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ASBESTOS

REPROTEXT ® System

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1.0 ADMINISTRATION

1.1 SYNONYMS

AMIANTHUS
AMOSITE (obsolete)
AMPHIBOLE
ASBEST (GERMAN)
ASBESTOS
ASBESTOS DUST
ASBESTOS FIBER
ASBESTOS FIBRE
ASBESTOSE (GERMAN)
ASCARITE
FIBROUS GRUNERITE

1. CONSTITUENTS OF THE GROUP

SERPENTINE ASBESTOS
 CHRYSOTILE (WHITE ASBESTOS)
AMPHIBOLE ASBESTOS
 ACTINOLITE
 AMOSITE (BROWN ASBESTOS)
 ANTHOPHYLLITE
 CROCIDOLITE (BLUE ASBESTOS)
 MYSORITE (BROWN ASBESTOS)
 TREMOLITE

1.2 IDENTIFIERS

1.2.1 CAS REGISTRY NUMBER:

CAS 1332-21-4

CAS 12001-29-5 (Chrysotile; white asbestos)
CAS 13768-00-8 (Actinolite)
CAS 12172-73-5 (Amosite; brown asbestos)
CAS 17068-78-9 (Anthophyllite)
CAS 12001-28-4 (Crocidolite; blue asbestos)
CAS 14567-73-8 (Tremolite)

1.2.2 NIOSH/RTECS NUMBER:

NIOSH/RTECS CI6475000
NIOSH/RTECS CI6478500orGC2625000 (Chrysotile; white asbestos)
NIOSH/RTECS CI6477000orBT6825000 (Amosite; brown asbestos)
NIOSH/RTECS CI6478000 (Anthophyllite)
NIOSH/RTECS CI6479000 (Crocidolite; blue asbestos)
NIOSH/RTECS CI6560000orXX2095000 (Tremolite)

1.2.3 UN/NA NUMBER:

UN 2212/2590 - Asbestos
UN 2590 - Chrysotile (white asbestos)
UN 2212 - Amosite (brown asbestos)
UN 2590 - Anthophyllite
UN 2212 - Crocidolite (blue asbestos)
UN 2590 - Tremolite

1.2.5 DESIGNATIONS:

NCI-C08991

1.2.6 ERG2000 GUIDE NUMBER:

171 - SUBSTANCES (LOW TO MODERATE HAZARD)
(UN/NA 2212; UN/NA 2590)

1.3 FORMULA

UVCB
 $\text{Mg}_6(\text{Si}_4\text{O}_{10})(\text{OH})_8$ (Chrysotile)
 $\text{Ca}_2(\text{Mg}, \text{Fe})_5(\text{Si}_8\text{O}_{22})(\text{OH})_2$ (Actinolite)
 $\text{Fe}_5\text{Mg}_2(\text{Si}_8\text{O}_{22})(\text{OH})_2$ (Amosite)
 $(\text{Mg}, \text{Fe})_7(\text{Si}_8\text{O}_{22})(\text{OH})_2$ (Anthophyllite)
 $\text{Na}_2\text{Fe}_3\text{Fe}_2(\text{Si}_8\text{O}_{22})(\text{OH})_2$ (Crocidolite)
 $\text{Ca}_2\text{Mg}_5(\text{Si}_8\text{O}_{22})(\text{OH})_2$ (Tremolite)

1.4 GENERAL TOXICITY HAZARD RATING

A. 3 ☹

1.5 REPRODUCTIVE HAZARD RATING

A. A- ☹

1.7 COMMENTS

A. Asbestos is a natural mineral fiber occurring in various forms. Some forms are more toxic than others. Asbestos can act as a carrier or "trap" for organic compounds.

2.0 INTRODUCTION

- A. Asbestos represents a group of naturally occurring impure magnesium silicate minerals (Clayton & Clayton, 1993; Lewis, 1997). On a macroscopic scale, asbestos occurs in white, gray, green, and brown fibrous forms (Lewis, 1997).
- B. The main forms are the serpentine subgroup, consisting of chrysotile (white), and a subgroup called amphiboles, which consists of actinolite, amosite (brown), anthophyllite, crocidolite (blue) and tremolite (Clayton & Clayton, 1993). Chrysotile represents 95 percent of natural mineral fiber asbestos used in the US and 99 percent of the world's production (Landrigan et al, 1999; ACGIH, 1991).
- C. Asbestos has been used for thermal insulation and resistance to high temperature or fire, saltwater, or corrosive chemicals (Lewis, 1998). Although the high-level exposures encountered by insulation workers and shipyard workers no longer occur, substantial exposures can occur today among PAINTERS (Selikoff, 1975) and DRYWALL INSTALLERS (Fischbein et al, 1979) who are renovating old buildings, as well as among asbestos-remediation workers.
- D. Commercial applications of asbestos are in the process of being phased out in the US, with the last group scheduled to be banned from distribution by 25 August 1997 (Clayton & Clayton, 1993). Because of widespread asbestos use in Europe, its proven role in human cancer and the inability to control its use, the Collegeum Ramazzini, a consortium of European health professionals, has called for an international ban on asbestos (Collegeum Ramazzini, 1999).

3.0 EFFECTS OF ACUTE EXPOSURE

- A. There is no evidence of any acute systemic effect from exposure to asbestos (Clayton & Clayton, 1993). Nearly all of the toxicologic literature on asbestos is concerned with its activity as a human carcinogen with chronic exposure.
- B. Asbestos is not acutely toxic, except for possible irritation of the eyes, skin, and respiratory tract due to mechanical action of the fibers. Skin irritation with corn formation can result from penetration of the skin by asbestos spicules (HSDB, 2000).
- C. The dose-response relationship for induction cancer from exposure to asbestos is not well understood for low-level exposures. It has been suggested that even a single, high-dose acute exposure might be sufficient to induce cancer (Stich, 1985).
- D. Asbestos fibers can stimulate the production of interleukin (IL)-8 in cultured lung cells. The mechanism of this induction involves redox changes and phosphorylation by means of staurosporine-sensitive and tyrosine kinase(s), activation of transcription factors that bind to the NF-kappaB/NF-IL-6 binding site of the IL-8 promoter, and upregulation of the IL-8 gene (Simeonova & Luster, 1996).
- E. Transforming growth factor (TGF)-alpha was also upregulated in the lungs of rats as a result of a single 5-hour exposure to asbestos. Increases in TGF-alpha mRNA and peptide were seen as early as 24 hours after the acute exposure and persisted for at least 2 weeks. These results support the idea that TGF-alpha is involved in the mechanism of asbestos-induced proliferation of epithelial and mesenchymal cells in the lung (Liu et al, 1996).

4.0 EFFECTS OF CHRONIC EXPOSURE

- A. Occupational exposure to asbestos dust is associated with chronic laryngitis, chronic bronchitis, chronic obstructive pulmonary disease, chronic inflammation of the lungs, pleural effusions, pleural plaques, and cancer (ACGIH, 1991; Harbison, 1998; ILO, 1998). The primary determinant seems to be fiber length (Clayton & Clayton, 1993). Fibers less than 5 micrometers in length are considered not pathogenic (ACGIH, 1991).
 - 1. Among insulation workers, 7 percent developed asbestosis, an interstitial fibrosis caused by inhaling fibers less than about 3 microns in diameter and 200 microns in length. In these same workers, 8 percent developed mesothelioma of the pleura and peritoneum, and 21 percent developed carcinoma of the lung (Stich, 1985).
- B. Asbestosis is pneumoconiosis resulting from asbestos exposure (ILO, 1998). Symptoms of asbestosis include shortness of breath and difficulty breathing, chest tightness, an initially non-productive then productive cough, and cyanosis (ILO, 1998; Zenz, 1994). Fibrosis decreases lung compliance, which increases the energy required to breath; decreased gas diffusion increases breathlessness (ACGIH, 1991).
- C. Signs of asbestosis include granular changes on chest X-ray, restrictive pulmonary function, rales and clubbing of fingers (Hathaway et al, 1991). Parietal pleura can undergo severe thickening, forming pleural hyaline plaques, which can become impregnated with calcium salts and opaque to X-ray even in the absence of asbestosis (ACGIH, 1991). Rheumatoid factor and anti-nuclear antibodies have also been found in patients with asbestosis (Lange, 1980).
- D. The unambiguous diagnosis of asbestosis is sometimes difficult. In one study of 176 exposed persons, nine had clinical signs of asbestosis, but no asbestos bodies were seen in the lung tissues (Gaensler et al, 1991). Diagnosis should be based on a history of known exposure and presence of diffuse interstitial pulmonary fibrosis, but when the exposure is difficult to ascertain, diagnosis must be based on pathological findings (Jones, 1991).
- E. Most of the literature on asbestos is concerned with its ability to cause various forms of cancer (see CARCINOGENIC EFFECTS section below).
 - 1. Mesothelioma is associated with asbestos exposure. The primary symptom is chest pain, then breathlessness, pleuritic pain, cough, weight loss and fatigue. Pleural effusions develop, with pleural thickening and densities seen on chest X-ray (Harbison, 1998).
 - 2. Studies have shown an increased risk of laryngeal cancer after occupational exposure to asbestos (IARC, 1998). Workers exposed to asbestos who develop hoarseness or pain or sore throat should be referred for examination for laryngeal cancer (HSDB, 2001).
- F. Consistent with the previous observation is the finding that humoral immunity was elevated in patients with asbestosis (Lange, 1980), although cellular immunity can be depressed (Deshazo et al, 1982). Cellular immunity is thought to be involved in host defense mechanisms against cancer cells.

5.0 CARCINOGENIC EFFECTS

- A. Asbestos is a known human carcinogen, classified as Group 1 (carcinogenic to humans) by IARC (1998). The ACGIH regards all forms of asbestos as confirmed human carcinogens (Group A1) (ACGIH, 2000).
 - 1. There is considerable literature on the relationship between occupational exposure to asbestos and risk for cancer, including mesothelioma (a cancer of the lining of

the pleural cavity or peritoneum), as well as lung cancer, laryngeal cancer, and gastrointestinal cancer (Dunn, 1989; Talcott Antman, 1988; IARC, 1998; Sittig, 1991).

B. MESOTHELIOMA -

1. Although asbestos was thought to be the only cause of mesothelioma, a recent reclassification of these tumors has concluded that some cases may be spontaneous or related to nonasbestiform agents (Ilgren & Wagner, 1991). The latent period for developing mesothelioma can be as long as 68 years (Mowe et al, 1984).
 2. All forms of asbestos have been linked with cancer in humans, but some forms are more potent than others in inducing cancer (ACGIH, 1991). Crocidolite seems to be the most potent form of asbestos for inducing tumors, followed by amosite, which in turn is more active than chrysotile (Stich, 1985). Ex-workers who had received exposure to crocidolite had increased risk of incidence of lung cancer, with squamous cell carcinoma being greater than adenocarcinoma (Deklerk et al, 1996).
 3. Although chrysotile is 2 to 4 times less active than crocidolite in causing mesothelioma, it is of comparable potency in inducing lung cancer (Stayner et al, 1997; Landrigan et al, 1999).
 4. A critical analysis of published studies has concluded that chrysotile is similar in potency to amphibole forms of asbestos for inducing malignant pleural mesothelioma (Smith Wright, 1998). Thus the "amphibole hypothesis", postulating the role of confounding exposure to amphiboles in chrysotile-linked cancers, has less experimental support. Some authors feel that chrysotile should be treated as being "virtually" as carcinogenic as the amphibole forms (Stayner et al, 1996).
 5. An occupational cohort exposed exclusively to amosite had duration-related excess deaths from respiratory cancer and pleural and peritoneal mesothelioma; significant excess deaths were seen even with less than 6 months of employment. This study confirms that amosite is a hazard for these forms of cancer (Levin et al, 1998).
 6. The rate of mesothelioma continues to rise, with estimated lifetime risks of 1.3 percent for persons born in the UK between 1893 and 1948, 1.0 percent in those born between 1943 and 1948, and 0.6 percent for those born between 1948 and 1953. According to one model, deaths from mesothelioma will peak in approximately the year 2020, and may account for 1 percent of all deaths for men born in the 1940s (Peto et al, 1995).
 7. Mesothelioma is currently occurring in epidemic proportions in Europe. One study estimates the death rate will double by 2018, with approximately 1 in 150 men born between 1945 and 1950 dying from it (Peto et al, 1999).
- C. With respect to occupations involving exposure to asbestos, British construction workers had the highest death rates from peritoneal cancer (PMR=990), and a relatively low rate (PMR=160) for pleural cancer. Other occupations had higher risks of death from pleural tumors, and no excess of peritoneal cancer. As a rule, the mortality risk for asbestosis followed that of peritoneal, rather than pleural, cancer (Coggon et al, 1995).
- D. Very small exposures to asbestos may be sufficient to increase the risk for cancer. Even a single, high-level acute exposure might be enough to increase the risk. IT IS NOT KNOWN IF THERE IS ANY SAFE DOSE FOR EXPOSURE TO ASBESTOS (Stich, 1985), although one survey suggests a threshold of 25-100 fibers/cc years for lung cancer (Browne, 1986).
1. A literature review concluded that a threshold for asbestos-induced mesothelioma may exist, based on a background of "spontaneous" and non-asbestos related cases

- (Ilgren Browne, 1991). Another reviewer has stated that the risk of LUNG cancer is higher in persons with asbestosis than in those in whom it is absent (Craighead, 1992).
2. There was no evidence for a threshold for induction of either lung cancer or asbestosis in a cohort mortality study of South Carolina textile workers. The excess lifetime risk for 45 years of exposure at the current OSHA standard was 5/1000 for lung cancer, and 2/1000 for asbestosis, in this cohort (Stayner et al, 1997). A literature review also found no evidence for a threshold for asbestos-induced mesothelioma (Hillerdal, 1999).
- E. In one ongoing study of persons occupationally exposed to asbestos in a nitric acid plant, cancers that have increased in incidence over time since the first exposure to asbestos are those of the lung, pleura, stomach, unknown origin, and total cancers (Hilt et al, 1991). This same group has been studied for more than 60 years, and will continue to be followed indefinitely.
- F. Danish men employed in the asbestos cement industry have been reported to be at increased risk for lung cancer. In one study, all Danish men with lung cancer from 1943 to 1984 were included, and cancers were stratified according to type. An increase in lung cancer incidence was confirmed, with the highest relative risk being for adenocarcinoma (3.31-fold). Risk was correlated with duration of employment and time since first employment (Raffn et al, 1993).
- G. In studies of Finnish cancer patients, lung fiber concentrations of greater than one million per gram of dry tissue were associated with increased risk for mesothelioma (Tuomi et al, 1991).
- H. Non-occupational exposure to asbestos has been associated with diffuse malignant pleural mesothelioma, in persons living in an area of high environmental asbestos levels. In this study, the latent time for development of mesothelioma was longer than with occupational exposure, and independent of duration of exposure (Metintas et al, 1999).
1. A few cases of mesothelioma have been reported in persons who washed asbestos-contaminated clothes. In one study, 13 of 262 total cases of pleural mesothelioma were thought to be due to such exposures (Dodoli et al, 1992). In another study, five fatal cases of mesothelioma were seen in wives of asbestos-exposed workers who cleaned their husbands contaminated clothes and shoes (Schneider et al, 1996).
- I. There is a well-known interaction between CIGARETTE SMOKING and exposure to asbestos in increasing the risk for lung cancer. There has been some controversy as to the quantitative effects between asbestos and tobacco smoke in the occurrence of lung cancer. It was hypothesized that embedded asbestos fibers may provide an area for the deposition of carcinogens from tobacco smoke (Clayton & Clayton, 1993).
1. More recent epidemiologic evidence, however, has suggested that regardless of smoking history, workers heavily exposed to asbestos may be at increased risk to develop lung cancer (Clayton & Clayton, 1993). Although asbestosis and lung cancer are related, the risk for mesothelioma seems to be separate and not related to smoking (EOSH, 1982; Berry et al, 1985).
- J. A meta-analysis of 69 occupational cohorts has concluded that asbestos exposure is linked with mesothelioma deaths in a dose-related manner, and a suggested association with laryngeal carcinoma (Goodman et al, 1999).
- K. Norwegian lighthouse keepers who drank cistern water contaminated with asbestos from runoff of asbestos-cement roof tiles for two decades had an excess risk for developing stomach cancer, but not malignant mesothelioma (Andersen et al, 1993). There is also a rare association of asbestos exposure and testicular cancer (Fligiel & Kaneko, 1976).

Excess ovarian cancer was found among female asbestos workers (HSDB, 2001).

- L. A meta-analysis of 30 published studies on asbestos and colorectal cancer found an overall relative risk of 0.99; this result does not support the idea that asbestos is related to colorectal cancer (Weiss, 1995).
- M. In a large mortality study on 4,943,566 persons, mortality ratios were slightly increased for esophageal, gastric, and colorectal cancer for occupations with asbestos exposure (Kang et al, 1997).
- N. A slight increase in standard incidence ratio for colorectal cancer was found in Danish asbestos cement workers (SIR 1.23, 95 percent CI 1.01 - 1.48). The SIR increased to 1.47 with a latency period of 15 years (Raffn et al, 1996).
- O. Among men newly diagnosed with adenocarcinoma of the lung, there was an increased prevalence of k-ras mutations among those with a history of occupational exposure to asbestos, compared with patients without asbestos exposure. The presence of k-ras mutation and asbestos exposure was independent of asbestosis, as determined by chest radiographs (Nelson et al, 1999).
- P. In a histological study on 414 consecutive cases of lung carcinoma, approximately 60 percent of the male cases could be attributed to asbestos (Bianchi et al, 1999).
- Q. Occupational exposure to asbestos was not a factor in kidney cancer, in a meta-analysis of 37 cohorts (Sali & Boffetta, 2000).
- R. Asbestos can be transferred to the ovary. Asbestos fibers have been found at significant levels in ovarian tissue of 13 women with household exposure. Counts were as high as >1 million/g wet weight in exposed women. These findings are consistent with reports linking asbestos with ovarian cancer (Heller et al, 1996). Asbestos was one of the risk factors found for incidence of ovarian cancer in a study on 892,591 Finnish women (Vasama-Neuvonen et al, 1999).
- S. Asbestos fibers have been found in lymph nodes of 13 out of 21 non-occupationally exposed individuals, at appreciably higher levels than in the lung. The authors suggest that lymph nodes may be a better indicator of lifetime exposure to asbestos than lung tissue (Dodson et al, 2000).

6.0 GENETIC EFFECTS

- A. Asbestos has been widely studied for possible genetic effects in a variety of systems. Its genetic effects have been reviewed (Daniel, 1983).
- B. Asbestos can damage DNA, and this damage can be enhanced several-fold in the presence of peroxides (Mahmood et al, 1993). The extent of damage in the presence of peroxides correlated with the carcinogenic potential of different forms of asbestos (Mahmood et al, 1994).
 - 1. Crocidolite fibers induced oxidative damage in DNA, in the form of 8-hydroxydeoxyguanosine, in a dose-dependent manner in cultured human-hamster hybrid cells, via reactive oxygen species (Xu et al, 1999).
- C. Ferrous iron complexed with asbestos can be oxidized to the ferric state by peroxide, generating free radicals, and the amount of DNA damage induced by asbestos is proportional to the amount of surface-complexed iron (Ghio et al, 1994). The iron in ferruginous bodies can also induce DNA damage, if it is in the reduced (ferrous) form (Lund et al, 1994).
 - 1. A two- to four-fold increase in double-stranded DNA breaks was seen in lymphocytes of persons occupationally exposed to asbestos, compared with those of non-exposed persons (Marczynski et al, 1994).

- D. In general, asbestos has not been mutagenic in bacteria, and is not clearly genotoxic in mammalian cells, except for some rodent cells in vitro (Daniel, 1983; Chamberlain & Tarmy, 1977). Amosite, crocidolite, and chrysotile were not mutagenic in the HGPRTase assay in rat cells (Reiss et al, 1982). Asbestos has been reported to be mutagenic in *E. coli* (Cleveland, 1984).
1. Recent developments in molecular genetics have enabled mutations induced by asbestos to be detected in mammalian cells. Asbestos can induce multi-locus deletions in human-hamster hybrid cells; these mutations are prevented by catalase or superoxide dismutase, anti-oxidant enzymes (Hei et al, 1995). Crocidolite, but not chrysotile, induced loss of heterozygosity in the HLA-A locus in human peripheral lymphocytes (Both et al, 1994).
- E. Mixed results have been obtained in cytogenetics assays.
1. Asbestos induced chromosomal mutations, aneuploidy, and chromosomal aberrations in various cultured mammalian cells; some of these alterations seemed non-random (Harbison, 1998).
 2. Asbestos did not cause sister chromatid exchanges in rat cells in vitro (Kaplan et al, 1980). Crocidolite did induce more sister chromatid exchanges than amosite in hamster cells (Livingston et al, 1982), but crocidolite did not induce sister chromatid exchanges or chromosome aberrations in chinese hamster V-79 cells (Price-Jones et al, 1980).
 3. Chrysotile was reported to increase sister chromatid exchanges in hamster cells, but did not have a dose-response relationship (Aravinda Babu et al, 1981). Asbestos induced SCEs in hamster cells, but not in human cells (Sincock et al, 1982).
 4. Crocidolite was positive for chromosome aberrations and mutations in Chinese hamster lung cells (Huang et al, 1978). Amosite and chrysotile were twice as mutagenic as crocidolite, but all were weak mutagens (Huang, 1979). Asbestos did not induce chromosome aberrations in cultured Chinese hamster cells (Farulla et al, 1978).
 5. Chrysotile and zeolite particles given intraperitoneally can induce chromosome aberrations in mice (Durnev et al, 1993). Chrysotile given orally to monkeys did not induce chromosome aberrations, but did induce such aberrations in hamster cells in vitro (Kaplan et al, 1980).
 6. Chrysotile induced chromosome aberrations in Chinese hamster cells (Aravinda Babu et al, 1980; Sincock & Seabright, 1975; Oshimura et al, 1984). Chinese chrysotile induced sister chromatid exchanges in human cells (Hong & He, 1985). Amosite, crocidolite, and chrysotile all induced micronuclei in cultured Syrian hamster embryo cells (Dopp et al, 1995).
 7. Short amosite fibers did not induce chromosome aberrations in cultured Chinese hamster cells, whereas longer fibers did (Donaldson & Golyasny, 1995).
 8. Sister chromatid exchanges were studied in the white blood cells of asbestos workers. There was a small increase associated with exposure to asbestos and a further increase with smoking (Rom et al, 1983). Increases in sister chromatid exchanges and chromosome aberrations were seen in cultured lymphocytes of asbestos cement workers (Fatma et al, 1991).
 9. Asbestos produced aneuploidy in human pleural mesothelial cells (Lechner et al, 1985) and in hamster cells (Hesterberg Barrett, 1985). It induced aneuploidy of sex chromosomes in *Drosophila* oocytes (Osgood & Sterling, 1991).
 10. Asbestos has been reported to induce chromosome aberrations in human cells (Valerio et al, 1983; Srb et al, 1984; Tokiwa et al, 1983; Valerio et al, 1980).

Previous in vivo exposure to asbestos has been associated with increases in stable chromosome aberrations in human lymphocytes, as visualized by fluorescent in situ hybridization with whole-chromosome probes ("chromosome painting") (Ramsey et al, 1995).

- F. Cell transformation by asbestos depends on fiber length; long thin fibers are more effective than short thick fibers (Harbison, 1998).
- G. Asbestos (as chrysotile or crocidolite) inhibited proliferation of human bronchial epithelial cells in culture; chrysotile was up to 300 times more potent. Chrysotile, but not crocidolite, induced micronuclei (a measure of chromosome breaks) in these cells. Structural aberrations were increased only after the longest incubation time (24 hours) (Kodama et al, 1993).
- H. Induction of mutations in oncogenes is thought to be part of the mechanism of carcinogenesis for some cancers.
 - 1. Lung tumor specimens from lung cancer patients had a high frequency of a specific kind of ras oncogene mutation: 57 percent of the adenocarcinoma samples had K-ras mutations. N-ras and H-ras mutations were not present. The K-ras mutations were increased 4.9-fold in samples from heavy smokers, and 2.2-fold samples from persons with occupational asbestos exposure (Husgafvel-Pursiainen et al, 1993).
 - 2. Although the latter increase was not statistically significant, it does indicate that asbestos may be involved in inducing K-ras mutations (Husgafvel-Pursiainen et al, 1993), and may favor the growth of cells containing the K-ras mutation (Vainio et al, 1993).
 - 3. Asbestos can also induce expression of c-fos and c-jun oncogenes in rat pleural mesothelial cells; crocidolite was more active than chrysotile for this effect, as it is for induction of mesothelioma (Heintz et al, 1993).
 - 4. Asbestos also induces c-jun mRNA in hamster tracheal epithelial cells, progenitors for bronchogenic carcinoma; this induction can respond to either asbestos or hydrogen peroxide, and confers the ability of cells to grow in soft agar (an endpoint of in vitro malignant transformation) (Timblin et al, 1995).
- I. There is a possibility that asbestos may carry mutagens into the cell because some substances can be strongly adsorbed to the fibers (Dunn, 1989). The possible genetic effects of asbestos in humans in vivo are not well understood.

7.0 REPRODUCTIVE EFFECTS

- A. Several studies have reported reproductive effects from occupational asbestos exposure. Among Russian railroad builders, 42 percent had abnormalities of the sex organs, but these workers were exposed to several other toxic substances in addition to asbestos, such as carbon monoxide, nitrogen dioxide, acrolein, and formaldehyde (Kogan et al, 1977).
- B. Russian workers exposed to asbestos cement dust had female reproductive system disorders (Kosolapova & Ulenkova, 1984). Another Russian study reported effects of asbestos on the genitals (Lebedeva, 1971).
- C. Asbestos is believed to cross the mammalian placental barrier (HSDB, 2001; Lemesch, 1980).
 - 1. Uncoated chrysotile asbestos fibers were found in lung, liver, and/or placenta digests of 5 stillborn infants, indicating transplacental transfer (Haque et al, 1992). Asbestos can cross the placenta to the fetuses in rats following maternal

intravenous injection (Cunningham & Ponternet, 1974).

2. Asbestos fibers were found in tissues of stillborn infants at higher frequencies and concentrations than for normal deliveries. Maximum concentrations were seen in lungs, then in liver and placenta. Although placentas from stillbirths averaged 164,500 fibers/g (n = 4), no asbestos fibers were seen in the placentas from normal births. Presence of asbestos fibers was strongly correlated with working status of the mothers (Haque et al, 1996).
- D. When administered in the drinking water, asbestos had no effect on embryo survival and was not teratogenic in rats (Schneider & Mauere, 1977). It has been reported to affect embryonic development in mice (Valerio et al, 1980). Chrysotile asbestos was not teratogenic in mice at an oral dose of 143 mcg (Shepards, 2001).
- E. No effects on sperm were seen in Swiss albino mice given chrysotile asbestos in the drinking water at a dose of 20 mg/kg/day (Rita & Reddy, 1986).
- F. Blastocyst exposure to asbestos did not result in decreased postimplantation survival (Shepards, 2001).

8.0 PREDISPOSING CONDITIONS

- A. **MEDICAL:** Immunocompromised persons, or those with pre-existing lung disease, might be at increased risk from asbestos exposure.
- B. **CHEMICAL:** Because asbestos can strongly adsorb other substances, persons also exposed to other carcinogens might be at increased risk.
- C. **SMOKING** increases the risk of asbestos-related lung cancer approximately 15 times (Hathaway et al, 1991).
- D. **GENETIC:**
 1. Asbestos insulators with the NAT2 slow-acetylator phenotype were more than twice as likely to develop both malignant and non-malignant pulmonary diseases, compared with the NAT2 fast-acetylator phenotypes, and their risk for malignant mesothelioma was approximately four-fold higher.
 2. Individuals who had both the NAT2 slow-acetylator phenotype and who were null for the GSTM1 gene had a five-fold increased risk for malignant and nonmalignant pulmonary diseases, versus those who were NAT2 fast-acetylators and present for the GSTM1 gene. In the latter group (slow-acetylators and null for GSTM1), their risk for malignant mesothelioma was 8-fold increased over the same comparison group (Hirvonen et al, 1996).

9.0 BIOMONITORING

- A. An effective method for biological monitoring is the detection of so-called ferruginous bodies in the sputum (Greenberg et al, 1976). Analysis of sputum for asbestos bodies is a fairly insensitive means of assessing exposure, but a positive sputum sample is indicative of high lung burden for asbestos (Teschler et al, 1996). Persons who work with asbestos should have periodic sputum analysis, chest X-rays, and pulmonary function tests.

11.0 SUMMARY AND CONCLUSIONS

- A. The greatest risks with occupational exposure to asbestos are mesothelioma and carcinoma of the lung, and asbestosis. While there are some reports that occupational exposure to asbestos may be associated with abnormalities of the sex organs, these

studies were in workers with mixed exposures to other agents.

- B. Asbestos is Class 3 (can cause irreversible changes which can be life-threatening) for general toxicity from its activity as a human carcinogen. It is in Class A- (unconfirmed human reproductive hazard) for reproductive hazard, based on several occupational studies with mixed or poorly defined exposures, and increased probability of finding asbestos fibers in tissues of stillbirths. The actual human reproductive hazard is unknown.
- C. As with all chemicals, unnecessary exposure should be avoided.

12.0 REFERENCES

12.1 GENERAL REFERENCES

- A. See ~~to~~: GENERAL REFERENCES

12.2 SPECIFIC REFERENCES

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