMED 6260/7 with **all of Section I completed.** If two exposures are required to obtain the P/A chest film, count these two chest films as one chest film, and prepare one NAVMED 6260/7 to request one evaluation. Place the NAVMED 6260/7 on top of each corresponding film (do not staple form to film) and stack up to 25 films in one x-ray jacket for efficient packaging. This will enable a mailing case to hold up to 100 AMSP films and forms. The B-reader is not responsible for sorting forms to match films. Films must be securely packed in the film mailing case. Mailing cases are furnished by the NAVENVIRHLTHCEN upon request.

e. AMSP films should be forwarded at least monthly in batches of 10 to 100 films. Facilities having less than 10 films in a month may batch those films with other facilities. Please contact NAVENVIRHLTHCEN to identify other clinics taking AMSP films in your

area, if needed.

f. Prepare a mailing label for the x-ray mailer case, containing the B- reader address (found in block 9 of the DD 1155.) Prepare a second mailing label with your address to be used by the B-reader in returning the AMSP chest films and NAVMED 6260/7s. Place the second label in the mailing case with the films, NAVMED 6260/7s and DD 1155.

g. **The films to the B-reader must always be mailed certified "priority 13" since films must be traceable in case they are lost in the mail. The DD 1155 must be used within 14 days (21 days for overseas activities) from the date found in block 3 of the DD 1155.**

3. The B-reader has thirty days to read the films. If the films and original NAVMED 6260/7s are not returned within two (2) months from the date you mailed the films, or by the date in block 10 of the order document DD 1155, contact NAVENVIRHLTHCEN.

4. B-reader interpretations (NAVMED 6260/7) are medical documents which must be incorporated into the permanent health record after review by the medical health provider.

#### **Requests for Authorization to Ship X-rays for B-readings**

Requests must be **in writing** and forwarded to NAVENVIRHLTHCEN by speed letter, regular mail, naval message, or telefax (Telefax: (804) 445-6873). An authorized signature is required unless the request is by naval message.

The format used in the following sample letter must be used to request authorization to ship AMSP chest x-rays for B-readings. Paragraph 1 requires information on the quantity of radiograph evaluations. If two exposures are required for an individual, count these two chest films as one. Use the UIC of the MTF shipping the AMSP chest x-ray.

DATE:

UIC:

From: (REQUESTING ACTIVITY) (Provide complete mailing address including building number, etc.)

To: Contracting Officer, Navy Environmental Health Center,  
2510 Walmer Avenue, Norfolk, Virginia 23513-2617

Subj: REQUEST FOR AUTHORITY TO SHIP ASBESTOS X-RAYS FOR B-READINGS

Ref: (a) OPNAVINST 5100.23D Chapter 17

1. Per reference (a), (**REQUESTING ACTIVITY**) has a total of (**QUANTITY**) chest radiograph evaluations available for shipping to the designated B-reader. The requested delivery date is (**DATE**: 45 days from the date of your request letter), Priority 13.

2. Please forward the order document (DD 1155) and the Chest Film Protocol for the AMSP.

3. Point of contact \_\_\_\_\_  
Telephone: DSN: \_\_\_\_\_ COMM: ( ) \_\_\_\_\_  
Telefax: DSN: \_\_\_\_\_ COMM: ( ) \_\_\_\_\_

**AUTHORIZED SIGNATURE**

**D. EVALUATION OF CHOLINESTERASE LEVELS**

**References**

Baker SR, Wilkinson CF, ed. *The Effects of Pesticides on Human Health*. Princeton: Princeton Scientific Publishing Co., Inc. 1990.

Bryson PD. *Comprehensive Review in Toxicology*. 2nd ed. Rockville, MD: Aspen Publishers, Inc; 1989:533-544.

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Hayes WJ. *Pesticides Studied in Man*. Baltimore: Williams and Wilkins. 1982:284-312,436-438.

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OPNAVINST 6250.4A. *Pest Management Programs*. 28 Nov 90.

**Mechanism of Action**

Most of the toxic effects of organophosphate and carbamate pesticides are due to their ability to inhibit the activity of acetylcholinesterase, an enzyme which normally inactivates acetylcholine. Acetylcholine is the neurotransmitter at the postganglionic parasympathetic nerve endings, preganglionic nerves to parasympathetic and sympathetic ganglia, somatic nerve endings to striated muscle, and certain central nervous system (CNS) synapses. When cholinesterase activity is inhibited, acetylcholine accumulates at cholinergic synapses, resulting in stimulation, then paralysis of transmission in those synapses.

**Routes of Absorption**

Organophosphates are absorbed through the respiratory and

gastrointestinal tracts, skin and conjunctival mucosa. Toxicity has been reported from skin absorption of organophosphates on clothing that had been laundered after contamination.

Carbamates are absorbed through the respiratory and gastrointestinal tracts. They are not appreciably absorbed through intact skin, but absorption may be increased in cases of dermatitis.

### **Elements of Medical Evaluation**

Workers undergo physical examinations before exposure and annually. The elements of the examination are contained in NEHC6260 TM96-1.

Cholinesterase levels are determined before exposure and at periodic intervals depending on the type and frequency of exposure. OPNAVINST 6250.4A contains the guidelines to be followed when monitoring cholinesterase levels.

### **Significance of Cholinesterase Levels**

The medical surveillance program tests for two kinds of cholinesterase:

1. Acetylcholinesterase (RBC cholinesterase) is found in the nervous system and red blood cells (RBC).
2. Butyrylcholinesterase (plasma cholinesterase, pseudocholinesterase) is found in the liver and plasma.

The syndrome observed with organophosphate or carbamate toxicity is due to the inhibition of acetylcholinesterase in the nervous system. Since this cannot be measured, RBC cholinesterase and plasma cholinesterase are used as surrogates in testing. Cholinesterase in the nervous system is reflected better by RBC cholinesterase than by plasma cholinesterase. Measurement of both is recommended because each yields different information:

1. Organophosphate and carbamate pesticides may cause a decline of RBC cholinesterase, plasma cholinesterase or both.
- 2, Plasma cholinesterase declines and returns to baseline values more rapidly than RBC cholinesterase. If there is complete inhibition of RBC cholinesterase by organophosphates, recovery takes place at the same rate as new RBC regeneration (approximately 1% per day). Plasma cholinesterase regenerates approximately 25% in the first 7 - 10 days.

Development of symptoms depends more upon the rate of decline in cholinesterase activity than upon the amount of the decline.

### **Considerations in the Interpretation of Laboratory Tests**

1. Normal laboratory values show a wide range, varying with the method and the laboratory. Therefore, it is preferable to compare a worker's follow-up cholinesterase values with his/her baseline

(obtained before exposure) rather than with the laboratory "normal" values. Cases have been reported of individuals whose cholinesterase levels are significantly depressed from their baseline, but fall within the laboratory range of normal.

2. Two baseline tests are recommended because for the same individual, cholinesterase values can vary by as much as 10 - 15%.

3. When baseline studies are not available for an individual who was overexposed to organophosphate, serial cholinesterase monitoring is advised. A rise in cholinesterase values indicates that there was post-exposure cholinesterase depression.

4. The complex formed by carbamates with cholinesterase is unstable. Cholinesterase monitoring is not helpful if a worker is exposed only to carbamates, unless the specimen can be examined within a few hours.

5. Decreased cholinesterase values have been reported in the following:

a. RBC and/or plasma cholinesterase - Overexposure to organophosphate or carbamate pesticides

b. RBC cholinesterase - anemia (if the cholinesterase measurement is not corrected for the hematocrit), quinine.

c. Plasma cholinesterase - liver damage, malnutrition, foods with xanthine related compounds (coffee, chocolate, tea), drugs (morphine, codeine, thiamine, ether, chloroquine), chemicals (organic mercury compounds, carbon disulfide, benzalkonium salts), acute infections, some types of anemia, stomach and kidney cancer.

6. Increased cholinesterase values have been reported in the following:

a. RBC cholinesterase - chronic low level exposure (as much as 10% above baseline).

b. Plasma cholinesterase - exercise, nephrotic syndrome.