

REPEALER

The following sections of the Washington Administrative Code are repealed:

WAC 296-62-07354	Appendices--Inorganic arsenic.
WAC 296-62-07525	Appendix A substance safety data sheet--Benzene.
WAC 296-62-07527	Appendix B substance technical guidelines--Benzene.
WAC 296-62-07529	Appendix C medical surveillance guidelines for benzene.

AMENDATORY SECTION (Amending WSR 05-01-172, filed 12/21/04, effective 3/1/05)

**WAC 296-849-11050 Training.**

**You must:**

. Provide training and information to employees:  
- At the time of initial assignment to a work area where benzene is present;

**AND**

- At least every twelve months after initial training for employees exposed to airborne concentrations at or above the action level (AL) of 0.5 parts per million (ppm).

. Make sure training and information includes all of the following:

- Specific information on benzene for each hazard communication training topic. For the list of hazard communication training topics, go to the Safety and health core rules, chapter 296-800 WAC, and find Inform and train your employees about hazardous chemicals in your workplace, WAC 296-800-17030;

**AND**

- An explanation of the contents of ~~((each of the following))~~ this chapter and guidance about where to find a copy ~~(of~~

~~. This chapter.~~

~~. The following found in another chapter, the General occupational health standards, chapter 296-62 WAC:~~

~~⊗ The substance safety data sheet benzene, found in WAC 296-62-07525, Appendix A.~~

~~⊗ The substance technical guidelines benzene, found in WAC 296-62-07527, Appendix B.~~

~~⊗ The medical surveillance guidelines for benzene, found in WAC 296-62-07529, Appendix C)) of it;~~

**AND**

- A description of the medical evaluation requirements of this chapter found in:

. Medical evaluations, WAC 296-849-12030;

**AND**

. Medical removal, WAC 296-849-12050.

**Reference:** To see additional training and information requirements in other chapters, go to the:  
. Respirators rule, chapter 296-842 WAC, and find the Training section, WAC 296-842-16005.  
. Safety and health core rules, chapter 296-800 WAC, and find the section titled, Inform and train your employees about hazardous chemicals in your workplace, WAC 296-800-17030.

AMENDATORY SECTION (Amending WSR 05-13-152, filed 6/21/05, effective 8/1/05)

**WAC 296-849-12030 Medical evaluations.**

**IMPORTANT:**

Medical evaluations conducted under this section will satisfy the medical evaluation requirement found in Respirators, chapter 296-842 WAC.

**You must:**

. Provide the relevant medical follow-up specified in Tables 4 and 5 to any employee exposed to benzene during an emergency.

. Make medical evaluations available to current employees who meet the following criteria:

- Potential or actual exposure to benzene at or above the action level (AL) for at least thirty days in any twelve-month period.

- Potential or actual exposure to benzene at or above either permissible exposure limit (PEL) for at least ten days in a twelve-month period.

- Past exposure to concentrations above 10 ppm benzene for at least thirty days in a twelve-month period before November 11, 1988.

- Current or past work as a tire building machine operator using solvents containing more than 0.1% benzene during tire building operations.

**You must:**

. Make medical evaluations available at no cost to employees.

- Pay all costs, including travel costs and wages associated with any time spent outside of the employee's normal work hours;

. Make medical evaluations available at reasonable times and places;

. Make medical evaluations available by completing Steps 1 through 6 of the medical evaluation process for each employee covered.

**Note:** . Employees who wear respirators need to be medically evaluated to make sure the respirator will not harm them, before they are assigned work in areas requiring respirators. Employees who decline to receive medical examination and testing to monitor for health effects caused by benzene are not excluded from receiving a separate medical evaluation for a respirator use.

. If employers discourage participation in medical monitoring for health effects caused by benzene, or in any way interfere with an employee's decision to continue with this program, this interference may represent unlawful discrimination under RCW 49.17.160, Discrimination against employee filing, instituting proceeding, or testifying prohibited--Procedure--Remedy.

**Helpful tool:**

**Declination form for nonemergency related medical**

**evaluations.**

. You may use this optional form to document employee decisions to decline participation in the medical evaluation process for exposure to benzene.

**Medical evaluation process:**

**Step 1:** Identify employees who qualify, as stated above, for medical evaluations.

**Step 2:** Make medical evaluations available for employees identified in Step 1 at the following times:

. Initially, before the employee starts a job or task assignment where benzene exposure will occur.

. Every twelve months from the initial medical evaluation.

. Whenever the employee develops signs or symptoms commonly associated with toxic benzene exposure.

. After benzene exposure from an emergency.

**Step 3:** Select a licensed health care professional (LHCP) who will conduct or supervise medical evaluations and make sure:

. Individuals who conduct pulmonary function tests have completed a training course in spirometry sponsored by an appropriate governmental, academic, or professional institution, if they are not licensed physicians;

**AND**

. Your LHCP uses an accredited laboratory, such as one accredited by a nationally or state-recognized organization, to conduct laboratory tests.

**Step 4:** Make sure the LHCP receives all of the following before the medical evaluation is performed:

. A copy of ((÷  
-)) this chapter.

~~((The following information found in the General occupational health standards, chapter 296-62 WAC:~~

~~Appendix A, the substance safety data sheet benzene, found in WAC 296-62-07525.~~

~~Appendix B, the substance technical guidelines benzene, found in WAC 296-62-07527.~~

~~Appendix C, the medical surveillance guidelines for benzene, found in WAC 296-62-07529.))~~

. A description of the duties of the employee being evaluated and how these duties relate to benzene exposure.

. The anticipated or representative exposure monitoring results for the employee being evaluated.

. A description of the personal protective equipment (PPE) each employee being evaluated uses or will use.

. Information from previous employment-related examinations when this information is not available to the examining LHCP.

. Instructions that the written opinions the LHCP provides, be **limited to** the following information:

- Specific records, findings, or diagnosis relevant to the employee's ability to work around benzene.

- The occupationally relevant results from examinations and tests.

- A statement about whether or not medical conditions were found that would increase the employee's risk for impairment from exposure to benzene.

- Any recommended limitations for benzene exposure.

- Whether or not the employee can use respirators and any recommended limitations for respirator or other PPE use.

- A statement that the employee has been informed of medical results and medical conditions caused by benzene exposure requiring further explanation or treatment.

**Step 5:** Provide the medical evaluation to the employee. Make sure it includes the content listed in Table 4, Content of medical evaluations, and Table 5, Medical follow-up requirements.

**Step 6:** Obtain the LHCP's written opinion for each employee's medical evaluation and give a copy to the employee within fifteen days of the evaluation date.

Make sure the written opinion is limited to the information specified for written opinions in Step 4.

**Note:** If the written opinion contains specific findings or diagnoses unrelated to occupational exposure, send it back and obtain a revised version without the additional information.

**IMPORTANT:** These tables apply when conducting medical evaluations, including medical follow-up for employees exposed to benzene during emergencies.

**Table 4**  
**Content of Medical Evaluations**

<b>When conducting</b>	<b>Include</b>
An initial evaluation	<p>A detailed history including:</p> <ul style="list-style-type: none"><li>- Past work exposure to benzene or other hematological toxins;</li><li>- Exposure to marrow toxins outside of current employment;</li><li>- Exposure to ionizing radiation;</li><li>- Family history of blood dyscrasias including hematological neoplasms;</li><li>- History of blood dyscrasias including genetic hemoglobin abnormalities, bleeding abnormalities, and abnormal function of formed blood elements;</li><li>- History of renal or liver dysfunction;</li><li>- History of medications routinely taken.</li></ul>

	<p>A complete physical examination:</p> <ul style="list-style-type: none"> <li>- Include a pulmonary function test and specific evaluation of the cardiopulmonary system <b>if</b> the employee is required to use a respirator for at least thirty days a year.</li> </ul> <p>A complete blood count including a:</p> <ul style="list-style-type: none"> <li>- Leukocyte count with differential;</li> <li>- Quantitative thrombocyte count;</li> <li>- Hematocrit;</li> <li>- Hemoglobin;</li> <li>- Erythrocyte count and indices (MCV, MCH, MCHC).</li> </ul> <p>Additional tests the examining LHCP determines are necessary based on alterations in the components of the blood or other signs that may be related to benzene exposure.</p> <p><b>Medical follow-up as required in Table 5.</b></p>
Annual evaluations	<p>An updated medical history covering:</p> <ul style="list-style-type: none"> <li>- Any new exposure to potential marrow toxins;</li> <li>- Changes in medication use;</li> <li>- Any physical signs associated with blood disorders.</li> </ul> <p>A complete blood count including a:</p> <ul style="list-style-type: none"> <li>- Leukocyte count with differential;</li> <li>- Quantitative thrombocyte count;</li> <li>- Hematocrit;</li> <li>- Hemoglobin;</li> <li>- Erythrocyte count and indices (MCV, MCH, MCHC).</li> </ul>

	<p>Additional tests that the examining LHCP determines necessary, based on alterations in the components of the blood or other signs that may be related to benzene exposure.</p> <p>A pulmonary function test and specific evaluation of the cardiopulmonary system every three years if the employee is required to use a respirator for at least thirty days a year.</p> <p><b>Medical follow-up as required in Table 5.</b></p>
Evaluations triggered by employee signs and symptoms commonly associated with the toxic effects of benzene exposure	An additional medical examination that addresses elements the examining LHCP considers appropriate.
Evaluations triggered by employee exposure during an emergency	<p>A urinary phenol test performed on the exposed employee's urine sample within seventy-two hours of sample collection.</p> <ul style="list-style-type: none"> <li>- The urine sample must be collected at the end of the work shift associated with the emergency;</li> <li>- The urine specific gravity must be corrected to 1.024.</li> </ul> <p><b>Medical follow-up as required in Table 5.</b></p> <p><b>Reference:</b></p> <p>Employees who are not covered by medical evaluation requirements in this chapter may be covered by medical evaluation requirements in other chapters such as Emergency response, chapter 296-824 WAC.</p>

**Table 5  
Medical Follow-up Requirements**

<b>If</b>	<b>Then</b>
The <b>complete blood count test</b> result is normal.	No further evaluation is required.
The <b>complete blood count test</b> shows any of the following abnormal conditions:	Repeat the complete blood count within two weeks:

<ul style="list-style-type: none"> <li>- A leukocyte count less than 4,000 per mm<sup>3</sup> or an abnormal differential count;</li>   <li style="text-align: center;"><b>OR</b></li>   <li>- A thrombocyte (platelet) count that is either: More than 20% below the employee's most recent values;</li>   <li style="text-align: center;"><b>OR</b></li>   <li>Outside the normal limit (95% C.I.) according to the laboratory;</li>   <li style="text-align: center;"><b>OR</b></li>   <li>- The hematocrit or hemoglobin level is either of the following, and can not be explained by other medical reasons: Below the normal limit (outside the 95% C.I.), as determined by the laboratory for the particular geographical area;</li>   <li style="text-align: center;"><b>OR</b></li>   <li>Persistently decreasing compared to the employee's preexposure levels.</li> </ul>	<ul style="list-style-type: none"> <li>- If the abnormal condition persists, refer the employee to a hematologist or an internist for follow-up medical examination and evaluation, unless the LHCP has good reason to believe it is unnecessary;</li>   <li>- The hematologist or internist will determine what follow-up tests are necessary;</li>   <li style="text-align: center;"><b>AND</b></li>   <li>Follow the requirements found in Medical removal, WAC 296-849-12050.</li> </ul>
<p>Results from the <b>urinary phenol test</b> conducted during an emergency evaluation show phenol levels less than 75 mg/L.</p>	<p>No further evaluation is required.</p>

<p>Results from the <b>urinary phenol test</b> conducted during an emergency evaluation show phenol levels equal or more than 75 mg/L.</p>	<p>Provide a complete blood count monthly for three months. Include a:</p> <ul style="list-style-type: none"> <li>- Leukocyte count with differential;</li> <li>- Thrombocyte count;</li> <li>- Erythrocyte count;</li> </ul> <p><b>AND</b></p> <p>If any of the abnormal conditions previously listed in this table for complete blood count results are found:</p> <ul style="list-style-type: none"> <li>- Provide the employee with periodic examinations, if directed by the LHCP;</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>- <b>Refer the employee</b> to a hematologist or an internist for follow-up medical examination and evaluation unless the LHCP has good reason to believe a referral is unnecessary;</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>- Follow the requirements found in Medical removal, WAC 296-849-12050;</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>- The hematologist or internist will determine what follow-up tests are necessary.</li> </ul>
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NEW SECTION

**WAC 296-849-500 Essential information.**

**Your responsibility:**

To make sure you meet the information requirements for employees and licensed health care professionals (LHCPs) as

specified in this chapter.

NEW SECTION

**WAC 296-849-50010 Health information about benzene.**

. Include an explanation of the contents of this section to employees as required in Training, WAC 296-849-11050.

. Provide a copy of this section to the licensed health care professional (LHCP) as required in Step 4 of the medical evaluation process found in Medical evaluations, WAC 296-849-12030.

**Table 7  
General Health Information About Benzene**

<b>What is benzene?</b>
Benzene is a clear, colorless liquid with a pleasant, sweet odor. It evaporates into air very quickly. The odor of benzene does not provide adequate warning of its hazard. In this chapter, "benzene " means: <ul style="list-style-type: none"><li>- Liquid benzene, benzene vapor, and benzene in liquid mixtures and the vapor released by these liquids. The CAS Registry Number that identifies benzene is 71-43-2.</li></ul> Synonyms for benzene include: Benzol, benzole, coal naphtha, cyclohexatriene, phenyl hydride, pyrobenzol. Benzin, petroleum benzin, and benzine are chemicals that do <b>not</b> contain benzene.
<b>How am I exposed to benzene?</b>
Benzene exposure occurs when you: <ul style="list-style-type: none"><li>- Breath in (<b>inhale</b>) vapor or liquid particles (from actions such as spraying or splashing) containing benzene;</li><li>- Have skin or eye contact with liquid or vapor containing benzene. Benzene is absorbed through the skin. Absorption occurs more rapidly with abraded skin or when benzene is present in solvents (as an ingredient or contaminant) which are readily absorbed;</li><li>- Swallow (<b>ingest</b>) benzene.</li></ul>
<b>What happens after I'm exposed to benzene?</b>
Some benzene that enters your body will be absorbed into the bloodstream. Once in the bloodstream, benzene travels throughout your body and can be temporarily stored in the bone marrow and fat.

Benzene is converted to products, called metabolites, in the liver and bone marrow. Some of the harmful effects of benzene exposure are caused by these metabolites. Most of the metabolites of benzene leave the body in the urine within 48 hours after exposure.

**Why is medical monitoring necessary?**

Medical monitoring is necessary to detect changes in your body's blood-forming system, including the bone marrow. These changes can occur due to repeated or prolonged, unprotected exposure to benzene, even at relatively low concentrations. Such changes can lead to various blood disorders, ranging from anemia to **leukemia**, an irreversible, fatal disease. Many of these disorders may occur without symptoms.

Benzene is classified as a confirmed **human carcinogen** (Group 1) by the International Agency for Research on Cancer (IARC).

To learn more about the medical monitoring process, see Medical evaluation, WAC 296-849-12030.

**What health effects are linked to benzene exposure?**

Unprotected exposure to benzene is associated with various health effects including symptoms and diseases associated with either short-term (**acute**) exposure or long-term exposure (**chronic**).

**Acute effects from inhaling high vapor concentrations:**

An **initial** stimulatory effect on the central nervous system (brain and spinal cord) can occur, characterized by exhilaration, nervous excitation (irritability), and/or giddiness. This may be followed by a period of depression, drowsiness, or fatigue.

Headache, dizziness, nausea, or a feeling of intoxication may develop.

A sensation of tightness in the chest may occur, accompanied by breathlessness. Ultimately the victim may lose consciousness.

In severe inhalation cases, tremors, convulsions, and death may follow due to respiratory paralysis or circulatory collapse in a few minutes to several hours.

**Acute effects from inhaling liquid benzene:**

Aspiration of small amounts of liquid benzene immediately causes pulmonary edema (excessive accumulation of fluid in lung tissues) and hemorrhage of pulmonary tissue.

**Skin contact:**

Direct contact may cause redness (erythema).

Benzene has a defatting action on skin. Repeated or prolonged contact may result in any of the following:

- Primary irritation;
- Dry skin;
- Scaling dermatitis (inflammation);

- Development of secondary skin infections.

**Effects on the eyes and mucous membranes:**

Localized effects from vapor or liquid contact on the eye are slight. High concentrations of benzene are irritating to eyes (causing a stinging sensation) and mucous membranes of the nose and respiratory tract.

**Effects due to prolonged exposure:**

The blood forming (hematopoietic) system is the main target for benzene's toxic effects. These effects can vary from anemia to **leukemia**, an irreversible, fatal disease. Many of the toxic effects may occur without symptoms. Most importantly, prolonged exposure to **small** quantities of benzene vapor is damaging to the blood forming system. This damage has occurred at concentrations of benzene that may not cause irritation of mucous membranes or unpleasant sensory effects.

**Early signs and symptoms** are varied and often not readily noticed and nonspecific. These include:

- Subjective complaints of headache, dizziness, and loss of appetite may precede or follow clinical signs;
- Rapid pulse and low blood pressure, in addition to a physical appearance of anemia, may accompany a subjective complaint of shortness of breath and excessive tiredness.

**Other symptoms may occur as the condition progresses:**

- Bleeding from the nose, gums, or mucous membranes;
- AND
- Development of purpuric spots (small bruises).

NEW SECTION

**WAC 296-849-50020 Medical guidelines for benzene.**

. Include an explanation of the contents of this section to employees as required in Training, WAC 296-849-11050.

. Provide a copy of this section to the licensed health care professional (LHCP) as required in Step 4 of the medical evaluation process found in Medical evaluations, WAC 296-849-12030.

**Table 8  
Medical Guidelines For Evaluating Employees Exposed  
to Benzene**

**Part 1: Becoming familiar with medical requirements in this chapter**

In addition to requiring employers to train employees and protect them from exposure to benzene, this chapter (the Benzene rule) requires employers to monitor their employees' health with assistance from licensed health care professionals (LHCPs).

- . For employees who will use respirators, the LHCP will also need to provide the employer with a written medical opinion clearing the employee for workplace respirator use.

These guidelines were designed to support an informed partnership between the LHCP and the employer when monitoring the health of employees exposed to benzene. The employer initiates this partnership by providing the LHCP with a copy of the chapter and other supporting information about the employee and job conditions. The LHCP can then become familiar with the medical monitoring requirements found in WAC 296-849-12030 through 296-849-12080, which address:

- . Frequency and content for routine (initial and periodic) medical examinations and consultations;
- . Emergency and other unplanned medical follow-up;
  
- . Medical opinions;
  
- . Employee medical removal;
  
- . Medical records retention and content.

**Part 2: Benzene toxicology**

Benzene is primarily an inhalation hazard. Systematic absorption may cause depression of the hematopoietic system, pancytopenia, aplastic anemia, and leukemia. Clinical evidence of leukopenia, anemia, and thrombocytopenia, singly or in combination, has been frequently reported among the first signs.

**Health information about benzene, WAC 296-848-50010**, provides **basic information** about the health effects and symptoms associated with benzene exposure.

**Reference:**

- . Other sources for toxicology information include:
  - ToxFAQs™ and the Toxicological Profile for Benzene. This free document is available from the Agency for Toxic Substances and Disease Registry (ATSDR) and can be obtained by:
    - . Visiting  
<http://www.atsdr.cdc.gov/toxprofiles>
    - OR
    - . Calling 1-888-422-8737
  - A variety of technical resources on benzene from the National Institutes for Occupational Safety and Health (NIOSH) by visiting <http://www.cdc.niosh/topics/chemicals.html>

**Part 3: Treatment of acute toxic effects**

When providing assistance to someone contaminated with benzene, make sure **you** are adequately protected and do not risk being overcome by benzene vapor. Remove the patient from exposure immediately.

Give oxygen or artificial resuscitation, if indicated.

Flush eyes, wash skin if contaminated and remove all contaminated clothing.

Recovery from mild exposures is usually rapid and complete. Symptoms of intoxication may persist following severe exposures.

**Part 4: Preventive considerations**

The principal effects of benzene exposure which form the basis for the requirements in this chapter are pathological changes in the hematopoietic system, reflected by changes in the peripheral blood and manifesting clinically as pancytopenia, aplastic anemia, and leukemia.

Consequently, the medical monitoring program is designed to observe, on a regular basis, blood indices for early signs of these effects, and although early signs of leukemia are not usually available, emerging diagnostic technology and innovative regimes make consistent surveillance for leukemia, as well as other hematopoietic effects, essential.

Symptoms and signs of benzene toxicity can be nonspecific. Only a detailed history and appropriate investigative procedure will enable a physician to rule out or confirm conditions that place the employee at increased risk.

Bone marrow may appear normal, aplastic, or hyperplastic, and may not, in all situations, correlate with peripheral blood forming tissues. Because of variations in the susceptibility to benzene morbidity, there is no "typical" blood picture.

The onset of effects of prolonged benzene exposure may be delayed for many months or years after the actual exposure has ceased and identification or correlation with benzene exposure must be sought out in the occupational history.

There are special provisions for medical tests in the event of hematologic abnormalities or for emergency situations.

- This chapter specifies that blood abnormalities that persist must be referred "unless the physician has good reason to believe such referral is unnecessary." Examples of conditions that could make a referral unnecessary despite abnormal blood limits are iron or folate deficiency, menorrhagia, or blood loss due to some unrelated medical abnormality.
- Blood values that require referral to a hematologist or internist are noted under Part 5: Hematology guidelines.

**Part 5: Hematology guidelines**

The following guidelines are established to assist the examining LHCP with regard to which laboratory tests are necessary and when to refer an employee to the specialist. A minimum battery of tests is to be performed using strictly standardized methods.

#### **Basic tests**

- . The following must be determined by an accredited laboratory:
  - Red and white cell counts;
  - Platelet counts;
  - White blood cell differential;
  - Hematocrit;
  - Red cell indices.
- . The normal ranges for the red cell and white cell counts are influenced by altitude, race, and sex, and therefore should be determined by the accredited laboratory in the specific area where the tests are performed.
- . Either a decline from an absolute normal or an individual's baseline to a subnormal value or a rise to a supra-normal value, are indicative of potential toxicity, particularly if all blood parameters decline.
  - The normal total white blood count is approximately 7,200/mm<sup>3</sup> plus or minus 3,000;
  - For cigarette smokers the white count may be higher and the upper range may be 2,000 cells higher than normal for the laboratory;
  - In addition, infection, allergies and some drugs may raise the white cell count;
  - The normal platelet count is approximately 250,000 with a range of 140,000 to 400,000. Counts outside this range should be regarded as possible evidence of benzene toxicity.
- . Certain abnormalities found through routine screening are of greater significance in the benzene-exposed worker and **require prompt consultation with a specialist**, namely:
  - Thrombocytopenia;
  - A trend of decreasing white cell, red cell, or platelet indices in an individual over time is more worrisome than an isolated abnormal finding at one test time. The importance of trend highlights the need to compare an individual's test results to baseline and/or previous periodic tests;

- A constellation or pattern of abnormalities in the different blood indices is of more significance than a single abnormality. A low white count not associated with any abnormalities in other cell indices may be a normal statistical variation, whereas if the low white count is accompanied by decreases in the platelet and/or red cell indices, such a pattern is more likely to be associated with benzene toxicity and merits thorough investigation;
  - . Anemia, leukopenia, macrocytosis or an abnormal differential white blood cell count should alert the physician to further investigate and/or refer the patient if repeat tests confirm the abnormalities. If routine screening detects an abnormality, follow-up tests which may be helpful in establishing the etiology of the abnormality are the peripheral blood smear and the reticulocyte count;
  - . The extreme range of normal for reticulocytes is 0.4 to 2.5 percent of the red cells, the usual range being 0.5 to 1.2 percent of the red cells, but the typical value is in the range of 0.8 to 1.0 percent;
  - . A decline in reticulocytes to levels of less than 0.4 percent is to be regarded as possible evidence (unless another specific cause is found) of benzene toxicity requiring accelerated surveillance. An increase in reticulocyte levels to about 2.5 percent may also be consistent with (but is not as characteristic of) benzene toxicity.

#### **Additional tests**

##### 1. Peripheral blood smears:

- . Collecting the sample: As with reticulocyte count, the smear should be with fresh uncoagulated blood obtained from a needle tip following venipuncture or from a drop of earlobe blood (capillary blood). If necessary, the smear may, under certain limited conditions, be made from a blood sample anticoagulated with EDTA (but never with oxalate or heparin).
- . Prepping the smear: When the smear is to be prepared from a specimen of venous blood which has been collected by a commercial Vacutainer type tube containing neutral EDTA, the smear should be made as soon as possible after the venesection. A delay of up to twelve hours is permissible between the drawing of the blood specimen into EDTA and the preparation of the smear if the blood is stored at refrigerator (not freezing) temperature.
- . Minimum mandatory observations:
  - The differential white blood cell count;

- Description of abnormalities in the appearance of red cells;
- Description of any abnormalities in the platelets;
- A careful search must be made throughout of every blood smear for immature white cells such as band forms (in more than normal proportion, i.e., over 10 percent of the total differential count), any number of metamyelocytes, myelocytes, or myeloblasts. Any nucleate or multinucleated red blood cells should be reported. Large "giant" platelets or fragments of megakaryocytes must be recognized;

- . An increase in the proportion of band forms among the neutrophilic granulocytes is an abnormality deserving special mention, for it may represent a change which should be considered as an early warning of benzene toxicity in the absence of other causative factors (most commonly infection). Likewise, the appearance of metamyelocytes, in the absence of another probable cause, is to be considered a possible indication of benzene-induced toxicity;

- . An upward trend in the number of basophils, which normally do not exceed about 2.0 percent of the total white cells, is to be regarded as possible evidence of benzene toxicity. A rise in the eosinophil count is less specific but also may be suspicious of toxicity if it rises above 6.0 percent of the total white count;

- . The normal range of monocytes is from 2.0 to 8.0 percent of the total white count with an average of about 5.0 percent. About 20 percent of individuals reported to have mild but persisting abnormalities caused by exposure to benzene show a persistent monocytosis. The findings of a monocyte count which persists at more than 10 to 12 percent of the normal white cell count (when the total count is normal) or persistence of an absolute monocyte count in excess of  $800/\text{mm}^3$  should be regarded as a possible sign of benzene-induced toxicity;

A less frequent but more serious indication of benzene toxicity is the finding in the peripheral blood of the so-called "pseudo" (or acquired) Pelger-Huet anomaly. In this anomaly many, or sometimes the majority, of the neutrophilic granulocytes possess two round nuclear segments - less often one or three round segments - rather than three normally elongated segments. When this anomaly is not hereditary, it is often but not invariably predictive of subsequent leukemia. However, only about two percent of patients who ultimately develop acute myelogenous leukemia show the acquired Pelger-Huet anomaly. Other tests that can be administered to investigate blood abnormalities are discussed below; however, such procedures should be undertaken by the hematologist.

## 2. Sucrose water test and Ham test:

An uncommon sign, which cannot be detected from the smear, but can be elicited by a "sucrose water test" of peripheral blood, is transient paroxysmal nocturnal hemoglobinuria (PNH), which may first occur insidiously during a period of established aplastic anemia, and may be followed within one to a few years by the appearance of rapidly fatal acute myelogenous leukemia. Clinical detection of PNH, which occurs in only one or two percent of those destined to have acute myelogenous leukemia, may be difficult; if the "sucrose water test" is positive, the somewhat more definitive Ham test, also known as the acid-serum hemolysis test, may provide confirmation.

### **Important clinical findings**

1. Individuals documented to have developed acute myelogenous leukemia years after initial exposure to benzene may have progressed through a preliminary phase of hematologic abnormality. In some instances pancytopenia (i.e., a lowering in the counts of all circulating blood cells of bone marrow origin, but not to the extent implied by the term "aplastic anemia") preceded leukemia for many years.

Depression of a single blood cell type or platelets may represent a harbinger of aplasia or leukemia. The finding of two or more cytopenias, or pancytopenia in a benzene-exposed individual, must be regarded as highly suspicious of more advanced although still reversible, toxicity.

"Pancytopenia" coupled with the appearance of immature cells (myelocytes, myeloblasts, erythroblasts, etc.), with abnormal cells (pseudo Pelger-Huet anomaly, atypical nuclear heterochromatin, etc.), or unexplained elevations of white blood cells must be regarded as evidence of benzene overexposure unless proved otherwise.

Many severely aplastic patients manifested the ominous findings of:

- 5 to 10 % myeloblasts in the marrow;
- Occasional myeloblasts and myelocytes in the blood;
- 20 to 30 monocytes.

It is evident that isolated cytopenias, pancytopenias, and even aplastic anemias induced by benzene may be reversible and complete recovery has been reported on cessation of exposure. However, since any of these abnormalities is serious, the employee must immediately be removed from any possible exposure to benzene vapor.

- Certain tests may substantiate the employee's prospects for progression or regression. One such test would be an examination of the bone marrow, but the decision to perform a bone marrow aspiration or needle biopsy is made by the hematologist.

2. The findings of basophilic stippling in circulating red blood cells (usually found in one to five percent of red cells following marrow injury), and detection in the bone marrow of what are termed "ringed sideroblasts" must be taken seriously, as they have been noted in recent years to be premonitory signs of subsequent leukemia.

3. Recently peroxidase-staining of circulating or marrow neutrophil granulocytes, employing benzidine dihydrochloride, have revealed the disappearance of, or diminution in, peroxidase in a sizable proportion of the granulocytes, and this has been reported as an early sign of leukemia. However, relatively few patients have been studied to date. Granulocyte granules are normally strongly peroxidase positive. A steady decline in leukocyte alkaline phosphatase has also been reported as suggestive of early acute leukemia.

- Peroxidase and alkaline phosphatase staining are usually undertaken when the index of suspicion for leukemia is high.

4. Exposure to benzene may cause an early rise in serum iron, often but not always associated with a fall in the reticulocyte count. Thus, serial measurements of serum iron levels may provide a means of determining whether or not there is a trend representing sustained suppression of erythropoiesis.

5. Measurement of serum iron, determination of peroxidase and of alkaline phosphatase activity in peripheral granulocytes can be performed in most pathology laboratories.