STEVENS & BALDO
A REGISTERED LIMITED LIABILITY PARTNERSHIP
ATTORNEYS AT LAW
550 FANNIN, SUITE 400
BEAUMONT, TEXAS 77701

R. LYN STEVENS*
NICHOLAS S. BALDO

JOHN R. DOLEZAL
MICHAEL R. WALZEL
MICHAEL K. ROSE
CHRISTINE S. KIBBE**

POST OFFICE BOX 4950
BEAUMONT, TEXAS 77704
TELEPHONE: (409) 835-5200
FACSIMILE: (409) 838-5638

* BOARD CERTIFIED
PERSONAL INJURY TRIAL LAW
TEXAS BOARD OF LEGAL SPECIALIZATION

** LICENSED TEXAS & LOUISIANA

July 26, 1995

Mr. Carl L. Tucker
Silber, Pearlman & Bruegger
SPB Building
3110 Webb
Dallas, Texas 75205

Re: Continuation of Dr. Robert Ross' Deposition

Dear Mr. Tucker:

Pursuant to your request in your correspondence of July 7, 1995, enclosed are copies of the following articles:

1. "Outline of Deposition Questions -- Pulmonary Specialist," Gary D. Elliston.

2. "If It's Not Mesothelioma, It's Not Asbestos Related," Gary D. Elliston and Stephanie L. Spardone.

Very truly yours,

R. Lyn Stevens

RLS/mjb
Enclosures

CUTLINE OF DEPOSITION QUESTION - PULMONARY SPECIALIST

BY GARY D. ELLISTON

QUALIFICATIONS & PERSONAL INFO.

Name:

Home Address: How Long:

Business Address: How Long:

Occupation or Profession: How Long:

Name & Address of Employer, Association or Business Entity: How Long:

Name & Specialty of Partners or Other Physicians Practicing in Association:

In what areas of medicine do you claim to be an expert or specialist?

Do you hold yourself out to the public as an expert in:

1. Pulmonary medicine
2. Cardiology
3. Industrial hygiene
4. Oncology
5. Pathology
6. Radiology
7. Epidemiology

Are you board certified? If so, please state:

1. What area of medicine:
2. Number of times examination taken:
3. Date of certification:

Are you a "B" reader? If not:

1. Have you taken examination or course:
2. How many times have you taken examination:

Appendix "E"

QUALIFICATIONS

Trace education since high school:

Institution:

Dates:

Major:

Degree:

Teacher/Mentor:

Thesis Subject:

Medical Text/Journals used for instruction:

Have you received additional training or education:

Internship:

Residency:

Fellowship:

During medical school, residency, internship, fellowship, how many cases did you observe of the following:

Mesothelioma:
Lung cancer:
Asbestosis:
Asbestos-related pleural changes:

What percentage of your education involved:

1. pulmonary diseases:

2. occupational diseases:

3. asbestos-related diseases:

What local industries were sources of occupational disease or asbestos exposure during medical school, internship, residency, and fellowship?

Is Exhibit _____ a true, correct, and current copy of your curriculum vitae?

What changes to your curriculum vitae have been made in the last five years?

QUALIFICATIONS

Have you testified in Court regarding asbestos-related diseases?
If so:

On how many occasions:
What percent of testimony at request of Plaintiff attorney:
Plaintiff attorney's name:
Plaintiff's Name:
Alleged illnesses or injuries involved:

Have you testified in deposition regarding asbestos-related diseases?
If so:

On how many occasions:
What percent of testimony at request of Plaintiff attorney:
Plaintiff attorney's name:
Plaintiff's Name:
Alleged illnesses or injuries involved:

Have you ever been called as an expert witness at the request of attorneys representing manufacturers of asbestos-containing products:

1. At trial
2. At deposition

If so, number of times:

When:
Where:
Style of case:
Injury alleged:
Name & address of defense attorney:

Have you ever been requested to evaluate an individual at the request of a manufacturer of asbestos-containing products?

If so, number of times:

When:
Where:
Style of case:
Injury alleged:
Name & address of defense attorney:
Deposition taken:

QUALIFICATIONS

How much is your charge for:

1. trial testimony time:
2. deposition testimony time:
3. investigation or research time:
4. consultation examination:

How much did you earn from medical/legal practice:

1988: % income:

1987: % income:

1986: % income:

1985: % income:

TOTAL:

How many evaluations or screening were performed in:

1988:

1987:

1986:

1985:

TOTAL:

What percent of time is spent in:

1. patient care:
2. teaching:
3. medical/legal
4. administrative:
5. other:

QUALIFICATIONS

Have you ever performed:

1. Epidemiological study:
2. Animal experiments:
3. Laboratory research:

If so:
   a. What subject:
   b. Results of study:
   c. When:
   d. Where results published:

Have you ever published:

1.	case report:	citation:
2.	article:	citation:
3.	abstract:	citation:

What seminars or meetings regarding occupational diseases:

1. attended as student:
2. attended as lecturer or speaker:

Do you consider yourself to be an expert in asbestos-related diseases?

Who else do you consider to be an expert in the area of asbestos-related diseases?

Are you familiar with the work, publications, or qualifications of the following individuals:

J. C. Wagner	Margaret Becklake
Irving J. Selikoff	Hans Weill
X Raymond Murphy	Elliot McCaughey
R. Keith Wilson	X John Craighead
Paul Stevens	X Francis Green
David Edelman	Edward Gaensler
E. C. Hammond	X Roger Mitchell
Jacob Churg	X Jerome Klinerman
Andrew Churg	Donald Greenberg
Phillip Enterline	X Corbet McDonald
X Gerrit Schepers	Joseph Wagoner
Anthony Lanza	X Samuel P. Hammar
Stuart Brooks	Victor Roggli
Bernard Gee	W. K. C. Morgan
Sir Richard Doll	X Barry Castleman
X Thomas Mancuso	H. Corwin Hinshaw
William Weiss	

Do you consider those individuals to be knowledgable experts in the area of asbestos-related diseases?

QUALIFICATIONS

How many cases of mesothelioma have you diagnosed:

1. in your career?
2. in the past year?
3. in individuals not referred by plaintiff's attorneys?

How many cases of lung cancer have you diagnosed:

1. in your career?
2. in the past year?
3. in individuals not referred by plaintiff's attorneys?

How many cases of GI tract cancer have you diagnosed:

1. in your career?
2. in the past year?
3. in individuals not referred by plaintiff's attorneys?

How many cases of asbestosis have you diagnosed:

1. in your career?
2. in the past year?
3. in individuals not referred by plaintiff's attorneys?

How many cases of asbestos-related pleural changes have you diagnosed:

1. in your career?
2. in the past year?
3. in individuals not referred by plaintiff's attorneys?

QUALIFICATIONS

Do you or does your organization maintain a medical library?

Please list the texts in your reference library on:

1. pulmonary medicine:

2. occupational medicine:

3. oncology:

4. epidemiology:

What medical journals do you subscribe to individually?

Do you consider each of those journals to be reputable, authoritative medical journals?

Do you maintain a library or file of significant medical articles regarding asbestos-related disease?

Will you agree to provide a list of the articles maintained in your file by author, journal, and date of publication?

If not, please list the articles maintained in your file by author, journal, and date of publication of the articles:

What faculty positions have you held:

Have you taught any courses, seminars, or training sessions regarding occupational disease:

If so, what texts or articles were used:

What memberships do you hold in any professional or medical organization such as the American Thoracic Society or the American College of Chest Physicians:

DIAGNOSTIC CRITERIA (See Quotable Quotes)

What is your diagnostic criteria for asbestosis?

What exposure history do you require to diagnose asbestosis within a reasonable degree of medical probability?

What is the minimum number or group of findings that you require before you will make a clinical diagnosis of asbestosis within a reasonable degree of medical probability?

Are you familiar with diagnostic criteria for asbestosis adopted and published by the American Thoracic Society in August, 1986?

Is ATS criteria different than your criteria?

Please explain all differences:

Can you identify exhibits as a copy of ATS Standards For Diagnosis Of Non-malignant Diseases?

Where was it published?

What is the American Thoracic Society?

Does that organization have as its official journal, The American Review of Respiratory Disease?

What is the relationship between the American Thoracic Society and the American Lung Association?

What is the American College of Chest Physicians?

Why was this special committee of experts formed?

Does this select committee include:

1. Pleural changes as part of its summary of diagnostic criteria:
2. Obstructive changes as part of its summary of diagnostic criteria:

ASBESTOS BODIES

What is significance of asbestos bodies?

Do asbestos bodies cause:

1. Disease
2. Harm
3. Pain
4. Reduced lung function
5. Further exposure

Isn't it true that once coated with iron asbestos fibers can no longer cause injury?

PULMONARY FUNCTION TESTING (See Quotable Quotes)

Explain what each test measures: What is range of normal for each:

FVC:
FEV^1:
FEV^1/FVC:
FEF^{25-75}:
VC:
RV:
TLC:
RV/TLC:
$DLCO_{SB}$:

Has ATS also appointed a select committee of experts to recommend standards for respiratory impairment as measured by PFT?

When did the committee render the latest report on standards for impairment?

Where was the report published?

Is Exhibit ____ a copy of those standards established by that ATS committee of experts:

Is Exhibit ____ a blow up of the standards for normal and slightly impaired measurements:

Isn't it true that if an individual with test measurements in the slight impairment category, according to ATS standards, should be able to perform virtually any job except the most unusually demanding:

Do these standards apply to people with asbestosis?

What pulmonary function test results demonstrate:

1. restrictive findings:
2. obstructive findings:
3. large airway obstruction (permanent/reversible):
4. small airways obstruction (permanent/reversible):
5. impairment:
6. combination of COPD and asbestosis:

What is significance of bronchodilator response:

If obstruction and restriction are present, can you designate a percentage of Plaintiff's shortness of breath to each within a reasonable degree of medical probability?

DIFFUSION CAPACITY

How is the $DLCO_{SB}$ measurement performed:

What does the $DLCO_{SB}$ measure:

Isn't it true that:

a. the diffusion capacity will be reduced in a person with emphysema?

b. a current smoker may have a reduced diffusion capacity if he smoked shortly before the test?

c. a reduction in the diffusion capacity in a current smoker may be as much as 10%?

EXERCISE TESTING:

Is exercise testing an accurate measurement of patient's ability to work:

Is exercise testing affected adversely if an individual is a compensation claimant:

In ideal circumstance explain value of exercise testing when:

DLCO up or down during exercise

ABG)
Arterial O_2) Up or Down
PO_2)

Healthy lungs

Fibrotic lungs

Emphysematous lungs

Explain how exercise physiologically affects lung mechanism to up or down PO_2 in healthy lung vs. diseased lung.

BLOOD GAS STUDIES

Please describe each blood gas study and what it measures.

For each blood gas study, what is the range of normal?

ASBESTOS: OBSTRUCTION (See Quotable Quotes)

Isn't it true that:

1. asbestosis is a restrictive disease?

2. the characteristics of asbestosis are those of a restrictive disease?

In your opinion, does asbestos cause:

a. chronic bronchitis?

b. emphysema?

c. clinically significant obstructive lung disease?

d. asthma?

e. pneumonia?

SMALL AIRWAY CHANGES (See Quotable Quotes)

Isn't it true that:

1. Small airways obstruction is reflected on pulmonary function testing by FEF^{25-75} or MMEF?

2. Smoking causes small airways obstruction?

3. Small airway obstruction is not responsive to bronchodilators?

4. FEF^{25-75} measurements should not be used for impairment evaluation?

5. Small airways fibrosis does not cause symptoms, therefore is not clinically significant?

Isn't it true that asbestos does not cause any obstruction that responds to bronchodilators?

RALES

What are:

1. Rales:
2. Rhonchi:
3. Wheeze:

Isn't it true that rales are non-specific finding:

What is significance if rales are:

1. inspiratory:
2. expiratory:
3. bilateral:
4. non-persistent on cough:

SHORTNESS OF BREATH (See Quotable Quotes)

Isn't it true that dyspnea (S.O.B.) is:

1. Non-distinct symptom (common to all lung disease):
2. Subjective symptom:
3. Deconditioning symptom:

What is significance if cough is:

1. Productive:
2. Dry:

OBESITY

Isn't it true that obesity causes:

1. SOB (on exertion)
2. Fatigue
3. Stress on heart
4. Stress on lungs
5. Restriction of pulmonary function
6. Decreased exercise tolerance

AGE

Isn't it true we all lose lung volume as we age?

If so, how much lung volume do we lose each year?

Isn't it true that our exercise tolerance decreases with age?

Isn't it true that the chest X-ray appearance changes with age?

P

PROGRESSION (See Quotable Quotes)

Will everyone exposed to asbestos develop asbestosis?

Please explain why:

If someone has prolonged exposure and develops asbestosis, will it necessarily progress?

Please provide basis and authority for opinion that asbestosis always progresses:

If someone develops progressive asbestosis, how slowly does it generally progress?

Would you agree that the lung's natural defense mechanisms will remove 90% of asbestos fibers inhaled?

Have you ever followed an individual:

1. with pleural changes to their death as a result of pleural changes?

2. from a 1/1 to their death as a result of interstitial fibrosis?

3. from a 2/2 to their death as a result of interstitial fibrosis?

4. from pleural changes to their ultimate death as a result of pleural or interstitial fibrosis?

How long have you been following individuals for asbestos-associated diseases?

Isn't it true that as exposure decreased with improved work conditions and industrial hygiene that progression rates have slowed:

CHEST X-RAY

Isn't it true that:

1/0 - 1/1 - 1/2 on ILO scale is slight or mild interstitial fibrosis?

2/1 - 2/2 - 2/3 on ILO scale is moderate interstitial change?

3/2 - 3/3 on ILO scale is severe interstitial change?

INTERSTITIAL FIBROSIS

What are all known causes of interstitial fibrosis?

Other physiological cause of CXR appearance of irregular small opacities:

Cigarette smoking:

Pneumonia:

Congestive heart failure:

Bilateral appearance:

PLEURAL

What are all known causes of:

1. pleural thickening:

2. pleural plaques:

3. pleural effusion:

Isn't it true that as general rule:

1. pleural plaques are asymptomatic:

2. pleural thickening is asymptomatic:

3. pleural effusions subside and disappear without any residual impairment:

4. Pleural plaques + thickening are not precursors of cancer

5. " " " do not develop into cancer

DISEASE

What is your definition of disease:

Under your definition, are the following changes considered a disease:

1. Callous
2. Wart
3. Scar
4. Mole
5. Freckle
6. Sunburn
7. Pimple
8. Broken leg
9. Bruise
10. Pulled muscle

EPIDEMIOLOGY

Please define:

1. SMR: Standard Mortality Ratio:

How elevated must a SMR be to be considered statistically significant:

2. Relative risk ratio

FIBER TYPE

Is there a difference between:

1. fibrogenic potential in the various types of asbestos fiber?

2. carcinogenic potential in the various types of asbestos fiber?

Please rank the commericially used asbestos fibers for their

1. fibrogenic potential:

2. carcinogenic potential:

Isn't it true, sir, that 95% of the asbestos fiber used in America was chrysotile?

CANCER (See Quotable Quotes)

In your opinion, does asbestos cause or contribute to cause any of the following types of cancer:

1. Leukemia
2. Lung cancer
3. Ovarian cancer
4. Stomach cancer
5. Pharyngeal cancer
6. Laryngeal cancer
7. Colon cancer
8. Rectal cancer
9. Testicular cancer
10. Breast cancer
11. Mesothelioma
12. Pancreatic cancer
13. Lymphoma
14. Brain cancer
15. Bone cancer
16. Esophogeal cancer
17. Prostate cancer
18. Kidney cancer

List the author and citation of all studies or reports which support your opinions:

Which cancers, if any, are dose-related:

For each cancer, what:

1. is most common cause in U.S.:
2. number of patients have you diagnosed in your career:
3. number of patients do you currently have hospitalized:
4. is the incidence rate in U.S.:
5. percentage of general population will develop:
6. percentage of asbestos workers will develop:
7. are all known contributing causes:
8. physical or pathological changes would you require to attribute to asbestos:

CANCER RISK

Isn't it true that:

1. 20 to 25% of the general population in America die of cancer:

2. 35 to 40% of Americans die of heart disease:

3. Smoking contributes to both heart disease and cancer:

4. Cancer is called disease of elderly

5. If all cancer was cured it would only increase life expectancy in the United States by 2 years or less

In your opinion, do pleural changes (i.e., thickening or plaques) increase a person's risk of mesothelioma over another individual with the same or similar exposure?

If so, please provide the author and publication that supports your opinion:

Does a person with "interstitial fibrosis" have an increased risk of mesothelioma over another person with the same or similar exposure but without the development of interstitial fibrosis?

If so, please provide the author and publication that supports your opinion:

Does a person with "asbestosis" have an increased risk of mesothelioma over another person with similar exposure but without the development of interstitial fibrosis?

If so, please provide the author and publication that supports your opinion:

In your opinion, do pleural changes (i.e., thickening or plaques) increase a person's risk of lung cancer over another individual with the same or similar exposure?

If so, please provide the author and publication that supports your opinion:

Does a person with "interstitial fibrosis" have an increased risk of lung cancer over another person with the same or similar exposure but without the development of interstitial fibrosis?

If so, please provide the author and publication that supports your opinion:

Does a person with "asbestosis" have an increased risk of lung cancer over another person with similar exposure but without the development of interstitial fibrosis?

If so, please provide the author and publication that supports your opinion:

In your opinion, is lung cancer, when associated with asbestos, a dose-related condition?

In your opinion, is lung cancer, when associated with smoking, a dose-related condition?

CANCER RISK

What are the relative and total lung cancer risks for the following occupations:

	Smoker	Non-Smoker
Household asbestos exposure:		
Electricians:		
Welders:		
Pipefitters:		
Painters:		
Sheetmetal workers:		
Shipyard workers:		
Insulators:		
Plasterers:		

With regard to each one, what studies, articles, publications, or authors do you rely upon?

Was smoking considered as a confounding variable in each of the studies you have relied upon?

What is the risk of mesothelioma for each of the above occupations:

With regard to each one, what studies, articles, publications, or authors do you rely upon?

CIGARETTE SMOKE

Have you ever diagnosed:

1. an individual with lung cancer who was a non-smoker?

2. an asbestos-worker with lung cancer who has never smoked?

If so, how many:

a. non-smokers diagnosed with lung cancer:
b. smokers diagnosed with lung cancer:

In your opinion, does smoking cause or contribute to cause:

1. a reduction in the dust clearance ability of the lung?

2. pleural plaques or thickening?

3. interstitial fibrosis?
- are they detectable on CXR? Size, type?

4. increased incidence of infection?

5. reduction in life expectancy?

6. bronchitis?

7. emphysema?

8. asthma?

9. destruction of cilia cells? for how long? per cigarette?

10. destruction of macrophages?

11. increased dust retention and distribution into periphery of lung?

12. increased mortality rate from asbestosis?

In your opinion, does smoking cause or contribute to cause increased extent or severity of:

1. pleural changes?

2. interstitial fibrosis?

3. bronchitis?

4. emphysema?

5. asthma?

CIGARETTE SMOKE

Is cigarette smoke:

1. Addictive:

2. Carcinogenic:

3. Fibrogenic:

Is there any safe level any carcinogen:

If so, which carcinogens:

What level is safe:

How many carcinogens are in every puff of cigarette smoke:

In your opinion, is lung cancer in a person exposed to any amount of any carcinogen, in reasonable medical probability, caused by that carcinogen:

Is there any safe level of cigarette smoke:

Would you agree that one cigarette is too many:

Do you advise all patients to stop smoking regardless of asbestos exposure:

Do you personally believe that cigarette smoking is hazardous?

Do you prescribe medication, hypnosis, or other therapy to help your patients stop smoking?

Did you prescribe any medication or therapy for the Plaintiff?

If you have a patient who smokes, what is the single most important thing you advise that patient? why?

CIGARETTE SMOKE

Isn't it true that cigarettes are the number one preventable cause of:

1. Heart disease
2. Bronchitis
3. Emphysema
4. Small airways disease - permanent & irreversible
5. Large airways disease
6. Lung cancer
7. other sites of malignancies? where?

Isn't it true that smoking causes or contributes to cause:

1. Adenocarcinoma
2. Squamous cell or epidermoid
3. Large cell
4. Small cell
5. All cell types of lung cancer
6. Carcinoma in every area or location in lung

Isn't it true that:

1. the earlier a person starts smoking the more damage is done to lungs:
2. 85% of lung cancer in America is attributable to cigarette smoking:

ALCOHOL

Isn't it true, sir, that alcohol consumption:

a. increases a person's risk of cancer?

b. acts as a depressant?

c. has been implicated in the reduction of dust clearance from the lungs?

d. reduces a person's life expectancy?

e. causes cirrhosis of the liver?

f. causes malnutrition A-E-21

g. deconditioning effect (sob, FATIGUE) A-141

HEART

Isn't it true that cor pulmonale:

1. is right sided heart failure?
2. only occurs with severe and longstanding lung disease?

Isn't it true that coronary artery disease is not asbestos-related?

Isn't it true that coronary artery disease may cause:

1. SOB (exertional)?
2. chest pain?
3. fatigue?
4. decreased exercise tolerance?

Isn't it true that risk factors for coronary artery disease are:

1. Smoking
2. Obesity
3. Familial history
4. Male
5. Age
6. Cholesterol
7. Hypertension
8. Lack of cardiovascular exercise or deconditioning

PNEUMONIA

Isn't it true that pneumonia may cause:

1. pleural effusion
2. pleural thickening
3. pleural plaques
4. Interstitial scarring
5. other permanent CXR changes and reduced pulmonary function

INDIVIDUAL CASE

Trial is set _____.

Do you know of any reason you can't attend?

Have you been asked to appear and testify?

Will you appear if asked by plaintiff attorney to do so?

May I see your complete file on this case?

Have there been any reports, documents, records, or information that you have reviewed or created that are not contained within the file?

If so,

1. please explain why those records, reports, information, and/or documents were removed or not included in the file.

2. please provide those.

What information in the file was not created by you?

1. who provided that information:

2. when was that information provided:

INDIVIDUAL CASE

Have you consulted any other person or expert with regard to this case?

In Plaintiff _____ case, who:

1. referred him to you?
2. paid the bill for examination and report?
3. scheduled the appointment with your office?
4. That attended any appointments with the π to your office?

In Plaintiff _____ case, did you or anyone from your office:

1. have any communication with Plaintiff prior to his appointment?
2. review any records on the plaintiff prior to his appointment?
3. review any chest X-rays prior to his appointment?

In Plaintiff _____ case, have you:

1. requested any information or medical records you have not received?
2. requested any chest X-rays you have not received?
3. planned or need any additional work, review of any additional records, review of any additional X-rays to support your opinions in this case?
4. planned or need future appointments or opportunities to evaluate Plaintiff?

If you do any further work, record review, or X-ray interpretation, would you agree to advise the plaintiff's counsel so that he may advise defense counsel of the additional work either which support or changes your opinions in this case?

INDIVIDUAL CASE

In Plaintiff _____ case, please state:

1. Each date the plaintiff was seen or evaluated by witness:
2. Where plaintiff was evaluated each time:
3. Who scheduled the evaluations:
4. Who paid the bill on each occasion:

In Plaintiff _____ case, please state Plaintiff's:

1. date of birth:
2. height & weight:
3. occupational history:
4. first & last alleged exposure to asbestos-containing insulation products:

SMOKING HISTORY:

Plaintiff's smoking history:

1. Date started:
2. Date stopped:
3. Average number of packs smoked per day over smoking history:
4. Total pack years accumulated:
5. Brands of cigarettes smoked during smoking history:
6. Years non-filter cigarettes smoked:
7. Smoking history of:
   a. father:
   b. mother:
   c. spouse:

8. Other tobacco use:
   a. pipe:
   b. cigars:
   c. chewing tobacco:
   d. snuff:

ALCOHOL HISTORY

Dates and amounts of alcoholic beverages consumed:

Type of alcohol consumed:

Whether Plaintiff had treatment for alcoholism or alcohol-related condition:

INDIVIDUAL CASE

PHYSICAL EXAMINATION:

Did you find:

Normal breath sounds:

Rales:

Rhonchi:

Wheezes:

Decreased breath sounds:

Increased chest diameter:

Clubbing:

Cyanosis:

Edema:

Cigarette/tobacco stains on fingers/lips:

CXR INTERPRETATION

What are dates and views of all chest X-rays taken and/or reviewed:

What is your ILO interpretation of all chest X-rays on:

1. Quality of films, techniques:
2. Small irregular opacities
3. Pleural changes

Do the chest X-rays demonstrate any:

1. signs of congestive heart failure?
2. emphysematous blebs or bullae:
3. hyperinflation:
   - flattened diaphragms
   - widened mediastinal spaces
4. pleural fat pads
5. any other disease process

INDIVIDUAL CASE

PULMONARY FUNCTION STUDIES:

Do they demonstrate:

1. restrictive defect?
2. obstructive defect?
3. combined defect?
4. any progression in any breathing defect present?

**Make certain you have actual numbers on all PFT tests in report. If none, require doctor to testify to numbers.

INDIVIDUAL CASE

FUTURE MEDICAL

Isn't it true that:

1. any smoker age 55 or older should have an annual chest X-ray?
2. any 55 year old smoker should have an annual physical examination?
3. you have recommended to the Plaintiff that he have a physical examination and chest X-ray every year?
4. unless the Plaintiff develops severe impairment or develops a cancer that his future medical expenses will be no greater than another individual his age without asbestosis?
5. you cannot testify in reasonable medical probability that Plaintiff will develop cancer?
6. you cannot testify that Plaintiff will reach a severe impairment category?

**If witness answers "no" to any question, please provide the author, publication, and citation of study or authority to support his opinion.

INDIVIDUAL CASE

PROGRESSION

Has there been any progression in the Plaintiff's condition over the number of years that you have followed the Plaintiff?

From your review of the records, has there been any progression of the Plaintiff's condition in the last ____ number of years?

Isn't it true the variables to consider in determining individual's progression include:

1. age:
2. latency between first exposure and manifestation of changes:
3. duration and extent of exposure:
4. smoking history:

LIFE EXPECTANCY

What is the Plaintiff's life expectancy?

What study or report to you rely upon for your calculation of the life expectancy of the Plaintiff?

What would the Plaintiff's life expectancy be if he had not been exposed to asbestos?

What other factors, not related to asbestos, reduce plaintiff life expectancy:

1. smoking:
2. obesity:
3. hypertension:
4. heart disease:
5. hereditary factors:

INDIVIDUAL CASE

CANCER CONCERN

What did you tell the Plaintiff concerning his condition?

Did you tell the Plaintiff he has:

1. cancer:
2. asbestosis:
3. impairment:
4. progression:
5. pleural changes:

Did you tell Plaintiff in reasonable medical probability he will develop cancer?

Exactly, as best you recall, what did you tell the Plaintiff concerning his cancer risk?

What did the Plaintiff say in response to you concerning his:

1. cancer risk:
2. asbestosis:
3. impairment:
4. progression:
5. pleural changes:

Provide the citation and/or study that you rely upon for calculating the cancer risk of Plaintiff:

Did you refer the Plaintiff to a counselor, psychiatrist, or psychologist?

QUOTABLE QUOTES: ASBESTOSIS

QUESTION:

Isn't it true that:

1....the term "asbestosis" should be reserved for interstitial fibrosis of pulmonary parenchyma where asbestos bodies or fibers may be demonstrated?

2....the minimum criteria for histological diagnosis of asbestosis are:

a. peribronchiolar fibrosis, and
b. two or more asbestos bodies in tissue

QUOTE:

PULMONARY ASBESTOSIS

DEFINITION

The term asbestosis should be reserved for the interstitial fibrosis of the pulmonary parenchyma in which asbestos bodies or fibers may be demonstrated. . .

American Thoracic Society, THE DIAGNOSIS OF NON-MALIGNANT DISEASES RELATED TO ASBESTOS, American Review of Respiratory Disease, 1986, Vol. 134, pp. 363-368

. . .

ASBESTOSIS

Fundamental to the diagnosis of asbestos-associated interstitial fibrosis, or asbestosis, is the microscopic demonstration of asbestos bodies. The Pneumoconiosis Committee of the College of American Pathologists has specified that the minimum criteria for the histologic diagnosis of asbestosis are (1) identification of peribronchiolar fibrosis and (2) at least two asbestos bodies in tissue sections.[46]

GREENBERG, S. DONALD, "Asbestos", Pulmonary Pathology, 1988, Chapter 22, p. 628

QUOTABLE QUOTES: LATENCY PERIOD

QUESTION:

Isn't it true that the common latency period for an asbestos-associated:

1....pleural effusion is 3 to 20 years.

2....pleural plaque is 10 to 20 years.

3....asbestosis is 10 to 20 years.

4....lung cancer is 20+ years.

5....mesothelioma is 25 to 50 years.

QUOTE:

ASBESTOS-ASSOCIATED DISEASES

Asbestos exposure may lead to pleural effusion, pleural plaques, fibrosis (asbestosis), and mesothelioma. It may act as a cocarcinogen in lung cancer. The latent periods commonly associated with these diseases and asbestos exposure are shown in Table 22-3.

TABLE 22.3. Latency of Asbestos-Associated Lung Diseases

Disease or condition	Latent period (years)
Pleural effusion	3-20
Pleural plaque	10-20
Asbestosis	10-20
Asbestos-associated lung cancer	20+
Asbestos-associated mesothelioma	25-50

GREENBERG, S. DONALD, "Asbestos", Pulmonary Pathology, 1988, Chapter 22, p. 627

QUOTABLE QUOTES: PLEURAL CHANGES

QUESTION:

Isn't it true that bilateral pleural plaques:

1....have no effect on life expectancy?
2....are not known to give rise to any complications?
3....are an index only of past asbestos exposure if other causes are excluded?

QUOTE:

Prognosis and Complications

Plaques themselves have no effect on life expectancy and are not known to give rise to any complications.

. . .

To Summarize

The pathogenesis of pleural plaques in asbestos-exposed persons is a fascinating enigma but their bilateral presence at autopsy and in chest radiographs is, for practical purposes, like asbestos bodies, an index only of past asbestos exposure if other causes are excluded.

W. Raymond Parkes, OCCUPATIONAL LUNG DISORDERS (Text), 2nd Ed., 1982, p. 249

. . .

4....cause no symptoms

PLEURAL PLAQUES

Pleural plaques develop on the parietal pleura in the intercostal spaces and the diaphragm and are usually incidental findings seen radiographically or at autopsy. The visceral pleura may also be involved. In themselves, they cause no symptoms, but are a marker of previous asbestos exposure in many cases [57].

Jerrold L. Abraham, Environmental Pathology of the Lung, ENVIRONMENTAL AND OCCUPATIONAL MEDICINE (Text), W. Rom, Editor, 1983, p. 141

. . .

5....should prompt no further investigation which would only alarm patient

PLEURAL PLAQUES

Pleural plaques are a benign condition, indicating exposure to asbestos in the past. They probably occur more frequently after exposure to amphiboles than to chrysotile, since they do not occur frequently in all parts of Quebec. They should not be taken to imply any more serious disease and should not prompt further investigation of follow-up, which will only needlessly alarm the patient.

W.K.C. Morgan, A. Seaton, M.D., OCCUPATIONAL LUNG DISEASES, 2nd Ed., 1984, p. 361

QUOTABLE QUOTES: DIAGNOSTIC CRITERIA

QUESTION:

Isn't it true that the diagnosis of asbestosis:

1....is a judgment based on careful consideration of all relevant clinical findings?

2....requires a reliable history of exposure and an appropriate time interval between exposure and detection?

3....has recognized clinical criteria of:

a. small irregular opacities on chest X-ray of a profusion of 1/1 or greater;
b. a restrictive pattern of lung impairment with a FVC below the lower limit of normal;
c. a reduced diffusion capacity below the lower limit of normal; and
d. persistent crackles at the lung bases

4....has as its most important clinical finding small irregular opacities on chest X-rays?

QUOTE:

SUMMARY

. . .The diagnosis of asbestosis is a judgment based on a careful consideration of all relevant clinical findings. In our opinion, it is necessary that there be:

1. A reliable history of exposure
2. An appropriate time interval between exposure and detection (see pages 9-10)

Furthermore, we regard the following clinical criteria to be of recognized value:

1. Chest roentgenographic evidence of type "s," "t," "u," small irregular opacifications of a profusion of 1/1 or greater
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

Of these, the findings on the chest roentgenogram are the most important. When this criteria is not met, considerable caution is warranted. The specificity of the above criteria increases with increasing numbers of positive criteria. As in all clinical judgments, confounding variables, such as the presence of other clinical conditions that affect these criteria, should be evaluated.

American Thoracic Society, THE DIAGNOSIS OF NON-MALIGNANT DISEASES RELATED TO ASBESTOS, American Review of Respiratory Disease, 1986, Vol. 134, pp. 363-368

QUOTABLE QUOTES: SYMPTOMS & IMPAIRMENT

QUESTION:

Isn't it true that:

1....in disability claimants the reliability of relationship between pulmonary function and shortness of breath breaks down?

2....disability claimants markedly exaggerate symptoms?

3....symptoms of SOB can no longer be relied on as index of impairment?

QUOTE:

PULMONARY PHYSIOLOGY

In disability claimants the reliability of the relationship between pulmonary function and shortness of breath breaks down. This is especially true where the financial rewards exceed what the subject earns at work . . . It is quite clear that disability claimants markedly exaggerate their symptoms, and as such the symptom of shortness of breath can no longer be relied upon as an index of impairment.

W.K.C. Morgan, A. Seaton, OCCUPATIONAL LUNG DISEASES (Text), 2nd Ed., 1984, p. 66

QUOTABLE QUOTES: SHORTNESS OF BREATH

QUESTION:

Isn't it true that dyspnea, shortness of breath, is:

1....a non-specific symptom, common in many cardiopulmonary disorders?

2....particularly subject to emotional factors present in suspected industrial-related disease?

QUOTE:

DYSPNEA

. . .Dyspnea, however, is a nonspecific symptom, common in many other cardiopulmonary disorders, and it is particularly subject to emotional factors likely to be relevant in instances of suspected industrially-related disease.

American Thoracic Society, THE DIAGNOSIS OF NON-MALIGNANT DISEASES RELATED TO ASBESTOS, American Review of Respiratory Disease, 1986, Vol. 134, pp. 363-368

QUOTABLE QUOTES: PFT & IMPAIRMENT

QUESTION:

Isn't it true that by pulmonary function testing:

1....FEV^1, FVC, FEV^1/FVC, and $DLCO_{SB}$ are the primary tests recommended for determination of respiratory impairment

2... a person with FEV^1 of 60% +, has slight impairment;
FVC of 60% +, have slight impairment;
DLCO of 60% +, have slight impairment;
FEV^1/FVC of 60% +, will only have slight impairment

3....a person with no or mild impairment would be able to perform all but the most unusually physically demanding of jobs

QUOTE:

IMPAIRMENT DIRECTLY RELATED TO REDUCED LUNG FUNCTION

Pulmonary Function Test (Primary Tests)

The FEV^1, FVC, FEV^1/FVC, and DL_{COsb} are the primary tests recommended for the determination of respiratory impairment.

. . .

Rating of Impairment

In the evaluation of respiratory impairment by pulmonary function testing, it is recommended that the first step include both forced spirometry measurements and testing for single breath diffusing capacity. With these results, the majority of subjects will be appropriately categorized as to their degree of impairment as follows:

Normal. FVC $\geq$ 80% of predicted, and
$FEV^1 \geq$ 80% of predicted, and
$FEV^1/FVC \times 100 \geq 75\%$, and
$DL_{COsb} \geq$ 80% of predicted.

Mildly Impaired. (Usually not correlated with diminishing ability to perform most jobs).

FVC 60% to 79% of predicted, or
FEV^1 60% to 79% of predicted, or
$FEV^1/FVC \times 100$ 60% to 74%, or
DL_{COsb} 60% to 79% of predicted.

. . .

Subjects with no or mild impairment (see Rating of Impairment) would be able to perform all but the most unusually physically demanding of jobs.

American Thoracic Society, EVALUATION OF IMPAIRMENT/DISABILITY SECONDARY TO RESPIRATORY DISORDERS, American Review of Respiratory Disease, March 6, 1986, pp. 1205-1209

QUOTABLE QUOTES: RESTRICTION

QUESTION:

Isn't it true that the characteristic features of pulmonary asbestosis are those of a restrictive lung disease?

QUOTE:

PULMONARY FUNCTION

. . .The characteristic features of pulmonary asbestosis are those of a restrictive lung disease, i.e., a reduction in lung volumes, with inspiratory capacity and vital capacity being primarily affected, functional residual capacity being less affected, and residual volume even less. These changes are consistent with a decrease in pulmonary compliance.

American Thoracic Society, THE DIAGNOSIS OF NON-MALIGNANT DISEASES RELATED TO ASBESTOS, American Review of Respiratory Disease, 1986, Vol. 134, pp. 363-368

QUOTABLE QUOTES: SMALL AIRWAYS OBSTRUCTION & IMPAIRMENT

QUESTION:

Isn't it true that:

1....clinically significant airways obstruction is not expected to occur as a result of asbestos exposure?

2....any airway changes resulting from asbestos exposure are not functionally significant?

QUOTE:

DIAGNOSIS OF ASBESTOS-RELATED DISEASE

. . . Peripheral airways dysfunction has been demonstrated in population studies and the pathologic analog described. However, clinical and epidemiologic evidence is now more than sufficient to firmly conclude that clinically significant chronic airways obstruction is not an expected consequence of asbestos exposure in the absence of far more important causal factors, most notably, smoking.

Hans Weill, M.D., F.C.C.P. Diagnosis of Asbestos-Related Disease, CHEST, Vol. 91, No. 6, June, 1987, p. 803

ASBESTOSIS

. . .

Microscopically, early lesions of asbestosis are concentrated at the level of the respiratory bronchiole, where the basic disease process is periobronchiolar fibrosis.[46] . . . Wright and Churg[87] suggested the term "asbestos airway disease" for the marked fibrosis found in the walls of respiratory bronchioles and alveolar ducts of some asbestos workers, for there is no proof that the lesion progresses to asbestosis. Such asbestos airway disease is not visible in chest x-rays and is not functionally significant.[40]

GREENBERG, S. DONALD, "Asbestos", Pulmonary Pathology, 1988, Chapter 22, p. 629

QUOTABLE QUOTES: SMALL AIRWAYS OBSTRUCTION & IMPAIRMENT

QUESTION:

Isn't it true that FEF^{25-75}, closing volume, closing capacity, and volume of isoflow on pulmonary function testing:

1....appear to detect small airway changes?

2....are not recommended for assessment of impairment?

QUOTE:

(B.) MISCELLANEOUS TESTS OF FLOW AND VOLUME

The $FEF^{25-75\%}$, closing volume, closing capacity, and volume of isoflow are tests that appear to detect changes in small airways of less than two millimeters internal diameter and are not recommended for the assessment of impairment...

American Thoracic Society, EVALUATION OF IMPAIRMENT/DISABILITY SECONDARY TO RESPIRATORY DISEASE, American Review of Respiratory Disease, Vol. 2, No. 2, 1982, pp. 945-950

Miscellaneous Tests of Flow and Volume

The FEV^{25-75}, closing volume, closing capacity, and volume of isoflow are tests for the detection of early changes of small airways of less than 2mm internal diameter. They are not recommended for the assessment of impairment because they may be normal when overall function as determined by the FEV is normal. On the other hand, one or more of these tests if almost always abnormal when overall function is abnormal, thus adding nothing of clinical significance to the determination of functional impairment.

American Thoracic Society, EVALUATION OF IMPAIRMENT/DISABILITY SECONDARY TO RESPIRATORY DISORDERS, American Review of Respiratory Disease, March 6, 1986, pp. 1205-1209.

QUOTABLE QUOTES: PROGRESSION

QUESTION:

Isn't it true that asbestosis:

1....may not progress?

2...,with first exposure since 1960, has become a rare disease?

3...,if it is progressive at all, the progression is very slow?

QUOTE:

PROGRESSION OF ASBESTOSIS

We have followed for up to 18 years 1,632 persons exposed in shipyards, paper mills, and asbestos product plants by clinical, physiologic and radiographic studies.

. . .

From this we concluded: 1) with first exposure since 1960, asbestosis has become a rare disease; 2) radiographic progression of two or more steps did occur but clearly was uncommon (among 447 persons followed yearly for 11±4 yrs, progression was recorded in only 13.2%, more often among 97 persons with continued low level exposure); 3) radiographic regression was almost as frequent (7%) as was progression (9%) among those with continued exposure, but regression of three or more steps was unusual; 4) in the great majority (80%), no parenchymal changes were noted during 11 years, and when progression did occur it was always very slow; 5) there was no statistical evidence that progression was more rapid or more severe in those with initially more advanced disease, perhaps because of the small number with severe asbestosis; and 6) there was also no evidence that initial readings of 0/1 or 1/0 carried a worse prognosis than initial readings of 0/0.

Edward A. Gaensler, FCCP; Peter J. Jederlinic and Theresa C. McLoud, Third International Conference on Environmental Lung Disease, Chest, Vol. 91, No. 2, February, 1987, p. 305

QUOTABLE QUOTES: OCCUPATION

QUESTION:

Isn't it true that:

1....the biological effects of asbestos differ not only with the kind of asbestos used, but also with the type of occupational exposure?

2....accurate statistics of the incidence and prevalence of asbestosis are few and valid comparisons between similar and dissimilar asbestos industries in one country or different countries are not possible?

3....statistics from one occupation cannot be applied to other occupation groups?

QUOTE:

Asbestos

. . .The biological effects of asbestos differ not only with the kind of asbestos but also with the type of occupational exposure--for example, mining and milling, manufacture, and insulation work.

William N. Rom, ASBESTOS AND RELATED FIBERS, Chapter 14, Environmental and Occupational Disease, p. 159, 1983

. . .

QUOTE:

Incidence and Prevalence

Accurate statistics of the incidence and prevalence of asbestosis are few, and valid comparisons between similar and dissimilar asbestos industries in one country or in different countries are not possible.

W. Raymond Parkes, Occupational Lung Disorders (Text), 2nd Ed., 1982, p. 248

. . .

QUOTE:

Information currently available concerning asbestosis has been derived largely from studies of employees of asbestos textile factories and should properly be referred to such individuals. It is inadequate to speak now of "asbestos workers." With the growth of asbestos utilization, including rapid multiplication of the number and variety of its applications, it would perhaps be more accurate to categorize workmen exposed to asbestos as "asbestos textile workers," "asbestos insulation workers," "asbestos miners," "asbestos mill workers," "asbestos-cement workers," etc. The different occupations vary widely in important respects; in intimacy, intensity and duration of exposure, in variety and grade of asbestos used, in working conditions, in concomitant exposure to other dusts or inhalants.

("The Occurrence of Asbestosis Among Insulation Workers in the United States", Selikoff, I.J., Churg, J., Hammond, E.C.; Annals of the New York Academy of Science, Vol. 132, Art. 1, p. 139)

QUOTABLE QUOTES: CIGARETTE SMOKE

QUESTION:

Isn't it true that cigarette smoke:

1....is the most significant source of preventable morbidity and premature mortality in America?

2....is the killer of over 350,000 people a year in the United States which is more than all American lives lost in all 20th century wars?

3....reduces a person's life expectancy by 5.5 minutes for each cigarette smoked?

4....reduces the average life expectancy of a smoker by 5 to 8 years?

QUOTE:

OVERALL TOLL OF SMOKING

Excess Mortality

Cigarette smoking has been identified in the U.S. Surgeon General's Reports since 1964 as the single most significant source of preventable morbidity and premature mortality. The estimated annual toll of excess mortality from cigarette smoking in the United States exceeds 350,000 people, more than the total number of American lives lost in all wars during the twentieth century.[1]

. . .

It has been estimated that an average of 5.5 minutes of life is lost for each cigarette smoked -- about the time taken to smoke it. This estimate is based on an average reduction in life expectancy for cigarette smokers of 5 to 8 years.

Jonathan E. Fielding, PUBLIC HEALTH AND PREVENTIVE MEDICINE (Text), Chapter 26: Smoking: Health Effects and Control, 1986, John M. Last, Editor, p. 999-1000

A-761

QUOTABLE QUOTES: LUNG CANCER

QUESTION:

Isn't it true that in deciding whether a tumor should be ascribed to asbestos that:

1....cell type cannot be utilized in making that determination?

2....the rule adopted and followed in the United Kingdom is that asbestosis must be present before a cigarette smoking worker can receive compensation?

3....asbestosis must be present before a lung cancer in a cigarette smoker can be attributed to asbestos exposure?

QUOTE:

ASSOCIATION WITH CARCINOMA

. . .Certainly one cannot use cell type in deciding whether a tumor should be ascribed to asbestos. When this question arises, I follow the rule adopted in the United Kingdom, which requires that asbestosis be present before a cigarette-smoking worker can receive compensation based on asbestos exposure for a carcinoma of the lung(36).

Andrew Churg, NONNEOPLASTIC ASBESTOS-INDUCED DISEASE, The Mount Sinai Journal of Medicine, Vol. 53, No. 6, June, 1986, p. 414

. . .

QUOTE:

ASBESTOS-ASSOCIATED LUNG CANCER

. . .

It has been reported that asbestos fibers in the lung contribute to the development of lung cancer only if asbestosis is also present.[40,79] It seems probable that in occupational settings where exposure to asbestos dust has been reduced to levels where asbestos is absent, excess lung cancer may not occur.[88]

GREENBERG, S. DONALD, "Asbestos", Pulmonary Pathology, 1988, Chapter 22, p. 631

QUOTABLE QUOTES: LUNG CANCER

QUESTION:

Isn't it true that:

1....a threshold exists for lung cancer above the threshold for asbestosis?

2....it takes a greater dose of asbestos to cause lung cancer than that necessary to cause asbestosis?

QUOTE:

EDITORIAL

IS ASBESTOS OR ASBESTOSIS THE CAUSE OF THE INCREASED RISK OF LUNG CANCER IN ASBESTOS WORKERS?

. . .

A causal relation between lung cancer and asbestosis cannot be established by epidemiological means.

. . .

There is therefore strong prima facie evidence that in occupational exposure to asbestos a threshold exists before the risk of lung cancer is increased.

. . .

It seems probable, in Merewether's terminology, that it is not asbestos per se but asbestosis which prepares the soil for subsequent malignancy. But a definitive answer to this question is still urgently awaited.

K. Browne, BRITISH JOURNAL OF INDUSTRIAL MEDICINE, 1986, Vol. 43, pp. 145-149

QUOTE:

A THRESHOLD FOR ASBESTOS RELATED LUNG CANCER

Whether a threshold exists for asbestos related lung cancer is question of great importance.

. . .

The data given above show that every industrial group of asbestos workers with adequate data on individual duration and intensity of exposure provides some evidence of a threshold of cumulative exposure below which the risk of lung cancer does not appear to be raised. The evidence for a threshold is also supported by one well documented study giving duration of exposure only, and by several studies showing no increase in lung cancer risks despite the presence of low levels of other asbestos related disease.

. . .

A threshold for asbestos related lung cancer at or above the threshold for asbestosis does not provide that the risks are linked. Nevertheless, it is consistent with the hypothesis that the increased risk of lung cancer due to exposure to asbestos occurs only where asbestosis is already present, a belief for which the evidence is now considerable.

K. Browne, BRITISH JOURNAL OF INDUSTRIAL MEDICINE, 1986, Vol. 43, pp. 556-558

QUOTABLE QUOTES: LUNG CANCER RISK

QUESTION:

Isn't it true that lung cancer:

1....is uncommon among asbestos insulation workers who have no history of cigarette smoking?

2....risk in non-smoking insulation workers, if it is increased, such increase is not great?

3....among insulation workers is largely confined to those men with a history of cigarette smoking?

QUOTE:

. . .

But this information is of tremendous importance. It is almost like saying that, if you work in a dynamite factory, you shouldn't smoke. And cancer of the lung could be wiped out in your trade if you people wouldn't smoke cigarettes, period.

DR. IRVING J. SELIKOFF; REPORT OF PROCEEDINGS OF THE TWENTY-FIRST CONVENTION OF THE INTERNATIONAL ASSOCIATION OF HEAT AND FROST INSULATORS AND ASBESTOS WORKERS, HELD AT CHICAGO, ILLINOIS, SEPT. 5-7, 1967, p. 71

. . .

QUOTE:

RELATION OF CIGARETTE SMOKING TO RISK OF DEATH OF ASBESTOS-ASSOCIATED DISEASE AMONG INSULATION WORKERS IN THE UNITED STATES

Lung Cancer Among Cigarette-Smoking Asbestos Insulation Workers

Recent experiences have confirmed that lung cancer among insulation workers is largely confined to those men with a history of cigarette smoking.

. . .

Lung Cancer Deaths Among Insulation Workers Who Do Not Smoke Cigarettes

. . .

Among the 2066 non-cigarette smoker in the nation-wide study, 73 deaths occurred between 1 January 1967 and 31 December 1971. Two were due to lung cancer. One of these two men was a cigar and pipe smoker, and the other never smoked regularly.

It seems clear, then, that lung cancer is uncommon among asbestos insulation workers who have no history of cigarette smoking and that if the risk is increased such an increase is not great.

Hammond, E. C. & Selikoff, I. J., BIOLOGICAL EFFECTS OF ASBESTOS, pp. 312-315, October, 1972

A#65

QUOTABLE QUOTES: HOUSEHOLD CANCER RISK

QUESTION:

Isn't it true that epidemiological studies have not demonstrated a risk of lung cancer among family or household exposures?

QUOTE:

POPULATIONS AT RISK

. . .So far, epidemiological studies have investigated lung cancer risk only for occupational groups--factory workers, insulators, miners and millers, shipyard workers, and others in the panolpy of asbestos trades. Studies of lung cancer risk for those less intensely exposed (e.g., family contacts) have not yet been completed.

Irving J. Selikoff, PUBLIC HEALTH AND PREVENTIVE MEDICINE (Text), Chapter 14: Occupational Respiratory Diseases, 1986, John M. Last, Editor, p. 529

QUOTABLE QUOTES: GASTROINTESTINAL CANCER

QUESTION:

What criteria should be met in order to establish a cause and effect relationship between an agent such as asbestos and a certain disease?

Do you agree with the criteria for establishing a cause and effect relationship between an agent and a disease stated by Selikoff and Lee as:

(1) a statistically significant association be established between exposures of subjects to the agent (asbestos) and the subsequent development of the syndrome;

(2) some degree of dose response relation should be demonstrable;

(3) in the event that the agent or its metabolic product can be shown in tissue, the concentration in exposed subjects should be greater than in unexposed subjects;

(4) the demonstration of pathological changes in animals after exposure to the agent, similar to those seen in man, would strengthen the evidence for causation, but the failure to obtain such changes would not negate other evidence supporting a causative relation; and

(5) the role of numerous attendant circumstances capable of influencing the appearance of manifestations of the disease initiated by the agent should be evaluated.

Isn't it true that:

1....there is no consistent statistical association between exposure to asbestos and gastrointestinal cancer?

2....the dose response relationship between asbestos and gastrointestinal cancer has not been demonstrated?

3....the results of ingestion studies in laboratory animals with asbestos have been negative for gastrointestinal cancer?

4....the criteria set forth in Selikoff & Lee to establish a cause and effect relationship between asbestos and gastrointestinal cancer have not been demonstrated in the literature?

5....the epidemiological, clinical, and experimental studies provide insufficient evidence to support a cause and effect relationship between exposure to asbestos and cancer of the gastrointestinal tract?

QUOTE:

DISCUSSION

. . .

The criteria that should be met to establish cause and effect relation have been stated in many different ways by numerous investigators. These criteria as restated by Selikoff and Lee[40] are that:

(1) a statistically significant association be established between exposures of subjects to the agent (asbestos) and the subsequent development of the syndrome;

(2) some degree of dose response relation should be demonstrable;

(3) in the event that the agent or its metabolic product can be shown in tissue, the concentration in exposed subjects should be greater than in unexposed subjects;

(4) the demonstration of pathological changes in animals after exposure to the agent, similar to those seen in man, would strengthen the evidence for causation, but the failure to obtain such changes would not negate other evidence supporting a causative relation; and

(5) the role of numerous attendant circumstances capable of influencing the appearance of manifestations of the disease initiated by the agent should be evaluated.

The present evaluation found no consistent statistical association between exposure to asbestos and gastrointestinal cancer, a dose response relation was not apparent, and results of ingestion studies in laboratory animals were negative. In terms of these criteria the findings of the present evaluation do not support a cause and effect relation between exposure to asbestos and gastrointestinal cancer. The third criterion was not evaluated since studies have not been conducted to evaluate the concentration of asbestos fibres or bodies in the gastrointestinal tissues of asbestos exposed and non-exposed subjects. Although various factors associated with an increased risk of gastrointestinal cancer have been identified, none of the 32 studies made any adjustments to the risk estimates for gastrointestinal cancer for any of these factors. Based on the epidemiological, clinical, and experimental studies evaluated, there is no evidence to support a cause and effect relation between exposure to asbestos and cancer of any gastrointestinal site.

Edelman, D., "Exposure to Asbestos and the Risk of Gastrointestinal Cancer: A Reassessment", British Journal of Industrial Medicine, 1988, Vol. 45, p. 81

QUOTABLE QUOTES: MESOTHELIOMA

QUESTION:

Isn't it true that:

1....a large proportion of mesotheliomas have no known cause?

2....about 50% of mesotheliomas in men have no known cause?

3....that 95% of mesotheliomas in women have no known cause?

QUOTE:

MALIGNANT MESOTHELIOMA

Epidemiology

However, a large proportion of mesotheliomas (probably about 50% of tumors in men and 95% of tumors in women) have no known cause.

Andrew Churg, M.D., Chest, Vol. 89, No. 4, April, 1986, p. 367S

IF IT'S NOT MESOTHELIOMA,

IT'S NOT ASBESTOS RELATED

An Updated Survey of the Epidemiologic Studies of Cancers Other than Mesothelioma and Lung Carcinomas Among Allegedly Asbestos-Exposed Populations

by

Gary D. Elliston
Stephanie L. Spardone

DeHay & Blanchard
Dallas, Texas

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INTRODUCTION

Epidemiology **does not** establish causation in an individual case. Yet, six or twelve lay jurors are sometimes asked to consider epidemiological evidence and decide whether asbestos exposure was a producing or proximate **cause** of an individual's cancer. Our goal in this paper is to provide a brief discussion of general epidemiological principles and review alleged association between asbestos and various cancers including pharyngeal, laryngeal, esophageal, stomach, colon, rectal, pancreatic, prostatic, and kidney cancer as well as lymphoma.

Despite numerous studies, there is still substantial debate in the medical profession about whether asbestos is a cause of certain cancers. Although there are many problems associated with epidemiological studies of asbestos exposure and disease in general, it is widely accepted that heavy exposure to asbestos may increase the risk for mesothelioma and lung cancer when antecedent asbestosis and smoking are present. Whether asbestos exposure increases the risk for other cancers is disputed. The medical literature discussed herein provides a strong evidence that asbestos does *not* cause or enhance an individual's risk for lymphoma or cancer of the:

A. pharynx
B. larnyx
C. esophagus
D. stomach
E. small intestine
F. colon
G. rectum
H. pancreas
I. prostate or
J. kidney

I. EPIDEMIOLOGICAL PRINCIPLES

Epidemiology is the study of the incidence and distribution of disease in human populations and the factors that influence these patterns. It combines concepts and methods from statistics, sociology, and biology to study disease. Lilienfeld, A.M., and Lilienfeld, D.E., Foundations of Epidemiology, p. 4 (1980).

The task of the epidemiologist is to detect unusual patterns of disease and to **associate** those patterns with certain environmental or biological risk factors. The ultimate goal of the epidemiologist is to establish causation. However, due to its statistical foundations, epidemiologic data is most useful in recognizing increased rates of affliction in **different** groups, rather than to identify the specific cause of a disease in a specific **individual**. Thus, epidemiological studies address the question whether exposure to X increases the **incidence** of disease Y, **not** whether exposure to X **causes** disease Y.

The data obtained from the epidemiologic study is typically used in one of three ways. First, such data is used to clarify the etiology of a specific disease by combining epidemiologic data with data from other scientific disciplines such as genetics, biochemistry, or microbiology. Second, epidemiologic studies may be used to evaluate pre-existing data with etiologic hypotheses for consistency. Finally, epidemiologic data can be instructive in developing and evaluating preventive measures and public policy. Id. at 5.

A. EPIDEMIOLOGIC METHOD

As in all areas of scientific research, the experimental study yields the most methodologically valid and reliable results. In the experimental study, a suspected risk factor is either introduced or eliminated. The results of a properly conducted experimental study are likely to allow conclusions regarding causation. Schottenfeld, D., Fraumeni, J.F., Cancer Epidemiology and Prevention, 3 (1982). Because implementation of the experimental method is not ethically feasible in human research, non-experimental studies compose the largest body of human cancer information.

Two types of non-experimental epidemiologic studies are employed in cancer research; the analytic and the descriptive. The descriptive or observational study examines the incidence and prevalence of a certain disease in a given population over time. The occurrence of disease is examined according to time, place and person and may be measured according to incidence or mortality. See id. at 3-6.

The analytic study takes the results obtained by the descriptive study and formulates a hypothesis which is then

evaluated by additional observational studies. Depending on the type of population studied, there are two forms of analytic studies; cohort and case control. The cohort study identifies subjects by their exposure while the case-control study identifies subjects by disease. The results derived from a cohort study may be expressed quantitatively as either attributable risk (the difference between the two incidences), or relative risk (the ratio of the two incidences). Id at 6-7.

Analytic studies, whether case control or cohort, may be either cross-sectional, retrospective, or prospective. See Lilienfeld at 193-195. In the retrospective study the epidemiologist identifies individuals who have and do not have the disease being studied. He then may obtain, through a variety of methods, their history of past exposure to the suspected risk factor under study. In the cross-sectional study, although the same groups are under study, disease experience is examined at a given point in time. Finally, prospective studies identify individuals with a certain exposure and then track their future morbidity or mortality. Id at 226.

B. RESULTS

As mentioned earlier, the goal of epidemiology is to establish causation. Note, however, that the identification of an association and its quantitative estimation does not establish causation. Alternative explanations for the results obtained must be considered and adjustments made for chance errors and confounding factors. See Schottenfeld and Fraumeni at 10. Adjusting for errors of chance is achieved by accompanying quantitative risk estimates with statistical confidence limits. Observed values of risk which include one (1.0) do not establish association. Id.

Errors in selection and/or classification may also explain a relative risk greater than one. When individuals are classified incorrectly as to the exposure under study, either a false-positive or a false-negative may result. Id. at 11. Errors may also arise from over-inclusion of subjects who are not representative of the group under study. Although these errors occur most frequently in case-control studies, they may also occur in prospective cohort studies where all cases occur after the population group has been identified. Id. Because the retrospective study examines exposed and non-exposed subjects after an effect has already occurred, selection bias is hard to avoid. The natural tendency is to include all those with the disease in the population. Id. Relative risk may also be artifactual due to the presence of various confounding factors, which are variables other than those under study. Id at 10. Age, sex, and socioeconomic

status are common confounding variables in almost all studies. The task of the epidemiologist is to separate the effect under study from the effect of extraneous or confounding factors which may be associated with the study factor. This is most efficiently achieved through matching, which is a process where both study subjects and control subjects are matched according to confounding factors. Id. at 12. If subjects are matched correctly, any differences in results may be more strongly explained in terms of the exposure under study rather than the confounding variable.

C. HEALTHY WORKER EFFECT

As mentioned above, age is a confounding factor routinely associated with disease risk and exposure frequency. The standardized mortality ratio (SMR) was developed to account for age. This is an age-standardized relative index of mortality which compares the mortality experience of the study population to that of a comparison or standard population; generally the total U.S. population. McMichael, A.J., "Standardized Mortality Ratios and the Scratching Beneath the Surface," Journal of Occupational Medicine, 1976, Vol. 18, pp. 165-168, 165. It is the use of the general population as the comparison group which produces the "healthy worker effect" in occupational epidemiologic studies. Since the population at large includes disabled, elderly, and sick people; their mortality experience is usually greater than the occupational population under study. Thus, the relative risk for the occupational cohort under study might be artificially low. Adjustments can be made to offset this "healthy worker effect," but one must necessarily allow for variation since the "healthy worker effect" does not act consistently across different age groups, races, work-status groups, causes of death, and/or periods of observation. Id. at 168.

D. CRITICAL REVIEW

Before the results of a study are considered authoritative, the study should undergo critical review. During critical review the methodology and results of a study are reviewed and critiqued by others in the scientific community.

The results of epidemiologic studies may be evaluated on many different levels. Sir Bradford Hill suggested the following criteria for determining the strength of the causal inference:

> 1. **Strength:** This criterion refers to the magnitude of the incidence ratio. Strong associations are more likely to be causal because if the association were due to some other bias or confounding factor, such factor

presumably would also be identifiable. However, weak associations cannot be automatically ruled out, but should be viewed relative to other possible causes.

2. **Consistency:** Have subsequent studies of different populations in different circumstances observed the same association? Repeated observations of similar results rules out the potential effects of chance and other errors.

3. **Specificity:** A cause should lead to a single, not multiple effect. Given that many diseases have multiple etiologies, this is not a plausible measure.

4. **Temporality:** The logical necessity that the cause, or the exposure in the occupational setting precede the effect or disease in time.

5. **Biologic gradient:** This criteria refers to the dose-response relationship. Thought to be the strongest positive evidence of an occupational hazard, dose-response refers to the relationship between intensity of exposure and subsequent incidence of disease. Unfortunately, outside of the laboratory setting, the measurement of intensity is very difficult.

6. **Plausibility:** Is causal inference biologically plausible? This criterion is of little value since what is biologically plausible depends on the biological knowledge of the day.

7. **Coherence:** Logical coherence requires that a cause and effect relationship not conflict with what is known of the natural history and biology of the disease.

8. **Experiment:** Does experimental evidence exist to support the causal inference? As mentioned earlier, experimental data is rarely available for human populations. Occasionally, crude semi-experimental data may be derived if some preventive action is taken, such as reducing dust levels. Strong support for the causal inference is found when the disease incidence subsequently decreases.

9. **Analogy:** Illustrated as, "if one drug can cause birth defects, perhaps another may as well." The importance of this criterion seems minimal.

Hill, Sir Austin Bradford, "The Environment and Disease: Association or Causation?" Proceedings of the Royal Society of Medicine - Section of Occupational Medicine, (1965), pp. 295-300.

Hill admitted that none of the "nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a sine qua non." Id. at 299. In any event, the results of all epidemiological studies should be evaluated with similar criteria.

E. EPIDEMIOLOGY AND ASBESTOS RELATED DISEASE

1. Problems of Extrapolation

Use of epidemiological studies in an attempt to establish an association between asbestos exposure and a particular disease can be quite problematic for a variety of reasons. First, the studies from which most of the available information was derived examined cancer rates in heavily exposed factory workers, shipyard workers, and insulators. Although some of these studies examined incidence of cancers other than mesothelioma and lung cancer, the majority focused on lung-related diseases. Furthermore, extrapolation of data from such studies which investigated non-routine cancer incidence can be misleading. Recent exposure levels may be quite different from the heavily exposed shipyard worker, insulator, or factory worker of the past. The fact that dose-response relationships have not been established for most non-lung related cancers, together with the exposure variance between the workers of the past and the Plaintiff of the 1990's, must be carefully considered when attempting to extrapolate epidemiological data.

2. Occupation and Exposure Distinctions

The degree, type, and duration of exposure are also important considerations. Exposures in one industry cannot necessarily be applied to those in another industry. Workers in various industries were exposed to different types and levels of asbestos under many different working conditions.

Dr. Irving J. Selikoff, when discussing asbestosis, acknowledged differences between the various occupational exposures:

> Information currently available concerning asbestosis has been derived largely from studies of employees of asbestos textile factories and should properly be referred to such individuals. It is inadequate to speak now of "asbestos workers." With the growth of asbestos utilization, including rapid multiplication of the number and variety of its applications, it would perhaps be more accurate to categorize workmen exposed to asbestos as "asbestos textile workers," "asbestos-cement workers," etc. The different occupations vary widely in important respects; in intimacy, intensity and duration of exposure, in variety and grade of asbestos used, in working conditions, in concomitant exposure to other dusts or inhalants. The importance of this distinction and parallel obligation to evaluate and study the experience of asbestos exposure in other trades, is emphasized by the fact that asbestos textile workers are now a minority of those exposed during the industrial use of asbestos.

Selikoff, I.J., Churg, J., and Hammond, E. C.: "The Occurrence of Asbestosis Among Insulation Workers in the United States," Annals of the New York Academy of Science, 1965, Vol. 132, p. 139.

Dr. William Rom has also written that the type of occupational exposure may affect the risk of disease:

> The biological effects of asbestos differ not only with the kind of asbestos but also with the type of occupational exposure -- for example, mining and milling, manufacture, and insulation work.

Rom, William N., Environmental and Occupational Medicine, p. 159, (1983).

Dr. Raymond Parkes indicated that valid comparisons between different asbestos industries are not possible for asbestosis:

> Accurate statistics of the incidence and prevalence of asbestosis are few, and valid comparisons between similar and dissimilar asbestos industries in one country or in different countries are not possible.

Parkes, Raymond W., Occupational Lung Disorders, pp. 248-249, (1982).

3. Latency

An additional complication which must be considered in the use of epidemiological studies is the long latency period between exposure and the manifestation of symptoms. Dr. Selikoff reports that the latency period between onset of asbestos exposure and death can be anywhere from two, three, four or more decades. Selikoff, I.J., Hammond, E.C., and Seidman, H., "Latency of Asbestos Disease among Insulation Workers in the United States and Canada," Cancer, 1980, Vol. 46, pp. 2736-2740, 2740.

4. Best Evidence v. Death Certificate

Another problem associated with certain studies is reliance on best evidence as opposed to death certificates. Since national mortality statistics are based on cause of death as reported on death certificates, when standardized mortality ratios are computed according to "best-evidence," valid comparison is impossible.

Drs. Morgan, Foliart, and Wong discussed the confounding effect of using best evidence in their review of eighteen cohort studies which provided data on gastrointestinal cancers:

> Although diagnostic inaccuracy is troubling, it is not easily remedied. Selikoff has used "best evidence" from numerous sources, rather than the certified cause of death, to calculate standardized mortality ratios (SMRs). However, 'best evidence' data cannot properly be compared with national mortality statistics, which are derived solely from death certificates. Unless one can also correct the statistics from the U.S. reference population, comparisons are invalid because of the underlying principle that both study and reference populations should have similar ascertainment and classification of death. Another statistically questionable practice is attributing to cancer those deaths previously certified as due to a cause other than cancer, but where cancer was present (Selikoff communication quoted by Miller). Again, without a similar mechanism for including cancer as a contributing cause of death in the national mortality statistics, such comparisons will either create an apparent excess of cancer in the study population or will exaggerate any excess already there.

Morgan, R.W., Foliart, D.E., and Wong, O., "Asbestos and Gastrointestinal Cancer," Western Journal of Medicine, 1985, Vol. 143, p. 61.

5. Reliance on Subject Memory

Retrospective or cross-sectional studies are frequently employed, therefore great reliance must be placed on the subject's recollection. The extent to which the subject accurately relates information about his background, family, health, and dietary habits is potentially confounding and can lead to an incorrect association. Since there can be multiple risk factors for disease, and exposure to such risk factors may act either alone or in concert, the epidemiologist must rely on the subject's recollection. The obvious way to avoid any confounding is to undertake a prospective study and control for confounding factors.

II. CANCER INCIDENCE AND MORTALITY

A. MORTALITY IN GENERAL POPULATION

Cancer is the second leading cause of death in the U.S. population. Cancer accounted for approximately 22.1 percent of deaths in 1985, 22.3 percent of deaths in 1986, and 22.5% of deaths in 1987. The mortality rates for leading causes of death in the United States in 1985, 1986, and 1987 are demonstrated in the following charts.

MORTALITY FOR LEADING CAUSES OF DEATH - 1985

Rank	Cause of Death	Number of Deaths	Death Rate per 100,000 Population	Percent of Total Deaths
	All Causes	2,086,440	739.0	100.0
1.	Heart Diseases	777,113	361.4	37.0
2.	Cancer	461,850	170.8	22.1
3.	Cerebrovascular Diseases	152,050	61.0	7.3
4.	Accidents	93,457	36.0	4.5
5.	Chronic Obstructive Lung Diseases	71,047	26.0	3.4
6.	Pneumonia & Influenza	67,815	23.0	3.2
7.	Diabetes Mellitus	35,969	13.1	1.8
8.	Suicide	29,453	11.2	1.4
9.	Cirrhosis of Liver	26,767	10.6	1.3
10.	Arteriosclerosis	23,925	7.6	1.1
11.	Nephritis	21,349	7.3	1.0
12.	Homicides	18,980	7.6	1.0
13.	Diseases of Infancy	18,248	6.9	0.9
14.	Septicemia & Pyemia	17,182	6.0	0.8
15.	Aortic Aneurysm	15,112	5.3	0.7
	Other & Ill-defined	259,691	99.1	12.5

Source: Vital Statistics of the United States 1985.

Ca-A Cancer Journal for Clinicians, Jan/Feb. 1990, Vol. 40, p. 8.

MORTALITY FOR LEADING CAUSES OF DEATH - 1986

Rank	Cause of Death	Number of Deaths	Death Rate per 100,000 Population*	Percent of Total Deaths
	All Causes	2,105,361	732.7	100.0
1.	Heart Diseases	765,450	267.5	36.4
2.	Cancer	469,376	170.8	22.3
3.	Cerebrovascular Diseases	149,643	48.5	7.1
4.	Accidents	95,277	38.3	4.5
5.	Chronic Obstructive Lung Diseases	76,585	26.5	3.6
6.	Pneumonia & Influenza	69,810	22.3	3.3
7.	Diabetes	37,164	13.1	1.8
8.	Suicide	30,904	11.6	1.5
9.	Cirrhosis of Liver	26,159	10.1	1.2
10.	Atherosclerosis	22,709	8.9	1.1
11.	Nephritis	21,757	7.8	1.0
12.	Homicide	21,731	8.1	1.0
13.	Septicemia	18,788	6.3	0.9
14.	Diseases of Infancy	18,291	8.6	0.9
15.	Aortic Aneurysm	15,287	5.2	0.7
	Other & Ill-defined	266,300	99.3	12.6

*Age-adjusted to the 1970 US standard population.
Source: Vital Statistics of the United States, 1986.

Ca-A Cancer Journal for Clinicians, Jan/Feb. 1990, Vol. 40, p. 12.

MORTALITY FOR LEADING CAUSES OF DEATH - 1987

Rank	Cause of Death	Number of Deaths	Death Rate per 100,000 Population*	Percent of Total Deaths
	All Causes	2,123,323	737.5	100.0
1.	Heart Diseases	760,353	250.5	35.6
2.	Cancer	476,927	170.4	22.5
3.	Cerebrovascular Diseases	149,635	47.7	7.1
4.	Accidents	95,020	35.6	4.5
5.	Chronic Obstructive Lung Diseases	78,360	26.5	3.7
6.	Pneumonia & Influenza	69,225	21.5	3.3
7.	Diabetes	36,532	13.2	1.6
8.	Suicide	30,796	11.4	1.5
9.	Cirrhosis of Liver	26,201	10.0	1.2
10.	Diseases of Arteries	22,610	7.6	1.1
11.	Atherosclerosis	22,474	6.7	1.1
12.	Nephritis	22,052	7.2	1.0
13.	Homocide	21,103	7.8	1.0
14.	Septicemia	19,516	6.6	0.9
15.	Diseases of Infancy	15,222	8.4	0.9
	Other & Ill defined	271,477	94.9	12.8

*Age-adjusted to the 1970 US standard population.
Source: Vital Statistics of the United States, 1987.

Ca-A Cancer Journal for Clinicians, Jan/Feb. 1991, Vol. 41, p. 22.

The American Cancer Society has projected that there will be over one million new cancer cases in 1991, excluding non-melanoma skin cancer. It is anticipated that California (110,000), New York (85,000), Florida (73,000), Pennsylvania (65,000), and Texas (59,000) will lead the nation in total new cases.

ESTIMATED NEW CANCER CASES FOR ALL SITES,
BY STATE - 1991

State	All Sites*	Major Sites								
	Number of Cases	Female Breast	Colon & Rectum	Lung	Oral	Uterus	Prostate	Skin (Melanoma)	Pancreas	Leukemia
Alabama	19,600	2,600	2,400	2,100	600	850	2,200	550	500	450
Alaska	1,200	175	150	200	30	40	75	50	25	25
Arizona	15,200	2,200	1,900	2,000	375	600	1,700	475	350	400
Arkansas	11,500	1,500	1,600	2,100	210	425	1,320	360	275	300
California	110,000	16,000	14,900	15,000	3,100	4,600	10,200	2,600	3,000	2,150
Colorado	10,300	1,800	1,600	1,300	250	350	1,100	400	300	275
Connecticut	15,600	2,800	2,400	2,100	475	650	1,600	450	450	350
Delaware	3,100	550	425	450	100	125	375	100	60	80
Dist. of Col.	3,600	550	500	450	125	200	550	100	70	80
Florida	73,000	10,500	10,600	11,500	2,500	2,500	9,000	2,200	1,900	1,900
Georgia	25,600	4,200	3,200	4,000	1,000	1,100	2,100	800	600	600
Hawaii	3,500	450	550	500	150	150	250	90	90	100
Idaho	3,600	500	500	450	100	175	500	150	125	80
Illinois	52,000	8,600	8,000	7,600	1,700	2,400	5,300	1,200	1,420	1,200
Indiana	28,700	3,900	3,800	3,800	650	1,000	2,900	650	650	650
Iowa	13,100	2,200	2,300	1,600	450	500	1,700	400	350	325
Kansas	10,400	1,700	1,700	1,500	300	475	1,200	325	300	350
Kentucky	17,300	2,300	2,400	3,100	475	700	1,600	450	400	375
Louisiana	19,100	2,400	2,700	3,000	650	1,000	2,000	425	500	400
Maine	6,300	800	950	850	225	300	600	150	150	175
Maryland	21,000	3,400	2,900	3,200	550	800	2,100	500	550	475
Massachusetts	29,700	5,550	4,700	4,000	800	1,200	3,000	850	750	700
Michigan	48,000	6,400	6,200	5,800	1,100	1,600	4,600	750	1,000	1,100
Minnesota	17,700	3,100	2,500	2,200	400	700	2,300	425	550	600
Mississippi	11,800	1,600	1,500	1,800	250	500	1,300	300	325	300
Missouri	24,700	4,000	3,500	3,800	550	950	2,800	600	600	600
Montana	3,400	500	500	450	100	175	500	100	90	80
Nebraska	6,500	1,100	1,200	1,000	100	225	800	275	150	175
Nevada	4,900	700	650	850	150	175	375	150	125	100
New Hampshire	4,800	850	750	650	150	200	550	125	125	100
New Jersey	39,100	6,800	6,100	5,400	1,200	1,700	4,100	1,100	900	900
New Mexico	5,100	800	700	650	100	175	650	150	150	150
New York	85,000	15,200	13,900	11,200	2,700	2,500	9,000	2,700	2,200	1,500
North Carolina	25,700	4,800	3,900	4,400	850	1,200	3,400	900	750	650
North Dakota	2,500	425	425	375	50	150	500	60	60	100
Ohio	50,000	8,200	7,800	7,800	1,400	2,400	5,200	1,300	1,200	1,300
Oklahoma	14,700	2,500	2,600	2,400	450	750	1,600	475	350	425
Oregon	13,000	1,900	1,700	2,100	375	550	1,700	425	325	375
Pennsylvania	65,000	10,200	10,100	9,100	1,500	3,000	7,000	1,550	1,500	1,650
Rhode Island	5,300	1,000	850	750	225	250	600	150	125	100
South Carolina	14,200	2,100	1,800	2,200	650	750	1,800	500	400	400
South Dakota	2,900	500	550	425	75	175	550	175	90	90
Tennessee	22,200	3,400	3,150	3,800	550	1,100	2,300	750	550	650
Texas	59,000	8,500	7,100	8,700	1,500	2,400	5,900	1,800	1,500	1,600
Utah	3,900	650	550	350	90	200	550	125	100	150
Vermont	2,400	475	350	350	60	100	350	75	70	80
Virginia	26,000	4,200	3,650	4,100	700	1,000	3,000	750	600	600
Washington	19,100	3,000	2,500	2,900	500	650	2,400	650	475	475
West Virginia	10,200	1,400	1,480	1,800	200	475	1,000	275	225	225
Wisconsin	21,200	3,500	3,100	2,600	550	800	2,600	550	550	550
Wyoming	1,900	275	150	200	30	60	175	50	45	60
United States	1,100,000	175,000	157,500	161,000	30,800	46,000	122,000	32,000	28,200	28,000
Puerto Rico	7,000	900	650	500	450	400	850	60	175	200

*Does not include carcinoma in situ or melanoma skin cancer.

These estimates are offered as a rough guide and should not be regarded as definitive. They are calculated according to the distribution of estimated 1991 cancer deaths by state. Experience data that year-to-year changes may only represent improvements in the base data.

Ca-A Cancer Journal for Clinicians, Jan./Feb. 1991, Vol. 41, p. 30.

The American Cancer Society also predicts over 500,000 deaths caused by cancer of all sites in 1991 with California (52,000), New York (39,500), Florida (34,000), Pennsylvania (30,500), and Texas (27,500) again leading the nation.

ESTIMATED CANCER DEATHS
FOR ALL SITES PLUS MAJOR SITES, BY STATE - 1991

State	All Sites		Major Sites								
	Number of Deaths	Death Rate per 100,000* Pop.	Female Breast	Colon & Rectum	Lung	Oral	Uterus	Prostate	Skin (Melanoma)	Pancreas	Leukemia
Alabama	9,200	176	650	900	2,700	150	175	575	100	450	300
Alaska	500	169	50	50	175	10	10	20	10	25	25
Arizona	7,000	154	550	750	1,900	75	125	450	90	325	250
Arkansas	5,700	167	400	600	1,900	75	90	325	70	275	200
California	52,000	188	4,000	5,700	13,900	800	1,000	3,200	800	2,700	2,000
Colorado	4,800	144	450	600	1,200	75	75	300	80	250	175
Connecticut	7,400	173	700	900	1,800	125	125	425	100	425	325
Delaware	1,400	150	150	150	375	20	20	100	20	50	50
Dist. of Col	1,700	222	150	200	400	50	50	150	20	60	50
Florida	34,000	183	2,700	4,100	10,300	650	550	2,300	450	1,700	1,100
Georgia	11,900	174	1,100	1,200	3,500	250	225	800	150	550	400
Hawaii	1,600	138	125	225	475	40	30	90	20	80	60
Idaho	1,700	146	125	200	400	25	40	125	30	100	60
Illinois	24,400	176	2,200	3,100	6,600	325	550	1,400	225	1,200	850
Indiana	12,000	177	1,100	1,450	3,500	175	225	750	125	550	425
Iowa	6,200	158	550	800	1,600	125	150	450	80	325	225
Kansas	4,900	152	450	650	1,200	50	100	325	70	275	225
Kentucky	8,100	181	600	950	2,800	100	150	475	90	350	250
Louisiana	9,000	187	600	1,000	2,700	175	225	550	90	475	250
Maine	2,900	180	200	375	800	75	70	150	30	125	100
Maryland	9,800	194	850	1,100	2,800	150	175	550	100	500	325
Massachusetts	12,900	175	1,400	1,850	3,600	225	275	800	175	700	450
Michigan	18,600	178	1,600	2,000	5,100	300	350	1,200	150	900	700
Minnesota	8,300	164	800	1,000	1,900	100	150	600	80	500	375
Mississippi	5,500	188	400	600	1,800	100	100	350	60	300	200
Missouri	11,600	171	1,000	1,300	3,400	150	200	725	125	550	400
Montana	1,600	160	125	225	400	30	40	125	20	80	50
Nebraska	3,200	154	275	450	850	35	50	200	50	150	125
Nevada	2,300	185	175	225	750	40	40	100	30	100	80
New Hampshire	2,300	179	200	300	600	40	50	150	25	125	70
New Jersey	18,400	185	1,700	2,400	4,800	300	375	1,100	225	850	600
New Mexico	2,400	144	225	275	550	30	40	175	30	125	100
New York	39,500	177	3,900	5,200	10,800	700	800	2,400	550	2,000	1,300
North Carolina	13,000	166	1,200	1,500	3,900	225	250	900	200	650	475
North Dakota	1,300	151	100	150	325	25	30	125	10	80	70
Ohio	24,300	182	2,100	3,000	6,900	350	500	1,400	275	1,100	850
Oklahoma	6,900	185	500	750	2,100	125	175	400	100	325	275
Oregon	6,100	167	500	650	1,800	100	125	450	90	300	225
Pennsylvania	30,500	179	2,600	3,900	8,100	375	650	1,800	375	1,400	1,100
Rhode Island	2,500	181	250	325	650	50	50	150	30	100	70
South Carolina	6,600	170	500	700	1,900	175	150	450	100	350	250
South Dakota	1,500	153	125	200	375	20	25	125	25	80	60
Tennessee	10,800	173	850	1,200	2,400	150	250	600	150	500	400
Texas	27,500	158	2,700	3,700	7,700	400	500	1,500	350	1,300	1,000
Utah	1,800	122	175	225	325	25	40	150	25	80	90
Vermont	1,100	177	125	175	325	20	20	90	20	50	60
Virginia	12,100	182	1,100	1,400	3,600	200	275	800	150	550	375
Washington	8,900	165	750	950	2,600	125	175	650	125	425	300
West Virginia	4,700	178	350	550	1,600	50	100	275	60	200	150
Wisconsin	9,900	161	850	1,200	2,300	150	175	700	125	500	375
Wyoming	700	149	75	90	175	10	20	50	10	40	50
United States	514,000	171	44,500	60,500	143,000	8,150	10,000	32,000	6,500	21,200	16,100
Puerto Rico	4,000	126	250	350	550	175	150	225	25	175	150

*Average annual mortality rate for 1983-1987, adjusted to the age distribution of the 1970 US Census Population.

Ca-A Cancer Journal for Clinicians, Jan/Feb. 1991, Vol. 41, p. 30.

B. OCCUPATIONAL CANCER

Since all forms of cancer are prevalent in the general population, the real question is whether plaintiff's occupation or exposure to asbestos contributed to cause plaintiff's cancer. Some general education about cancer and occupational risk of cancer can be effective and beneficial to establish a proper perspective for the jury. Maintaining proper perspective on occupational cancer is emphasized by Drs. Morgan and Seaton:

> Before discussing preventive measures, it is important to place occupational cancer in perspective. First, cancer is generally a disease of the elderly, and it has been calculated that if all forms of cancer were eradicated in the United States, average life expectancy would rise by only two (2) years. Second, there does not seem to be an epidemic of cancer, the only important type noted to be on the increase being bronchial carcinoma. Third, any occupational factor in bronchial carcinogenesis pales in significance when compared with the effect of tobacco, which may be calculated to cause some 120,000 to 125,000 excess deaths from cancer each year in the United States, including an excess of about 80,000 to 85,000 lung cancers.

Morgan & Seaton, Occupational Lung Diseases, p. 662 (1984).

Since 1775, certain occupational exposures have been recognized as causing cancer. For example, British surgeon Sir Pervical Pott (1714-1788) observed that a unique tumor, scrotal carcinoma, often developed in chimney sweeps. Since that time, exposure to various carcinogens in the work place has been the subject of great interest and debate in the scientific and medical community.

In 1959, R. E. Eckardt, assembled a compilation of data pertaining to various historical studies linking cancer to exposure to industrial carcinogens on a world-wide basis.

Table 15.1 Historical Data on Occupational Cancer*

Year	First Reported By	Reported Agent or Process	Site	Probable Total Number of Cases Reported To Date
1775	Pott	Soot	Scrotum	190
1822	Paris	Arsenic	Skin	<25
1875	Volkmann	Crude Wax from Coal	Skin	254
1876	Volkmann	Coal Tar	Skin	>3000
1876	Bell	Shale Oil	Skin	>200
1879	Harring & Hesse	Ionizing Radiation	Lung	>300
1894	Unna	Ultraviolet Radiation	Skin	Unknown
1895	Rehn	Aromatic Amines	Bladder	>1200
1898	Mackenzie	Creosote	Skin	20
1906	Frieben	X-rays	Skin	>125
1910	Wilson	Shale Oil and Mineral Oil Lubricants	Skin	2000
1911	Pfeil	Chromate Producing	Lung	140
1917	Leymann	Crude Anthracene (coal tar?)	Skin	20
1926	Prunes	Saltpeter	Skin	17
1929	Hartland	Radium	Bone	9
1932	Grenfell	Nickel Refining	Lung & Sinuses	135
1935	Lynch & Smith	Asbestos Production with Asbestosis	Lung	59
1952	Weil et al	Isopropyl Alcohol Manufacture	Sinuses	10

*By permission. From Industrial Carcinogens, Modern Monographs in Industrial Medicine. Grune & Stratton, New York, 1959

Eckardt, R. E.: "Industrial Carcinogens: Modern Monographs in Industrial Medicine," Grune and Stratton, New York, (1959).

Drs. Rutherford T. Johnstone and Suwarde E. Miller also referred to and incorporated Eckardt's 1959 compilation with the caveat that they had not accepted arsenic, salt peter, or asbestos as adequately proven carcinogens, but rather they were believed to act only as cocarcinogens. Johnstone and Miller, Occupational Diseases and Industrial Medicine, p. 323.

Surveys in England and Wales have shown that, although certain occupations are associated with a greater or lesser cancer risk than occurs in the general population, almost ninety percent of such variation disappears when comparison is made between individuals of similar habits and social class. Registrar General (1978), Office of Population Censuses and Surveys: Occupational Mortality. Decennial Supplement for England and Wales, 1970-72. Long; HMSO. Fox and Adelstein, "Occupational Mortality: Work or Way of Life?" Journal of Epidemiology and Community Health, (1978), Vol. 32, pp. 73-78. The cancers which are of non-occupational origin are primarily related to "life style" factors - these being understood as the "total cultural, behavioral and dietary environment" of the individual. Parkes, W. R., Occupational Lung Disorders, p. 499 (1982).

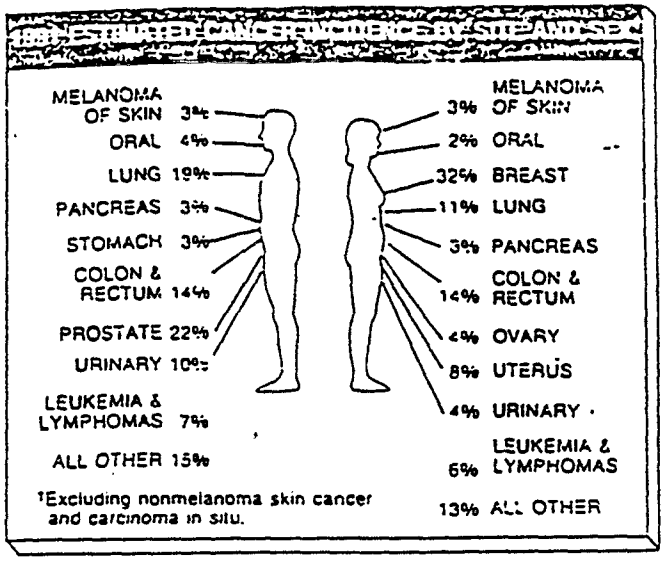
A majority of the available medical evidence indicates that industrial carcinogens are responsible for only a small portion of cancers. Doll and Peto, The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today, (1981). While it is true that the continuing search for occupational hazards has uncovered more human carcinogens than any other approach, this is far from saying that these carcinogens are responsible for most human cancer. The evidence available from epidemiological studies indicates that both the age standardized incidence and mortality for all forms of cancer are beginning to fall and that the existence of an "epidemic" of cancer is fallacious. Howard, J. K., "Occupationally Related Cancer," The Practitioner, 1981, Vol. 225, p. 810.

Dr. John Higginson, then director of the International Agency for Research on Cancer, originally proposed that 80 percent of cancers were dependent on environmental factors relating them to a wide range of factors such as life style, social habits, diet, and cooking methods, and not primarily to the result of industrial activity. Dr. Higginson has subsequently remarked that the "over emphasis on chemical carcinogens has distorted an approach to the environmental theory for many years." Higginson, J., "Proportion of Cancers Due to Occupation," Preventive Medicine, 1980, Vol. 9, pp. 180-188.

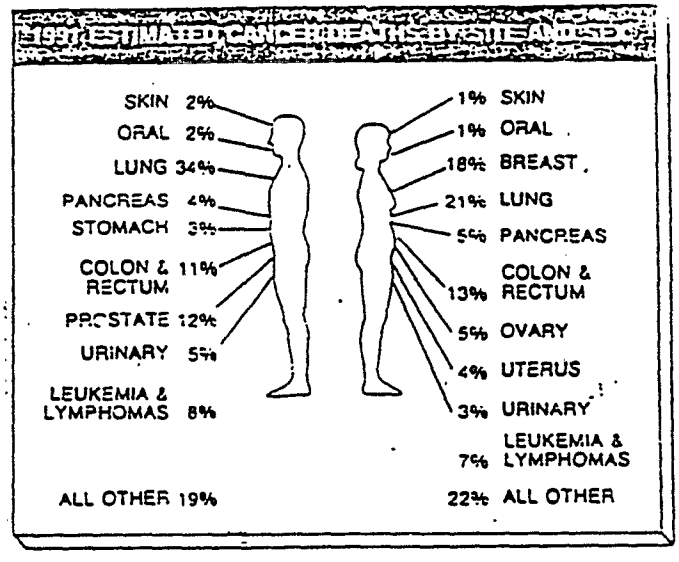
It is critical to convince the jury that the mere presence of carcinogens in the work place proves little. Various studies demonstrate that carcinogens are present in not only the work place, but virtually every aspect of our life. Therefore, there is inherent difficulty in diagnosing a particular cancer as being a result of exposure to a specific agent, such as asbestos. Seldom is it possible to say with probability or certainty that the plaintiff's cancer is related to occupational exposure.

C. INCIDENCE OF NON-LUNG RELATED CANCERS

When defending any cancer case, it is imperative that the jury be educated on the overall incidence of the specific disease. Although the lung is a common site for cancer it is not the most common site in males or females. In men, 22 percent of new cancers occur in the prostate, while only 19 percent occur in the lung. In women, 32 percent of cancers occur in the breast with only 11 percent occurring in the lungs. However, lung cancer accounts for 34 percent of cancer deaths in men and 21 percent of cancer deaths in women. In 1991, the American Cancer Society estimate that the most common cancer sites will be the prostate (22%), lung (19%), colon/rectum (14%), urinary (10%), leukemia and lymphoma (7%), oral (4%) and pancreas (3%). In women the more common sites are estimated to be the breast (32%), colon/rectum (14%), lung (11%), uterus (8%), leukemia and lymphoma (6%) and oral (2%).



[1]Excluding nonmelanoma skin cancer and carcinoma in situ.



Ca-A Cancer Journal for Clinicians, Jan/Feb. 1991, Vol. 41, p. 19.

In 1991 the estimated new cases of cancer are as follows:

Site	Total	Male	Female
All Sites	1,100,000*	545,000*	555,000*
Buccal Cavity & Pharynx (ORAL)	30,800	20,600	10,200
Lip	3,600	3,100	500
Tongue	6,200	3,900	2,300
Mouth	11,600	6,900	4,700
Pharynx	9,400	6,700	2,700
Digestive Organs	240,600	125,400	115,400
Esophagus	10,900	7,600	3,300
Stomach	23,600	14,500	9,200
Small Intestine	2,900	1,600	1,300
Large Intestine } (COLON &	112,000	54,000	58,000
Rectum } RECTUM)	45,500	25,000	20,500
Liver & Biliary Passages	15,000	7,800	7,200
Pancreas	28,200	13,700	14,500
Other & Unspecified Digestive	2,500	1,200	1,300
Respiratory System	178,000	114,000	64,000
Larynx	12,500	10,000	2,500
LUNG	161,000	101,000	60,000
Other & Unspecified Respiratory	4,500	3,000	1,500
Bone	2,000	1,100	900
Connective Tissue	5,800	3,100	2,700
SKIN	32,000**	17,000**	15,000**
BREAST	175,900	900	175,000
Genital Organs	201,000	129,300	71,700
Cervix } (UTERUS)	13,000		13,000
Corpus & Unspecified } (UTERUS)	33,000		33,000
Ovary	20,700		20,700
Other & Unspecified Genital, Female	5,000		5,000
Prostate	122,000	122,000	
Testis	6,100	6,100	
Other & Unspecified Genital, Male	1,200	1,200	
Urinary Organs	75,500	52,800	22,700
Bladder	50,200	37,000	13,200
Kidney & Other Urinary	25,300	15,800	9,500
Eye	1,700	900	800
Brain & Central Nervous System	16,700	9,000	7,700
Endocrine Glands	13,900	4,100	9,800
Thyroid	12,400	3,300	9,100
Other Endocrine	1,500	800	700
Leukemias	28,000	15,800	12,200
Lymphocytic Leukemia	11,700	6,800	4,900
Granulocytic Leukemia	11,600	6,300	5,300
Other & Unspecified Leukemias	4,700	2,700	2,000
Other Blood & Lymph Tissues	56,900	30,000	26,900
Hodgkin's Disease	7,400	4,200	3,200
Non-Hodgkin's Lymphomas	37,200	19,600	17,600
Multiple Myeloma	12,300	6,200	6,100
All Other & Unspecified Sites	41,000	21,000	20,000

Note: ACS six major sites appear in boldface caps.

*Carcinoma in situ and nonmelanoma skin cancers are not included. Carcinoma in situ of the uterine cervix accounts for about 50,000 new cases annually; carcinoma in situ of the female breast accounts for about 15,000 new cases annually; and melanoma carcinoma in situ accounts for about 6,000 new cases annually. Overall, about 100,000 new cases of carcinoma in situ of all sites of cancer are diagnosed each year. Basal and squamous cell skin cancer accounts for more than 600,000 new cases annually.

**Melanoma only.

Incidence estimates are based on rates from NCI SEER program 1985-1987.

Ca-A Cancer Journal for Clinicians, Jan/Feb. 1991, Vol. 41, p. 28.

The chart below details cancer death rates over the last 30 years and indicates which cancers have decreased and/or increased as the cause of death per 100,000 population:

30-YEAR TRENDS IN AGE-ADJUSTED CANCER DEATH RATES PER 100,000 POPULATION
1953-55 to 1983-85

SITES	SEX	1953-55	1983-85	PERCENT CHANGES	COMMENTS
ALL SITES	Male	[illegible]	[illegible]	+ [illegible]	[illegible]
	Female	[illegible]	[illegible]	+ [illegible]	Slight decrease
PLATOMA	Male	[illegible]	[illegible]	[illegible]	Slight decrease in recent years
	Female	[illegible]	[illegible]	[illegible]	Some fluctuations; generally decreasing
BRAIN	Male	[illegible]	[illegible]	[illegible]	Early increase in both sexes later showing off, reasons unknown
	Female	[illegible]	[illegible]	[illegible]	
BREAST	Male	6.1	6.2	+	Constant rate
	Female	[illegible]	[illegible]	[illegible]	Slight fluctuations; overall no change
COLON & RECTUM	Male	[illegible]	[illegible]	+	Slight fluctuations; overall no change
	Female	[illegible]	[illegible]	[illegible]	Slow, steady decrease
COLON	Male	[illegible]	[illegible]	[illegible]	Slow steady increase showing in recent years
	Female	[illegible]	[illegible]	[illegible]	Slow steady decrease.
RECTUM	Male	[illegible]	[illegible]	[illegible]	Slow steady decrease.
	Female	[illegible]	[illegible]	[illegible]	Slow steady decrease
ESOPHAGUS	Male	[illegible]	[illegible]	[illegible]	Some fluctuations; small increase.
	Female	[illegible]	[illegible]	+	Slight fluctuations; overall no change.
KIDNEY	Male	[illegible]	[illegible]	[illegible]	Steady slight increase.
	Female	[illegible]	[illegible]	+	Slight fluctuations; overall no change
LARYNX	Male	[illegible]	[illegible]	+	Slight fluctuations; overall no change in both males and females.
	Female	[illegible]	[illegible]	+	
LEUKEMIA	Male	[illegible]	[illegible]	[illegible]	Early increase, later leveling off and decrease
	Female	[illegible]	[illegible]	[illegible]	Early slight increase; later leveling off and decrease.
LIVER**	Male	[illegible]	[illegible]	[illegible]	Decreasing random rate; later showing off.
	Female	[illegible]	[illegible]	[illegible]	Some fluctuations; steady decrease.
LUNG	Male	[illegible]	[illegible]	[illegible]	Steady increase in both sexes due to cigarette smoking.
	Female	[illegible]	[illegible]	[illegible]	
LYMPHOMAS	Male	[illegible]	[illegible]	[illegible]	Slow steady increase in both males and females
	Female	[illegible]	[illegible]	[illegible]	
ORAL	Male	[illegible]	[illegible]	+	Slight fluctuations; overall no change in both males and females.
	Female	[illegible]	[illegible]	+	
OVARY	Female	[illegible]	[illegible]	[illegible]	Steady increase; later showing off and decrease
PANCREAS	Male	[illegible]	[illegible]	[illegible]	Steady increase in both sexes, then showing off, reasons unknown.
	Female	[illegible]	[illegible]	[illegible]	
PROSTATE	Male	[illegible]	[illegible]	[illegible]	Fluctuations throughout; overall slight increase
SKIN	Male	[illegible]	[illegible]	[illegible]	Slight fluctuations; slight increase.
	Female	[illegible]	[illegible]	[illegible]	Slight fluctuations; overall no change.
STOMACH	Male	[illegible]	[illegible]	[illegible]	Steady decrease in both sexes; reasons unknown.
	Female	[illegible]	[illegible]	[illegible]	
UTERUS	Female	[illegible]	[illegible]	[illegible]	Steady decrease.

*Percent changes not listed because they are not meaningful.

**Primary and non-specified.

American Cancer Society: "Cancer Facts & Figures - 1989," P. 29

D. Smoking v. Asbestos Exposure -- The Proper Perspective

Without question or debate smoking is the single most preventable cause of cancer in the U.S.. The table below provides estimates regarding additional etiological factors in the causation of cancer in man:

Table 1 - Etiological factors in the causation of cancer in man (estimates compiled from several sources)

Causative Factor	Estimated percentage of all cancer cases Males	Females
Congenital/genetic	2	2
Environmental		
Diet and life-style	35	60
Smoking	30	8
Alcohol	3	3
Sunlight	<8	<8
Occupation	5	2
Radiation	1	1
Medication/drugs	<1	<1
Unknown	15	15

Howard, J., "Occupationally Related Cancer," The Practitioner (1981), Vol. 225, p. 810.

It should be emphasized that 30 percent of **ALL** cancer deaths are caused by tobacco not limited to lung cancer deaths. Further, it should be emphasized that 4 percent refers to **ALL** occupations not just occupations involving asbestos exposure. A table taken from Doll and Peto's article estimates the percentage of cancer deaths caused by various factors:

> By far the largest reliably known percentage is 30% of the current U. S. cancer deaths are due to tobacco, although it is possible that some nutritional factor(s) may eventually be found to be of comparable importance.
>
> . . .
>
> The proportion of current U. S. deaths attributable to occupational factors is provisionally estimated at 4%, lung cancer being the major contributor to this.

. . .

Table 20 - Proportions of cancer deaths attributed to various different factors

Text Section No.	Factor or class of factors	Percent of all cancer deaths	
		Best estimate	Range of acceptable estimates
5.1	Tobacco	30	25-40
5.2	Alcohol	3	2-4
5.3	Diet	35	10-70
5.4	Food additives	<1	-5 -2
5.5	Reproductive and sexual behavior	7	1-13
5.6	Occupation	4	2-8
5.7	Pollution	2	<1-5
5.8	Industrial products	<1	<1-2
5.9	Medicines and medical procedures	1	0.5-3
5.10	Geophysical factors	3	2-4
5.11	Infection	10 ?	1-?
5.12	Unknown	?	?

Doll, R. and Peto J., The Causes of Cancer, Quantitative Estimates of Avoidable Risks of Cancer in the United States Today, (Oxford Univ. Press, p. 1196, 1256 (1981).

This chart may be useful not only because it demonstrates that tobacco causes 30 percent and occupation only 4 percent of all cancer deaths, but in addition, that alcohol causes 3 percent of all cancer deaths, almost as many as all occupations combined. Furthermore, diet causes 35 percent of cancer deaths, almost nine times as many as occupation. This may assist defendants' efforts to put the alleged cancer risk from asbestos in perspective.

In a recent study, the National Cancer Institute estimated that cigarette smoking will cause more than 157,000 cancer deaths this year. Lung cancer, therefore, now kills more smokers than does heart disease. This new study also implicates smoking in cancers of the mouth, esophagus, pancreas, larynx, bladder, and kidney. According to this study smoking is the main risk for 91.5 percent of oral cancer cases among men and 86.7 percent of larynx cancer cases among women. Significantly, the study reported that the statistical risk of dying from lung cancer has doubled in the last three decades for male smokers and quadrupled for their female counterparts. "Smoking, Cancer Cases Studied," Dallas Morning News, Aug. 22, 1991, p. 7A.

The American Cancer Society also provides strong evidence of the overwhelming effects of tobacco.

> The American Cancer Society estimates that cigarette smoking is responsible for 85% of lung cancer cases among men and 75% among women - about 83% overall. The cancer death rate for male cigarette smokers is more than double that of nonsmokers, and the rate for female smokers is 67% higher than for nonsmokers. The American Cancer Society estimates that 40% of male smokers and 28% of female smokers die prematurely, or about 35% overall. The higher cancer rates for men reflect the fact that in the past, more men than women smoked, and smoked more heavily. In recent years, however, the gap between male and female smoking has been narrowing.
>
> Smoking also has been implicated in cancers of the mouth, pharynx, larynx, esophagus, pancreas, cervix, uterus and bladder. Smoking accounts for about 30% of all cancer deaths, is a major cause of heart disease, and is linked to conditions ranging from colds and gastric ulcers to chronic bronchitis and emphysema.
>
> Smoking is related to 390,000 deaths each year. A September 1985 study by the U. S. Congress Office of Technology Assessment estimates the cost of smoking to the economy from $38 billion to $95 billion, with a middle estimate of $65 billion. This amounts to $2.17 in lost productivity and the treatment of smoking-related diseases for each pack of cigarettes sold.

American Cancer Society, "Cancer Facts and Figures - 1989," P. 20

In an editorial on dust, disability, and death, Dr. Keith Morgan compares the role of occupation to smoking in cancer causation:

> "That the role of occupation relative to other factors as a cause of respiratory disease has been unduly exaggerated is all too evident from the most recent publications of Doll and Peto and the Surgeon General (3,4).

. . .

Finally, the study of Foxman and colleagues places in perspective the relative contributions of dust versus cigarette smoking. This should indicate to those whose responsibility it is to devise the most effective means of reducing morbidity and mortality that a relatively greater effort must be made to control cigarette smoking than to control dust levels. This is not to say that the latter can be ignored, but clearly, if priorities are to be established on sound scientific principles, it is far more important to dissuade workers, and indeed everybody else, from smoking than it is to lower dust levels by 20 to 25 percent."

Morgan, W.K.C., "American Review of Respiratory Disease, 1986, Vol. 134, pp. 539-641.

E. ENVIRONMENTAL CARCINOGENS

Dr. Bruce Ames has reported on an exhaustive database of animal cancer tests. The studies indicated that of the 392 chemicals tested in both rats and mice at the maximum tolerated dose levels, more than 50 percent were carcinogenic in at least one species of animals. His study concluded that the proportion of chemicals found to be carcinogens is strikingly high. Dr. Ames predicted from considerations of carcinogenesis mechanisms, that it is plausible that a large proportion of all chemicals tested in the future, both natural and man made, will prove to be carcinogens. Ames, B., "What are the Major Carcinogens in the Etiology of Human Cancer," Important Advances in Oncology (J.B. Lippincott Co. - 1989).

Below is Dr. Ames' table reflecting a ranking of possible carcinogenic hazards:

Table 14a-1
Ranking of Possible Carcinogenic Hazards*

Possible Hazard: HERP (%)	Daily Human Exposure	Carcinogen Dose per 70-kg Person	Potency of Carcinogen TD50 (mg/kg)	
			Rat	Mouse
		Environmental Pollution		
0.60	Tap water: 1 L	Chloroform, 53 μg (US average)	(116)	6
0.60	Well water: 1 L contaminated (worst well in Silicon Valley)	Trichloroethylene, 2560 μg	(—)	63
0.0074	Well water: 1 L contaminated (98 cases)	Trichloroethylene, 267 μg	(—)	63
0.0022		Chloroform, 12 μg	(116)	6
0.0003		Tetrachloroethylene, 21 μg	101	(32)
0.009	Swimming pool, 1 h (for child)	Chloroform, 250 μg (average pool)	(116)	6
0.6	Conventional home air (14 h/d)	Formaldehyde, 586 μg	1.9	1.2
0.002		benzene, 155 μg	(15)	(2)
2.1	Mobile home air (14 h/d)	Formaldehyde, 2.2 mg	1.9	1.2
		Pesticides and Other Residues		
0.0002	PCBs: daily dietary intake	PCBs, 0.2 μg (US average)	1.7	(5.4)
0.0003	DDE/DDT: daily dietary intake	DDE, 2.2 μg (US average)	(—)	15
0.0004	EDB: daily dietary intake (from grains and grain products)	Ethylene dibromide, 0.42 μg (US average)	1.5	(5.1)
		Natural Pesticides and Dietary Toxins		
0.003	Bacon, cooked (100 g)	Dimethylnitrosamine, 0.5 μg	(0.2)	0.2
0.006		Diethylnitrosamine, 0.1 μg	0.02	(—)
0.003	Sake (250 ml)	Urethane, 43 μg	(61)	22
0.03	Comfrey herb tea (1 cup)	Symphytine, 36 μg (750 μg of pyrrolizidine alkaloids)	1.9	(?)
0.03	Peanut butter (32 g; one sandwich)	Aflatoxin, 64 ng (US average, 2 ppb)	0.003	(—)
0.06	Dried squid, broiled in gas oven (54 g)	Dimethylnitrosamine, 7.9 μg	(0.2)	0.2
0.07	Brown mustard (5 g)	Allyl isothiocyanate, 4.6 mg	95	(—)
0.1	Basil (1 g of dried leaf)	Estragole, 5.8 mg	(?)	52
0.1	Mushroom, one raw (*Agaricus bisporus* 15 g)	Mixture of hydrazines, etc.	(?)	20,300
0.2	Natural root beer (12 ounces; 354 ml; now banned)	Safrole, 6.6 mg	(436)	56
0.005	Beer, before 1979 (12 ounces; 354 ml)	Dimethylnitrosamine, 1 μg	(0.2)	0.2
2.5	Beer (12 ounces; 354 ml)	Ethyl alcohol, 18 ml	9110	(?)
4.3	Wine (250 ml)	Ethyl alcohol, 30 ml	9110	(?)
6.2	Comfrey–pepsin tablets (nine daily)	Comfrey root, 2700 mg	626	(?)
1.3	Comfrey–pepsin tablets (nine daily)	Symphytine, 1.8 mg	1.9	(?)
		Food Additives		
0.0002	AF-2: daily dietary intake before banning	AF-2 (furylfuramide), 4.5 μg	28	(130)
0.06	Diet cola (12 ounces; 354 ml)	Saccharin, 95 mg	2143	(—)
		Drugs		
[0.3]	Phenacetin pill (average dose)	Phenacetin, 300 mg	1246	(2137)
[5.6]	Metronidazole (therapeutic dose)	Metronidazole, 2000 mg	[542]	508
[14]	Isoniazid pill (prophylactic dose)	Isoniazid, 300 mg	[156]	30
16	Phenobarbital, one sleeping pill	Phenobarbital, 60 mg	(—)	3.6
17	Clofibrate (average daily dose)	Clofibrate, 2000 mg	169	(?)
		Occupational Exposure		
5.8	Formaldehyde workers' average daily intake	Formaldehyde, 6.1 mg	1.9	1.2
140	EDB workers' daily intake (high exposure	Ethylene dibromide, 150 mg	1.5	(5.1)

Reprinted with permission from: Ames, B.N., Magaw, R., Gold, L.S. Ranking possible carcinogenic hazards. Science 236: 271–280, 1987.

Ames, B.N., Important Advances in Oncology, "What are the Major Carcinogens in the Etiology of Human Cancer," p. 239 (J.B. Lippincott Co. - 1989).

III. ASBESTOS AND "OTHER" CANCERS

A. Selected Studies/Publications: 1960-1979

1. Selikoff, Churg, and Hammond 1964

In 1964, Drs. Selikoff, Churg, and Hammond in their landmark article, "Asbestos Exposure and Neoplasia," suggested **the possibility** of a relationship between asbestos and gastrointestinal cancer. The authors stated:

> Gastrointestinal Cancer - Rather to our surprise, the death rate from cancer of the stomach and the death rate from cancer of the colon and rectum were higher among the asbestos workers than would be expected from the rates reported for the US white male population, calculated in the same way as for lung cancer. Twelve deaths from gastric cancer occurred among the asbestos workers, as compared with only 4.3 expected. Seventeen deaths from cancer of the colon and rectum occurred among the asbestos workers, as compared with 5.2 expected.
>
> . . .
>
> Cancer of All Other Sites. - The combined death rate from cancer of all sites other than lung and pleura, and stomach, colon, and rectum was not increased. Twenty-one such deaths occurred among asbestos workers, as compared with 20.5 expected.
>
> "Gastrointestinal Carcinoma - Isolated instances of gastrointestinal carcinoma in the presence of asbestosis have been known, but there have been no data to indicate that these were more than coincidental findings. Among the asbestos workers studied here, cancer of the stomach, colon, and rectum was three times as frequent as expected. These data **suggest** that there **may perhaps be** an etiological relationship between industrial asbestos exposure and carcinoma of the gastrointestinal tract. (emphasis added)

Selikoff, I.J., Churg, J. and Hammond, C., "Asbestos Exposure and Neoplasia," Journal of the American Medical Association, 1964, Vol. 188, pp. 22-26, 25-26.

2. Selikoff, Hammond, and Churg 1968

In 1968, Drs. Selikoff, Hammond and Churg reported on deaths among 632 members of the International Association of Heat & Frost Insulators and Asbestos Workers. The death rates reported from cancer of the stomach, colon, and rectum were higher than expected; but the authors acknowledged that **this may have been due to chance.**

> Cancer of Stomach, Colon, and Rectum - In our earlier study of asbestos workers, there were more deaths than expected from cancer of the stomach, colon and rectum (9.4 expected, 29 observed). As compared with a total 1.8 expected deaths from these causes, there were eight observed deaths in this study, due to cancer of the following sites: stomach, three; colon, four; and rectum, one.
>
> Although this bears out our earlier findings, **the number of deaths from these causes was so small that we still refrain from drawing any conclusion at this time.** (emphasis added)

Selikoff, I.J., Hammond, C.E., and Churg, J., "Asbestos Exposure, Smoking, and Neoplasia," Journal of the American Medical Association, 1968, Vol. 204, pp. 106-112, 108.

3. Selikoff, Hammond, and Churg 1972

In 1972, Dr. Selikoff, et al. published "Carcinogenicity of Amosite Asbestos" which tracked the mortality experience of 230 amosite asbestos factory workers. The study stated:

> We have investigated the mortality experience of a group of workmen occupationally exposed solely to amosite whose employment started between June 1941 and December 1945. This cohort has been observed through June 30, 1971.
>
> . . .
>
> It may be of interest that more deaths from cancer of the stomach, colon and rectum have occurred than expected. **The increase is only threefold, however. As with similar previous experiences, further observations are required before this association can be regarded as clearly established.** (emphasis added)

Selikoff, I.J., Hammond, C.E., Cuyler, E., and Churg, J., "Carcinogenicity of Amosite Asbestos," Archives of Environmental Health, (1972), Vol. 25, pp. 184-185.

4. Meurman, Kiviluoto, and Hakama 1974

In 1974, Dr. Meurman reported on 1,092 Finnish anthophyllite asbestos workers whose cancer rates were compared to control group and Finland death rates. They found no excess in the numbers of gastrointestinal cancers among asbestos miners. Workers with more than 10 years of exposure experienced only two gastrointestinal cancers when 2.1 were expected.

TABLE 3
OBSERVED AND EXPECTED[1] NUMBERS OF LUNG CANCER AND CANCER OF DIGESTIVE ORGANS IN DEATHS AMONG ASBESTOS EMPLOYEES AND CONTROLS, BY AGE

Age	Lung Cancer			Cancer of Digestive Organs		
	Asbestos	Controls	Expected	Asbestos	Controls	Expected
15-24	--	--	0.0	--	--	0.0
25-34	--	--	0.1	--	--	0.3
35-44	1	--	0.7	1	--	1.2
45-54	10	6	3.4	1	4	3.2
55-64	7	4	5.6	1	1	5.3
65-74	3	3	2.6	4	4	4.2
75-	--	--	0.2	--	--	0.7
All ages	21	13	12.6	7	9	14.9

[1]Assuming age-specific rates for deaths from lung cancer and cancers of digestive organs in Finland 1958.

TABLE 4
OBSERVED AND EXPECTED[1] NUMBERS OF LUNG CANCER AND OF CANCER OF DIGESTIVE ORGANS IN DEATHS AMONG ASBESTOS EMPLOYEES WITH MORE THAN 10 YEARS OF EXPOSURE, BY AGE

Age	Lung Cancer		Cancer of Digestive Organs	
	Observed	Expected	Observed	Expected
35-44	1	0.0	--	0.0
45-54	5	1.0	1	0.8
55-64	2	1.0	--	0.8
65-74	--	0.4	1	0.5
Total	8	2.4	2	2.1

[1]Assuming age-specific rate for deaths from lung cancer and cancer of digestive organs in Finland 1958

Meurman, L.O., Kiviluoto, R., and Hakama, M. "Mortality and Morbidity Among the Working Population of Anthophyilite Asbestos Miners in Finland," British Journal of Industrial Medicine, 1974, Vol. 31, pp. 105-112, 108.

6. Peto, Doll, Howard, Kinten, and Lewinsohn 1977

In 1977, Dr. Peto and others reported on 1,106 men and women who worked at English textile factory. The subjects were divided into five groups based upon duration of work. Cohorts one and two consisted of those men with twenty or more years of exposure at least 10 of which were worked prior to the implementation of asbestos regulations in 1932. They found excesses of lung cancer and mesothelioma but **no excess of gastrointestinal cancer.** Only sixteen (16) cases of gastrointestinal cancer were reported when 15.7 were expected. Peto, J., Doll, R., Howard, S.V., Kinten, L.J., and Lewinsohn, H.C., "A Mortality Study Among Workers in an English Asbestos Factory." British Journal of Industrial Medicine, 1977, Vol. 34, pp. 169-173, 171.

7. Selikoff and Lee 1978

In his text Asbestos and Disease, Dr. Selikoff states:

> The evidence for carcinogenic or cocarcinogenic action of asbestos in tumors developing in the gastrointestinal tract is highly suggestive but **not conclusive**; for tumors in other sites the evidence so far is equivocal. (emphasis added)

Selikoff, I. J. and Lee, D.H.K., Asbestos and Disease, (Academic Press, 1978), p. 301.

8. Nicholson, Selikoff, Seidman, Lilis, and Formby 1979

In 1979, Dr. Nicholson and others reported on 544 asbestos miners and millers and found no increased incidence of gastrointestinal cancer. They found only 10 gastrointestinal tract cancers when 9.5 were expected. There was a deficit of all cancers other than lung cancer, gastrointestinal cancer, and mesothelioma. Table 5 from this study summarizes the results:

Table 5

EXPECTED AND OBSERVED DEATHS AMONG 544 ASBESTOS MINERS AND MILLERS. THETFORD MINES, QUEBEC. JAN. - NOV., 1961-AUG. 1977*

	Total		
	Exp.	Obs.	O/E
Total deaths	159.9	178	1.11
Total cancer all sites	36.7	49	1.34
Lung cancer	11.1	28	2.52
Pleural mesothelioma	**	1	-
Cancer of the gastrointestinal tract	9.5	10	1.05
All other cancers	16.1	10	0.62
Total Noninfectious pulmonary diseases	6.7	30	4.48
Asbestosis	**	26	-
All other causes	116.5	99	0.85
Person-years		7,408	

*Expected deaths are based upon age-specific death rate data for Canadian white males.
**Death rates not available but these have been rare causes of death in the general population.

Nicholson, W.J., Selikoff, I.J., Seidman, H., Lilis, R. and Formby, P., "Long-term mortality experience of chrysotile miners and miller in Thetford Mines, Quebec," Annals of the New York Academy of Sciences, 1979, Vol. 330, pp. 11-21, 16.

9. Rubino, Piolatto, Newhouse, Scanscoti, Arsini, and Murray 1979

In 1979, Dr. Rubino and others reported on the mortality experience of over 900 workers first employed at a chrysotile mine between 1930 and 1965, and found an excess of laryngeal cancer but no statistically significant excess of lung cancer, mesothelioma, or gastrointestinal cancer:

Table 3 Number of deaths observed and expected by period since first exposure, and cause. (Period of observation from 1946 to 1975)

Period since first exposure (yr)	Up to 19			20 and over			Total		
Person-years observation	12683			8776			21459		
Cause of Death	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR
All Causes	112	54.2	207**	220	160.2	137**	332	214.4	155**
All malignant neoplasms (140-205)	12	10.0	120	38	37.0	103	50	47.0	106
Lung and pleura (162-163)	1	1.7	59	10	8.7	115	11	10.4	106
Larynx (161)	2	0.4	500	4	1.5	267	6	1.9	316*
Gastrointestinal (151-159)	4	4.8	83	15	14.5	103	19	19.3	98
Other sites	5	3.1	161	9	12.3	73	14	15.4	91
Non-malignant respiratory diseases (470-527)	12	2.3	522**	20	11.8	169*	32	14.1	227**
Influenza and pneumonia (480-493)	8	1.6	500**	4	4.6	87	12	6.2	194*
Other respiratory diseases (470-475, 500-527)	4	0.7	571**	16	7.2	222**	20	7.9	253**
Asbestosis (523.2)	2	---	---	7	---	---	9	---	---
Tuberculosis of the lung (001-008)	13	3.9	333**	5	3.3	152	18	7.2	150**
Cardiovascular diseases (400-468)	22	14.8	149	100	67.7	148**	122	82.5	148**
Cirrhosis of the liver (581)	9	2.1	429**	22	7.8	282**	31	9.9	313**
Accidents (800-999)	30	7.8	385**	15	9.5	158	45	17.3	260**
All other causes	9	13.3	68	17	23.1	74	26	36.4	71
Unknown	5	---	---	3	---	---	8	---	---

* $p<0.05$; ** $p<0.01$.

These numbers include one suspected case of mesothelioma of the pleura.
Figures in parentheses are ICD (7th Revision) Code numbers.

Rubino, G.F., Piolatto, G.F., Newhouse, M.L., Scanscoti, G., Arsini, G.A., and Murray, R., "Mortality of Chrysotile Asbestos Workers at the Balangero Mine, Northern Italy," British Journal of Industrial Medicine, 1979, Vol. 36, pp. 187-194.

10. Selikoff, Lilis ,and Nicholson 1979

Drs. Selikoff, Lilis, and Nicholson studied asbestos disease in U. S. shipyards and found no statistically significant excess of gastrointestinal cancer or other cancers except lung cancer and mesothelioma:

> As a first approximation to evaluation of the problem, we have investigated the mortality

experience of insulation workers in U.S. shipyards, to ascertain whether this experience reflected the sort of asbestos-associated diseases seen with asbestos exposure in general and whether such experience varied substantially from that of insulation workers not employed in shipyards.

Table 10
Deaths Among 440 U.S. Shipyard Insulation Workers
Observed Prospectively
January 1, 1967 - January 1, 1977

Number of men	440		389	
Man-years of observation	3986		2876	
Cause of Death	Observed	Expected*	Observed	Expected
Total deaths	79	75.2	73	66.4
Cancer-all sites	39	16.2	37	14.4
Lung Cancer	21	5.7	20	5.1
Pleural mesothelioma	3	**	3	**
Peritoneal mesothelioma	5	**	5	**
G.I. Cancer	3	3.1	3	2.8
All other cancer	7	7.4	6	6.5
Noninfectious pulmonary disease	14	3.2	14	3.0
Asbestosis	13	**	13	**
All other causes	26	55.8	22	49.0

* Expected deaths are based upon white male age specific mortality data of the U.S. National Center for Health Statistics for 1967-1976.
** These are rare causes of death in the general population.

Table 11
Deaths Among 12,051 Insulation Workers in the U.S. and Canada
with Twenty or More Years from Onset of Exposure,
January 1, 1967 - January 1, 1977
(Comparison of shipyard with nonshipyard employment)

	Insulators: Shipyard		Insulators: other than Shipyards	
Number of men			38911,662	
Man-years of observation			287674,515	
Cause of Death	Observed	Expected*	Observed	Expected
Total deaths	73	66.4	1873	1309.7
Cancer-all sites	37	14.4	875	262.7
Lung Cancer	20	5.1	430	88.6
Pleural mesothelioma	3	**	58	**
Peritoneal mesothelioma	5	**	104	**
G.I. Cancer	3	2.8	90	50.4
All other cancer	6	6.5	193	123.7
Noninfectious pulmonary disea	14	3.0	190	51.0
Asbestosis	13	**	147	**
All other causes	22	49.0	808	996.0

* Expected deaths are based upon white male age specific mortality data of the U.S. National Center for Health Statistics for 1967-1976.
** These are rare causes of death in the general population.

Selikoff, I.J., Lilis, R., and Nicholson, W.J., "Asbestos Disease in the United States Shipyards," Annals of the New York Academy of Sciences, 1979, Vol. 330, pp. 295-311, 301-302.

11. Selikoff, Hammond, and Seidman 1979

In "Mortality Experience of Insulation Workers in the United States and Canada 1943-1976" Drs. Selikoff, Hammond, and Seidman noted that colon-rectal cancer ranked third as cause of cancer death among asbestos workers and that the mortality ratios ranged from 1.59 to 1.81:

> It must be emphasized that only one group of asbestos workers is included in this investigation, namely members of the insulation workers union, ... mortality ratios ranged from 1.59 to 1.81, the mortality ratios having been calculated from four different sets of figures. In this particular case, all four sets of comparisons led us to the conclusion that death rates from colon-rectum cancer are increased by exposure to asbestos dust, **but it would be folly to suppose that we have precisely determined the degree of association even in this group of asbestos workers** (emphasis added).
>
> . . .

Table 3
Expected and Observed Deaths Among 632 New York-New Jersey Asbestos Insulation Workers January 1, 1943 - December 31, 1976 (13,925 Man-years of Observation)

Underlying Cause of Death	Expected*	Observed
Total deaths, all causes	328.9	478
Total cancer, all sites	57.0	210
Cancer of lung	13.3	93
Pleural mesothelioma	**	11
Peritoneal mesothelioma	**	27
Cancer of esophagus	1.4	1
Cancer of stomach	5.4	19
Cancer of colon-rectum	8.3	23
Cancer of larynx, pharynx, buccal cavity	2.8	6
Cancer of kidney	1.3	2
All other cancer	24.5	28
Noninfectious pulmonary diseases, total	9.3	45
Asbestosis	**	41
All other causes	262.6	223

* Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1976. Rates for specific cause of death for 194301948 were extrapolated from rates for 1949-1955.

** Rates are not available, but these have been rare causes of death in the general population.

Selikoff, I.J., Hammond, C.E., and Seidman, H., "Mortality Experience of Insulation Workers in the United States and Canada 1943-1976, Annals of the New York Academy of Sciences, 1979, Vol. 330, pp. 91-116, 94.

B. Selected Studies/Publications: 1980-1990

1. Beaumont and Weiss 1980

In 1980, Drs. Beaumont and Weiss reported on the mortality of welders, shipfitters and other trades in two shipyards and field construction as compared to the U.S. death rates for white males. The authors found a low risk for all digestive cancers primarily due to a deficit of cancer of the large intestine:

Table 3

All workers: standardized mortality ratios (SMR) for selected disease classifications

Disease classification*	SMR	(No. observed)
All causes (000-999)	0.99	(2019)
All malignant neoplasms (140-205)	1.01	(396)
Malignant neoplasms of buccal cavity and pharynx (140-148)	1.00	(13)
Malignant neoplasms of digestive organs and peritoneum (150-159)	0.84	(100)
Malignant neoplasms of respiratory system (160-164)	1.17	(147)
Malignant neoplasms of prostate (177)	1.10	(32)
Malignant neoplasms of kidney (180)	1.14	(11)
Malignant neoplasms of bladder (181)	1.13	(15)
Malignant neoplasms of brain and other central nervous system (193)	1.27	(13)
Lymphopoietic cancer (200-205)	0.92	(34)
Mental, psychoneurotic, and personality disorders (300-327)	1.99	(17)**
Vascular lesions of the central nervous system (330-334)	0.88	(143)
Diseases of circulatory system (400-468)	0.86	(845)**
Respiratory diseases (470-527)	1.25	(146)**
Diseases of digestive system (530-587)	1.08	(102)
Accidents (800-962)	1.14	(114)
Suicide (963, 970-979)	1.26	(46)

*International Classification of Diseases, Adapted (Seventh Revision).
**$p < 0.01$.

Beaumont, J.J. and Weiss, N.S., "Mortality of Welders, Shipfitters, and other Metal Trades Workers in Boilermakers' Local No. 104, AFL-CIO", American Journal of Epidemiology, 1980, Vol. 112, pp. 775-786, 779.

2. Rossiter and Coles 1980

In a study of 6,300 shipyard workers, no statistically significant excess mortality due to gastrointestinal cancers was found by Drs. Rossiter and Coles.

To investigate the effect of occupational exposure to asbestos on mortality, names of all 6292 men born on or after 1 January 1910 and employed as industrial workers in the Royal Naval Dockyard, Devonport on 1 January 1947 were submitted to the Office of Population Censuses and Surveys for tracing. Follow-up continued until the end of 1978: over 99% were traced; 3% emigrated; and there were 1043 (17%) deaths.

On the basis of the mortality in England and Wales for each five years of age and each five calendar years, the standardized mortality ratio (SMR) was 96. Adjusting the rates for the lower mortality in southwest England, the SMR was 104. No relation was found between SMR and date of birth, and there was only a very slight excess among those more heavily exposed to asbestos.

Table 2. Observed and expected deaths by cause among dockyard workers

Cause of death	No. of deaths	England & Wales Expected	England & Wales SMR[a]	Southwest estimates[b] Expected	Southwest estimates[b] SMR	
All deaths	1043	1081.2	96	998.4	104	
All cancers	265	282.1	94	255.6	104	
Mesothelioma	31c	0.5	6400	0.4	7700	P << 0.001
Lung cancer	84[c]	119.7	70	100.3	84	
Gastrointestinal cancer	63	83.3	76	76.2	83	
Others	87[d]	78.6	111	78.7	111	
Asbestosis, pulmonary fibrosis	9	0.03	27,000	0.03	2,000	P << 0.001
Other respiratory diseases	67	97.3	69	81.9	82	
Circulatory diseases	518[d]	< 64.2	112	440.8	118	P < 0.001
Other causes	174	237.6	73	220.1	79	P < 0.01
Unknown causes	10	-	-	-	-	

[a] SMR, standardized mortality ratio
[b] Estimated deaths rates in Southwest Britain (including Devonport)
[c] Three also had asbestosis
[d] One also had asbestosis

Rossiter, C. E. and Coles, R.M., "H. M. Dockyard, Davenport: 1947 Mortality Study, Biological Effects of Mineral Fibres," IARC. Sci. Pub., Vol. 2, pp. 713-21, 715, 1980.

3. McDonald, Liddell, Gibbs, Eyssen, and McDonald 1980

In 1980, Dr. McDonald and others reported on a cohort of 11,379 asbestos miners and reported some excess of mortality from upper gastrointestinal tract cancer but no excess of lower gastrointestinal cancer:

> We report a further follow-up of a birth cohort of 11,379 workers exposed to chrysotile. The cohort consisted of all 10,939 men and 440 women, born 1891-1920, who had worked for at least a month in the mines and mills of Asbestos and Thetford Mines in Quebec."

. . .

7(d) Gross Service: 20 or More Years

Cause of death (see table 2)	Accumulated dust exposure (see table 4)							
	Low		Medium		High		Very High	
	O	SMR	O	SMR	O	SMR	O	SMR
All causes	367	0.98	253	0.89	183	1.07	295	1.50
Pneumoconiosis	4	10.49	7	23.75	5	30.10	20	101.51
Malignant neoplasms:								
Lung	28	1.21	20	1.08	24	2.20	32	2.65
Oesophagus and stomach	17	1.36	6	0.64	8	1.44	19	2.89
Colon and rectum	7	0.56	4	0.43	1	0.18	9	1.39
Other abdominal	10	1.18	3	0.46	2	0.51	6	1.35
Larynx	2	1.07	1	0.69	0	0	1	1.03
Other	33	1.23	16	0.79	11	0.90	19	1.36
Heart disease	138	0.87	115	0.95	77	1.06	94	1.12
Respiratory tuberculosis	5	1.01	5	1.31	3	1.27	9	3.06
Other respiratory	18	0.92	10	0.68	14	1.62	17	1.74
Cerebrovascular	32	1.15	18	0.89	10	0.84	22	1.58
Accidents	16	0.82	19	1.16	9	0.85	12	1.01
All other known causes	52	0.92	29	0.68	18	0.70	33	1.10
Cause not known	5	---	0	---	1	---	2	---

> As in earlier reports on the Quebec cohort, the patterns of gastrointestinal cancer are difficult to interpret. There was unquestionably a substantial excess in mortality from cancer of the upper gastrointestinal tract in men most heavily exposed. This excess was confined to Thetford Mines where most of the long and heavy exposures occurred. The exposure-response curves were far from regular, however, and it appears that some other

important factors were also operating -perhaps environmental. The SMR for cancer of the lower gastrointestinal tract for the complete cohort was 0.78 (table 6); nevertheless, there was some evidence of an exposure response trend.

McDonald, J.C., Liddell, F.D.K., Gibbs, G.W., Eyssen, G.E., and McDonald, A.D., "Dust Exposure and Mortality in Chrysotile Mining, 1910-75," British Journal of Industrial Medicine, 1980, Vol. 37, pp. 11-24, 18, 22.

4. Thomas, Benjamin, Elwood, and Sweetwood 1982

In 1982, Dr. Thomas and colleagues reported on 1592 Welsh asbestos cement factory workers employed for six months or more from 1936 to 1977 and found no excess of gastrointestinal cancer:

Table 2 Mortality by all causes, all neoplasms, and selected concerns for the total male population, men alive 15 years or longer after first exposure, and for men employed in 1935-6

Cause of Death (ICD)	Study Group	Expected Deaths	Observed Deaths	Standardized Mortality Ratio (SMR)
All cases	Total population	343.3	351	102
	Alive ≥ 15 years after first exposure	243.2	261	107
	Employed in 1935-6	88.3	83	94
All neoplasms (140-239)	Total population	80.7	74	92
	Alive ≥ 15 years after first exposure	61.0	58	92
	Employed in 1935-6	21.5	22	103
Cancers of lung and/ pleura (162, 163)	Total population	33.0	30	93
	Alive ≥ 15 years after first exposure	25.8	24	93
	Employed in 1935-6	9.2	7	76
Cancers of gastrointestinal tract (151-154)	Total population	19.6	18	92
	Alive ≥ 15 years after first exposure	14.1	14	99
	Employed in 1935-6	5.0	6	120

Deaths due to cancer of the gastrointestinal tract were not increased in the total male population (SMR 92) or in those men alive 15 or more years after first exposure (SMR 99). The raised SMR (120) for men employed in 1935 and 1936 is due to one extra death (6 observed, 5.0 expected). These figures do not suggest that the chrysotile asbestos cement workers are at an excess risk of gastrointestinal cancer, a finding consistent with the results of studies of chrysotile miners and millers and chrysotile asbestos textile workers.

Thomas, H.F., Benjamin, I.T., Elwood, P.C., and Sweetnam, P.M., "Further Follow-up Study of Workers from an Asbestos Cement Factory," British Journal of Industrial Medicine, 1982, Vol. 39, pp. 273-276, 274, 275.

5. Dement, Harris, Symons, and Shy 1983

In 1983, Dr. Dement and colleagues in "Exposures & Mortality Among Chrysotile Asbestos Workers Part II: Mortality," studied 1,261 males with one month or more in textile production operations and found no statistically significant cancer of the digestive system (SMR=131). Cancer incidence cancer for "all other sites" besides the digestive system and the lung were not elevated. A total of 33,141 person-years at risk was experienced by this cohort between 1940 and 1975. The results of this study have been set out below in Table II.

TABLE II. Observed and expected Deaths by Cause for White Male Asbestos Textile Workers 1940-1975.

Cause of Death	ICDA 7th List No.	Observed	Expected	SMR
All causes		308	205.66	150*
Malignant neoplasms		59	35.06	168*
Digestive system	150-159	13	9.89	131
Trachea, bronchus, lung	162-163	35	11.10	315*
All other sites		11	14.07	78
Vascular lesions affecting the central nervous system	330-334 345	15	10.97	137
Diseases of the circulatory system	400-468	105	83.74	125*
All tuberculosis	001-019	6	3.48	172
Nonmalignant respiratory diseases		28	9.53	294*
Acute upper respiratory infection	470-475	0	0.03	-
Influenza	480-483	0	0.04	-
Pneumonia	490-493	4	4.19	95
Bronchitis	500-502	0	0.55	-
Other respiratory disease	510-527	24	4.35	552*
Accidents	800-962	34	25.38	134*
Other violent deaths	963-964 970-985	9	9.37	96
All other known causes		29	26.91	108
Unknown causes including 17 missing death certificates		23	2.55	-

*$p < 0.05$.

Dement, J.M., Harris, R.L., Symons, M.J. and Shy, C.M., "Exposures and Mortality Among Chrysotile Asbestos Workers Part II: Mortality, American Journal of Industrial Medicine, 1983, Vol. 4, pp. 421-433, 424.

6. Acheson, Gardner, Winter, and Bennett 1984

In 1984, Dr. Acheson and others studied the mortality of 5,969 men. Four thousand eight hundred and twenty (4,820) men were involved in the manufacture of asbestos containing products. An excess mortality among asbestos workers was virtually limited to cancer of the lung and pleura. There was no large or significant excess of cancer of all other sites combined. A total of 48 deaths were observed compared to 45.3 expected.

When the SMRs for individual sites are considered, none were significantly increased.

TABLE 5 Observed deaths, expected deaths and SMRs from cancer by site amongst asbestos and other workers

	Asbestos workers (68922)+			Other workers (16609)+		
Cancer of:--	Obs	Exp	SMR	Obs	Exp	SMR
Oesophagus (150)	2	2.0	100	1	0.6	161
Stomach (151)	7	7.5	94	4	2.5	159
Colon (153)	6	4.4	137	2	1.4	142
Rectum (154)	4	3.2	124	0	1.1	0
Pancreas (157)	3	3.1	96	0	1.0	0
Lung (162,163)^	61+	29.1	210**	10	9.4	106
Skin (172,173)	1	1.0	102	0	0.3	0
Prostate (185)	2	2.1	94	2	0.9	218
Testis (186)	0	1.1	0	1	0.3	377
Bladder (188)	2	2.2	89	1	0.8	124
Other Urinary (189)	2	1.4	139	0	0.4	0
Brain etc. (191,192)	5	3.0	165	0	0.8	0
Hodgkin's disease (201)	1	1.6	64	0	0.4	0
Leukaemia (204-208)	4	2.6	154	0	0.7	0
Other cancers	9++	10.0	90	3	2.9	103
All malignant neoplasms (140-209)	109	74.4	147**	24	23.5	102

+ 4 of the 61 deaths were from mesothelioma of the pleura.
++1 of the 9 deaths was from mesothelioma of the peritoneum.
* significant at 5% level.
**significant at 1% level.
^ the SMR for lung cancer for the District in which the factory is situated was 107 during 1968-78.

> Another difference between our findings and those of the Patterson workers is that men in our study have no evidence of excess risks of cancers other than lung cancer for example of cancers of the stomach, colon, rectum and pancreas.[8-9]
>
> . . .
>
> It has been suggested that the excess mortality from for example, cancer of the stomach and large bowel experienced by the Patterson workers, American insulators and certain British factories may be due to substances other than asbestos in the working environment.[1,10] Although some such cases may represent misdiagnosed peritoneal mesotheliomas this is unlikely to account for all of them.[10]

Acheson, E.D., Gardner, M.J., Winter, P.D., and Bennett, C., "Cancer in a Factory Using Amosite Asbestos," International Journal of Epidemiology, 1984, Vol. 13, pp. 3-10.

7. Berry and Newhouse 1983

In 1983, Drs. Berry and Newhouse reported on 13,460 British friction products workers. The only type of asbestos used was chrysotile, except during two well-defined periods before 1945 when crocidolite was used. Over 90 percent of the population was traced. In excess of two-thirds started work by 1960 and thus would have been followed for at least 20 years. Of the workers studied, no excess of gastrointestinal cancer was reported. The results of this study are reported in Tables 7 and 8 below.

Table 7 Observed and expected mortality after 10 years from first exposure. (Number of pleural mesotheliomas included in parentheses)

Cause of Death	No/Subject-years			
	Men 7474/104193		Women 3708/58816	
	Obs.	Exp.	Obs.	Exp.
All causes	1339	1361.8	299	328.0
Lung and pleural cancer	151(8)	139.5	8(2)	11.3
Gastrointestinal cancer	103	107.2	29	27.4
Other cancers	77	87.7	51	60.0
Other causes	1008	1027.4	211	229.3

Table 8 Observed and expected mortality after completing 10 years employment.

Follow-up after 10 years' exposure (years)	Men				Women			
	0-10		>10		0-10		>10	
No/Subject-Years	2484/21860		1808/19025		627/5578		457/6377	
Cause of Death	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs	Exp.
All Causes	185	195.7	432	450.8	14	21.3	76	66.5
Lung & Pleural Cancer	23	21.3	58(7)	47.4	0	0.7	2(1)	2.2
Gastrointestinal Cancer	23	16.3	25	35.8	0	1.8	8	5.7
Other cancers	7	12.6	21	28.2	3	4.5	14	10.7
Other causes	132	145.5	328	339.4	11	14.3	52	47.9

Berry, G., and Newhouse, M.L., "Mortality of Workers Manufacturing Friction Materials Using Asbestos," British Journal of Industrial Medicine, 1983, Vol. 40, pp. 3-4.

8. Kolonel, Yoshizawa, Hirohata, and Myers 1985

In 1985, Dr. Kolonel, et al. reported on 7,971 men employed at the Pearl Harbor Naval Shipyard with follow-up for up to 29 years. They found an increased risk of lung cancer for those with greatest exposure and longest

latency period (1.77 RR). However, they found no significant increases for any other cancers, including gastrointestinal cancers (45 observed/47 expected):

> Selikoff and Hammond (24) followed a cohort of 440 shipyard insulators in the United States and found a somewhat higher risk ratio of 3.9 for lung cancer after a minimal interval of 20 years from onset of employment; there was no increase in gastrointestinal cancers.
>
> . . .
>
> The relationship of asbestos exposure to cancer risk has been the subject of much epidemiological research. Of special concern in recent years has been the extent to which workers in naval shipyards, in particular, are at increased risk. One reason for this interest is the very large size of shipyard work forces, particularly at certain periods in the past [an estimated 4.5 million United States men worked in shipyards during World War II, for example (20)].
>
> . . .

Table 6
Mortality from gastrointestinal cancers (esophagus, stomach, colon, rectum) among shipyard workers by duration of exposure and latency interval For person-years at risk, Table 3.

Duration of exposure (yr)	Latency interval (yr)	Observed deaths	Expected deaths	SMR	95% CI
Nonexposed	0-19	5	7.8	0.6	0.2-1.5
	20-29	4	7.7	0.5	0.1-1.3
	30 +	9	10.1	0.9	0.4-1.7
		18	25.6	0.7	0.4-1.1
< 15	0-19	8	13.2	0.6	0.3-1.2
	20-29	12	9.5	1.3	0.7-1.1
	30 +	11	4.9	2.2	1.1-4.0
		31	27.6	1.1	0.8-1.6
≥ 15	15-19	0	1.8	0.0	
	20-29	4	7.9	0.5	0.1-1.3
	30+	10	9.7	1.0	0.5-1.9
		14	19.4	0.7	0.4-1.2

Kolonel, L.M., Yoshizawa, L.N., Hirohata, T., and Myers, B.C., "Cancer Occurrence in Shipyard Workers Exposed to Asbestos in Hawaii," Cancer Research, August, 1985, Vol. 45, p. 3927.

9. Levine 1985

In 1985, Dr. Levine posed the question "Does Asbestos Exposure Cause Gastrointestinal Cancer?" The abstract of his article indicated the jury is still out:

> The relationship between asbestos exposure and gastrointestinal malignancies is unlike the well-established correlation between occupational asbestos exposure and the subsequent development of pleuropulmonary neoplasms and mesotheliomas. Cohort studies on occupationally exposed workers suggest an association between asbestos and gastrointestinal cancer, but evaluation of dose-response, tissue analysis, animal experiment, and cell culture data yield inconsistent conclusions. No simplistic cause-effect relationship can be ascribed to asbestos at the present time, and the answer to the question, "Does asbestos exposure cause gastrointestinal cancer?" must await the results of additional studies.

Levine, D.S., "Does Asbestos Exposure Cause Gastrointestinal Cancer?", Digestive Diseases and Sciences, 1985, Vol. 30, pp. 1189-1197, 1189.

10. Doll and Peto 1985

In 1985, Drs. Doll and Peto again expressed doubt that gastrointestinal cancer was caused by asbestos.

> The laboratory evidence weighs against the possibility that asbestos causes cancer in sites other than the lung, pleura, peritoneum.
>
> . . .
>
> More importantly, asbestos has failed to produce gastro-intestinal or any other type of cancer in animals when given by mouth. (Bolten et al 1982; Condie, 1983).
>
> . . .
>
> The simplest explanation of the excess mortality of gastrointestinal cancer, however, and in our opinion the most likely one, is that it results largely or wholly from misdiagnosis of cancer of the lung and mesothelioma of the pleura or peritoneum. We cannot,

> of course, rule out the possibility that asbestos may cause a small number of cancers in many different organs, even though there is no strong evidence that it does. In particular, we do not wish to rule out the possibility that it may cause cancer of the oesophagus. The diagnosis is usually easy, misdiagnosis in place of cancer of the lung is rare, and in several studies the relative risk attributed to it is notably raised (Selikoff, Hammond, and Seidman, 1979; McDonald et al, 1930; Peto et al, 1985).

Doll, R. and Peto, J., "ASBESTOS - Effects on Health of Exposure to Asbestos," Health and Safety Commission, Her Majesty's Stationary Office, 1985, p. 6.

11. Morgan, Foliart, and Wong 1985

In 1985, Drs. Morgan, Foliart and Wong reviewed more than 45 published articles and discussed whether asbestos caused gastrointestinal cancer:

> To determine the role of occupational asbestos exposure in the risk of gastrointestinal cancer, we attempted to identify all relevant publications from the indexed literature.
>
> . . .
>
> Exposure to asbestos is among several factors cited as possible causes of esophageal, gastric and colo-rectal cancer. More than 45 published studies have presented mortality data on asbestos-exposed workers. For each cohort, we listed the observed and expected rates of deaths from types of gastrointestinal cancer based on the latest published follow-up. Summary standardized mortality ratios (SMRs) were then derived. Finally, we calculated summary SMRs for total gastrointestinal tract cancer for three occupational groups; asbestos factory workers, insulators/shipyard workers and asbestos miners.
>
> Statistically significant elevations in summary SMRs were found for esophageal, stomach and total gastrointestinal tract cancer in all asbestos-exposed workers. Esophageal cancer summary SMR remained significantly elevated when data were reanalyzed

to include only those cohorts with death certificate diagnoses for cause of observed deaths. However, summary SMRs were not statistically significant for stomach and total gastrointestinal tract cancer after reanalysis. Summary SMRs by occupational group showed a significant elevation for total gastrointestinal cancer in insulators/shipyard workers. The elevation was not significant after reanalysis.

Based on the results after reanalysis, the elevations in summary SMRs for stomach and total gastrointestinal tract cancer are of a magnitude that could result from diagnostic investigator error. We conclude that more studies are required before stomach and colorectal cancers are documented as asbestos-related diseases.

Table 3. -- Summary SMRs

Site of Cancer	Obs	Exp	SMR	95% Confidence Interval*	References
Esophagus	21	9.8	214**	132.6-327.6	2***, 17, 22
Stomach	43	23.5	183**	132.4-246.5	2***, 17, 22
Colorectal	176	156.4	113	96.5-130.4	2***, 17, 22, 33
Total gastrointestinal tract	912	840.9	108**	101.5-115.7	2***, 7, 8, 12 13, 17, 22, 24 28, 33, 38, 41 44, 46, 48

SMR = standardized mortality ratio

* Reference 54.
** $P < .05$.
*** NY-NJ cohort and U.S. Canadian cohort.

Table 4. -- Summary SMRs Deleting 'Best Evidence' Data

Site of Cancer	Obs	Exp	SMR	95% Confidence Interval*	References
Esophagus	20	8.4	238**	145-368	2***, 17, 22
Stomach	24	18.1	133	85-197	2***, 17, 22
Colorectal	153	148.1	103	88-121	2**, 17, 22, 23
Total gastrointestinal tract	869	825.8	105**	98-113	2***, 7, 8, 12, 13, 17, 22, 24, 28, 33, 38, 41, 44, 46, 48

SMR = standardized mortality ratio

* Reference 54.
** $P < .05$.
*** U.S-Canadian cohort; NY-NJ cohort excluded.

> Although there are statistically significant elevations of SMR for esophageal and gastric cancer for all groups and for total gastrointestinal tract cancer for insulators and shipyard workers, we are not convinced of the relationship to asbestos exposure, especially for stomach cancer, where the finding is inconsistent and possibly erroneous in the largest positive study. For colo-rectal cancer, at this time there is no discernible relationship to asbestos exposure. We hope that the occupationally exposed cohorts now under study will provide more conclusive evidence soon - refuting or supporting such an association.

Morgan, R.O., Foliart, D.E., and Wong, O., "Asbestos and Gastrointestinal Cancer," Western Journal of Medicine, 1985, Vol. 143, pp. 61-65.

12. Hodgson and Jones 1986

In 1986, Drs. Hodgson and Jones published a study on 31,150 male asbestos workers in England and Wales and found no excess incidence of gastrointestinal cancer:

> The question as to whether exposure to asbestos leads to increased risk of cancers of the alimentary tract was initially posed by Selikoff's report on the mortality of U.S. insulation workers, in which a threefold excess of gastrointestinal cancer was observed. The evidence from later studies is mixed, with some cohorts showing significant excesses and others not. The small size of many of these studies no doubt explains a certain amount of this variability, but clearly there are genuine differences between the observed results. In a recent review, Doll and Peto conclude that where excesses of alimentary tract cancer have been observed, these are most probably due to misdiagnosis of mesothelioma. This hypothesis is consistent with the fact that the strongest excesses of gastrointestinal cancers have been recorded in cohorts that also display a high risk of peritoneal mesothelioma.

The present study shows no excess from cancer at any of the four main alimentary tract sites examined (oesophagus, stomach, colon, rectum), either overall or in association with increasing exposure to asbestos nor among insulation workers, who showed heavy excesses of the established asbestos related diseases. The present results therefore weigh against the hypothesis that exposure to asbestos is responsible for an increase in the incidence of cancer of the alimentary tract. (emphasis added)

Table 2 Mortality of workers exposed to asbestos before and after 1969 regulations

Cause of Death	Exposure before Regulations				Exposure only after regulations			
	Total period of follow up		Excluding follow up for initial 10 years after 1st exposure to asbestos		Total period of follow up		Excluding follow up for initial 10 years after 1st exposure to asbestos	
	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SMR
All causes	897/1011.8	88.7^{AA}	834/931.6	89.5^{AA}	231/273.7	84.4^{AA}	9/9.5	94.8
Cancer of:								
Oesophagus	6/9.4	63.7	6/8.8	68.5	1/2.3	44	0/0.9	-----
Stomach	27/27	100.2	24/24/9	96.3	5/6.1	82.7	0/.2	-----
Colon	6/16.7	36.0^{AA}	5/15.4	32.5^{A}	4/4.1	97.2	0/.2	-----
Rectum	10/12.9	77.3	9/12	75.0	0/3.1	----	0/.1	-----
Lung	157/121.0	129.7^{AA}	152/112.1	135.6^{AA}	29/26.9	108.0	1/1.0	96.2
Circulatory disease	426/509.7	83.6^{AA}	395/471.5	83.8^{AA}	101/122.3	82.6	6/4.6	129.6
Respiratory disease	64/92.4	69.3^{AA}	61/85.4	71.4^{AA}	14/20.7	67.6	1/.8	123.5
Asbestosis	11(1.1%)	11(1.2%)	1(.04%)	0				
Mesothelioma	34(3.4%)	34(3.6%)	1(.04%)	0				

$^{A}p < 0.05$; $^{AA}p < 0.01$.

Table 3. Mortality at selected alimentary tract cancer sites by cumulative exposure

OBS/EXP (SMR)	Cumulative exposure (years)			All exposures
	< 10	10-20	> 20	
Cancer of:				
Oesophagus	0/1.4	2/3.14 (65)	4/5.0 (80)	6/9.4 (64)
Stomach	6/4.0 (150)	10/8.6 (116)	11/14.3 (77)	27/26.9 (100)
Colon	1/2.5 (40)	2/5.5 (36)	3/5.6 (35)	6/16.7 (36)
Rectum	1/1.9 (52)	2/4.2 (47)	7/6.8 (103)	10/12.9 (77)
Total	8/9.8 (82)	16/21.4 (75)	25/34.7 (72)	49/65.9 (74)

Hodgson, R.T. and Jones, R.D., "Mortality of Asbestos Workers in England and Wales 1971-81," British Journal of Industrial Medicine, 1986, Vol. 43, pp. 158-164.

13. Enterline, Hartley, and Henderson 1987

Dr. Enterline and others conducted a study of asbestos workers who retired between 1941 and 1987 from a U.S. asbestos company. The authors found some elevations in cancer incidence.

> The mortality experience of 1,074 white men who retired from a United States asbestos company during the period 1941-67 and who were exposed to asbestos working as production and maintenance employees for the company is reported to the end of 1980 when 88% of this cohort was known to be dead. As noted in earlier reports, the mortality for respiratory and gastrointestinal cancer was raised. A more detailed examination of causes of death shows that the excess in gastrointestinal cancer was largely due to a statistically significant excess in stomach cancer. A statistically significant excess was also noted for kidney cancer, cancer of the eye, and non-malignant respiratory disease.

Table 2

Observed and expected deaths and SMRs for 1074 retirees from a United States asbestos company by cause of death 1941-80

Cause of Death (7th revision codes)	Obs	Exp	SMR
All causes of death	944	762.77	123.8**
Tuberculosis (001-019)	14	4.47	313.1**
All malignant neoplasms (140-205)	208	129.87	160.2**
Buccal cavity & pharynx (140-148)	5	3.60	139.0
Digestive organs & peritoneum (150-159)	64	45.70	140.0*
Oesophagus (150)	4	2.95	135.6
Stomach (151)	20	11.09	180.4*
Large intestine (153)	14	14.24	98.3
Rectum (154)	9	5.66	159.0
Biliary passage & liver (155-156)	4	3.52	113.6
Pancreas (157)	8	7.37	108.6
All other digestive organs.(residual)	5	0.87	571.4**
Respiratory system (160-164)	79	30.57	258.4**
Larynx (161)	2	1.75	114.1
Bronchus, trachea, lung (162-163)	77	28.44	270.7**
All other respiratory system (residual)	0	0.38	---
Prostate (177)	17	18.17	93.6
Testis & other male genital (178-179)	0	0.34	---
Kidney (180)	7	2.54	275.8*
Bladder & other urinary (181)	5	6.13	81.5
Malignant melanoma of skin (190)	0	1.74	---
Eye (192)	2	0.13	1544.5*
Central nervous system (193)	3	1.19	251.2
Thyroid gland (194)	0	0.28	---
Bone (196)	0	0.66	---
All lymphatic & hematopoietic tissue (200-205)	9	10.76	83.7
Lymphosarcoma, reticulosarcoma (200)	2	2.24	89.4
Hodgkins (201)	0	0.74	---
Leukaemia & aleukemia (204)	3	5.36	56.0
All other lymphatic (202, 203, 205)	4	2.44	163.9
All other malignant neoplasms (residual)	17	8.06	210.9**
Benign neoplasms (210-239)	3	1.19	251.6
Diabetes mellitus (250)	15	11.62	129.0
Stroke (330-334)	85	92.00	92.4
All heart disease (440-443)	395	353.87	111.6*
Rheumatic heart disease (400-416)	6	4.11	146.0
Coronary heart disease (420)	315	280.80	112.2*
Hypertensive heart disease (440-443)	21	21.92	95.8
All other heart disease (residual)	53	47.04	112.7
Hypertension without heart disease (444-447)	7	4.96	141.2
Non-malignant respiratory disease (470-527)	86	49.35	174.3**
Influenza & pneumonia (480-493)	27	24.23	111.4
All other respiratory disease (residual)	59	25.12	234.9**
Asbestosis (523.2)	22	---	---
Ulcer of stomach & duodenum (540-541)	3	5.65	53.1
Cirrhosis of liver (581)	13	6.30	206.3*
Chronic nephritis (592)	2	4.23	47.3
All external causes of death (800-998)	22	24.82	88.6
Accidents (800-962)	16	18.95	84.4
Motor vehicle accidents (810-835)	6	6.30	95.2
All other accidents (residual)	10	12.65	79.1
Suicides (963, 970-979)	6	5.10	117.7
Homicides & all other (residual)	0	0.77	---
All other causes of death (residual)	57	74.44	76.6*
Unknown	34	---	---

*p < 0.05; **p < 0.01.

Enterline, P.E., Hartley, J., and Henderson, V., "Asbestos and Cancer: a Cohort Followed Up to Death," British Journal of Industrial Medicine, 1987, Vol. 44, p. 397.

14. Sanden and Jarvholm 1987

In 1987, in a group of Swedish shipyard workers with more than 20 years since first exposure, Drs. Sanden and Jarvholm found no increased incidence of gastrointestinal cancer. The authors concluded that it was highly improbable that workers in that shipyard had an increased risk of gastrointestinal cancer due to asbestos exposure.

Table 2. Cancer morbidity in 1978-1983 in shipyard workers

Site	All		95% confidence interval of rate ratio
	Observed	Expected	
All (140-209)[c]	54[b]	66.2	0.61-1.1
Lung (162)	11	9.8	0.56-2.0
Pleural mesothelioma (163)	4	—[a]	—
Peritoneal mesothelioma (158)	0	—[a]	—
Gastrointestinal tract (150-158)	11*	22.2	0.25-0.89
Stomach (151)	3	3.4	0.18-2.6
Colon/rectum (152-154)	3	7.8	0.08-2.6
Urinary bladder (188)	6	4.5	0.49-2.9
Kidney (189)	2	3.3	0.07-2.2
Prostate (185)	10	8.5	0.57-2.2

*$P < 0.05$
[a]There is no incidence of data for calculating expected values
[b]In addition to the sites mentioned there were four cases of pancreatic cancer and one case each of lymphoma, leukemia
[c]Figures in parentheses, ICD number 8th revision

Table 3. Cancer morbidity in shipyard workers where at least 20 years have elapsed since onset of asbestos exposures

Site	All		Heavy or very heavy exposure to asbestos[a]	
	Observed	Expected	Observed	Expected
All	49	54.5	16	25.6
Lung	10	8.2	3	3.9
Mesothelioma	4	—[b]	3	—[b]
Gastrointestinal	8	14.2	5	6.7
stomach	3	2.8	1	1.3
rectum	3	6.6	2	3.1
Urinary bladder	6	3.8	1	1.8
Kidney	1	2.7	0	1.3
Prostate	9	7.4	4	3.5

[a]According to answers in the questionnaire of the individuals
[b]Data lacking for calculation of expected values

Some studies indicate an increased risk of gastrointestinal cancer in workers exposed to asbestos, while others do not find such an association. In a previous study, covering 1961-1979, we found no increased risk of gastrointestinal cancer. In the present study the number of cases was significantly lower than expected (95% confidence interval of the rate ratio of 0.2 to 0.9). It thus seems highly improbable that workers have an increased risk of gastrointestinal cancer due to asbestos exposure in the shipyard industry. The increase of gastrointestinal cancer found in some other studies might be an effect of other contemporary exposure, or exposure to other types of asbestos.

Sanden, A. and Jarvhölm, B., "Cancer Morbidity in Swedish Shipyard Workers I978-1983", International Archives of Occupational Environmental Health, 1987, Vol. 59, p. 461.

15. Edelman 1988

In 1988, David Edelman published a review article on 32 cohorts of asbestos workers. He concluded that **asbestos workers do not have an increased risk of gastrointestinal cancer.**

ABSTRACT. In 1964 it was first reported that asbestos workers had a higher risk of gastrointestinal cancer. This notion has persisted despite several studies that have found no increased risk. The risks of gastrointestinal cancer to workers exposed to asbestos were reassessed, based on the results of published studies on 32 independent cohorts of asbestos workers. Not all studies provided risk estimates (SMRs) for all gastrointestinal sites (ICD codes 150-159). No consistent evidence was found to indicate that exposure to asbestos increases the risk of gastrointestinal cancer. Generally, the higher SMRs came from studies conducted in the United States or Canada and might reflect factors not related to exposure to asbestos. In studies in which asbestos exposed and non-asbestos exposed workers were evaluated the SMRs were not consistently higher for the group exposed to asbestos. There was no apparent dose

response relation between accumulated asbestos dose and the risk of gastrointestinal cancer. It is concluded there is no dose response relation between exposure to asbestos and the risk of gastrointestinal cancer, and **asbestos workers are not at an increased risk of gastrointestinal cancer.** (emphasis added)

. . .

Study Methods

Thirty-two cohorts of asbestos-exposed workers were identified that provided data on their risks of gastrointestinal cancer. Table 1 summarizes the types of occupational exposures to asbestos of cohorts evaluated.

. . .

Table 1

Occupational Exposures to Asbestos of Cohorts Evaluated

Industry Occupational Exposure	No. of Cohorts
Asbestos cement	4
Insulation work	1
Manufacturing:	
Gas masks	2
Paper, millboard, friction products, etc.	9
Textiles	2
Mining and milling	5
Muric acid production plant	1
Railroad	1
Shipyard dockyard	3
Workers reported to registries, pneumocomosis panels or applying for workman's compensation	4

. . .

Numerous articles have identified factors that might place an increased risk of cancer to any gastrointestinal site (ICD codes 150-159). These risk factors include smoking; diet

including alcohol, beer, and beef; familial/inheritance factors - for example, adenomatosis; history of ulcerative colitis; and place of residence.

Small but significantly increased relative risks (relative risks less than 2, for example) may occur because of spurious associations or failure to account for the effects of other risk factors, such as diet or smoking, that might affect the relative risk. For relative risks that lie between 1 and 2 it is extremely difficult to disentangle the various contributions of biased information, confounding of two or more factors, and cause and effect.

. . .

If asbestos has a carcinogenic effect on the gastrointestinal tract it should be possible to show this effect through lifetime ingestion studies in laboratory animals. Selikoff and Lee noted that "attempts to induce carcinoma in the intestinal epithelium or mesothelioma in the peritoneum by feeding asbestos have been uniformly disappointing...." In a later review of published studies of asbestos administered by mouth Condie concluded, "the bulk of the experimental evidence indicates that the long-term, high-level ingestion exposure to various types of asbestos fibres failed to produce any definite, reproducible, organ-specific carcinogenic effect.

Doll and Peto noted that unless local death specific rates are used, ratios (SMRs) under 1.5 may be largely or wholly artifactual.

. . .

The present evaluation found no consistent statistical association between exposure to asbestos and gastrointestinal cancer, a dose response relation was not apparent, and results of ingestion studies in laboratory animals were negative. In terms of these criteria the findings of the present evaluation do not support a cause and effect relation between exposure to asbestos and gastrointestinal cancer. The third criterion was not evaluated since studies have not been

conducted to evaluate the concentration of asbestos fibres or bodies in the gastrointestinal tissues of asbestos exposed and non-exposed subjects. Although various factors associated with an increased risk of gastrointestinal cancer have been identified, none of the 32 studies made any adjustments to the risk estimates for gastrointestinal cancer for any of these factors. Based on the epidemiological, clinical, and experimental studies evaluated, there is **no evidence to support a cause and effect relation between exposure to asbestos and cancer of any gastrointestinal site.** (emphasis added)

Edelman, D., "Exposure to Asbestos and the Risk of Gastrointestinal Cancer: A Reassessment", British Journal of Industrial Medicine, 1988, Vol. 45, p. 81.

16. Churg and Green 1988

Dr. Andrew Churg, in his text on occupational lung disease, confirmed there is no pathological means to determine if a gastrointestinal tract cancer is caused by asbestos.

OTHER NEOPLASMS CLAIMED TO BE ASSOCIATED WITH ASBESTOS EXPOSURE

For the pathologist, the problem is one of dealing with tumors which are common in the general population, and which, in many instances, clearly have other strong etiologic associations. Carcinoma of the larynx in particular is related to cigarette smoke, esophageal cancers to smoking and alcohol consumption, and stomach and colon cancers to a variety of postulated dietary factors.

Given the lack of uniformity in regard to the question of whether these tumors are even associated with asbestos exposure, and given their common occurrence in nonexposed populations, I know of no scientific way for the pathologist to associate a specific case of one of these neoplasms with asbestos exposure. **Certainly, there are no pathologic or mineralogic findings that permit the pathologist to decide that an individual case was caused by asbestos exposure. (emphasis added).**

Churg, A. and Green, F., Pathology of Occupational Lung Disease, p. 319, (1988).

17. Mossman, Bignon, Corn, Seaton, and Gee 1989

In their famous 1989 Science article, Drs. Mossman and others questioned whether gastrointestinal cancers are caused by asbestos:

> Tumors of the gastrointestinal tract, larynx, and other organs including the kidney, ovary, pancreas, pericardium, eye, and lymphatic system, have been reported in some cohorts of asbestos workers. In general, the enhanced SMRs for these tumors are not statistically distinguishable from normal SMRs and have not been confirmed in most cohorts. Both laryngeal and gastrointestinal tumors have other etiologies such as smoking, alcohol, diet, and intestinal polyposis that confound the interpretation of epidemiologic data.

Mossman, B. T., Bignon, J., Corn, M., Seaton, A., and Gee, J.B.L., "Asbestos: Scientific Developments and Implications for Public Policy," Science, Vol. 247; P. 295-296

18. Selikoff 1990

Dr. Selikoff has presented updated statistics on 17,800 insulators in "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place." He followed the entire membership of International Association of Heat and Frost Insulators and Asbestos Workers for twenty years beginning January 1, 1967 through December 31, 1986. Selikoff did not find an increased incidence of any of the following cancers: bladder, urinary, leukemia, lymphoma, melanoma, brain, or liver. Therefore, Dr. Selikoff agreed that the notion that asbestos produces cancer in every organ it reaches is fallacious:

> Spectrum of asbestos-associated diseases
>
> On January 1, 1967, the entire membership of the International Association of Heat and Frost Insulators and Asbestos Workers was registered in a prospective epidemiological investigation, undertaken by the Mount Sinai School of Medicine and the American Cancer Society. The observation of this group continues.

> From January 1, 1967 to December 31, 1986, 4,951 deaths occurred among the 17,800 men originally listed. These have been analyzed and the results are contained in Tables 1-4, covering 301,592.6 person-years of observation.
>
> . . .
>
> Of both practical and theoretical interest, these experiences did not demonstrate an increased incidence in a variety of other cancers (urinary bladder, prostate, leukemia, lymphoma, melanoma, brain tumors, primary cancer of the liver) (Table 4). Theoretical interest, because some thought has been given to the possibility that a carcinogenic agent such as asbestos would be likely to produce cancer in whatever organ it was found. At least in the present investigation, this was not the case.

Selikoff, I.J., Mount Sinai School of Medicine, "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place", Copyright 1990, Andrews Communications, Inc., p. 3.

Dr. Selikoff further states that clinically evident asbestos associated disease is not generally found less than 20, 30, 40 years from first exposure. He also admitted that his earlier calculations of 8 to 10 thousand asbestos associated excess cancer deaths predicted each year have to be modified. In fact, the relative risk ratio for all cancer and lung cancer is decreasing.

(1) All Cancer Risk (Best Evidence)

'67-'72	'73-'79	'80-'86
3.41	3.09	2.74

(2) Lung cancer:

5.16	4.57	3.81

Various tables concerning the mortality experience in the cohort of insulation workers are reproduced below:

Table 2

Deaths among 17,800 asbestos insulation workers in the United States and Canada January 1, 1967 - December 31, 1986

Principal cause of death

Cause of Death	Expected Deaths[1]	Observed deaths: Death Certificate Number	Death Certificate SMR	Observed deaths: Best Evidence[2] Number	Best Evidence[2] SMR[3]
All causes	3453.50	4951	143[c]	4951	143[c]
All cancer	761.41	2127	279[c]	2295	301[c]
Lung cancer	268.66	1008	375[c]	1168	435[c]
Pl. meso[4]	---	89	---	173	---
Perit. meso[4]	---	92	---	285	---
G.I. Cancer[5]	135.69	188	139[c]	189	139[c]
G.I. Cancer-extended[6]	191.66	324	169[c]	269	140[c]
Non-Infectious respiratory disease	144.82	465	321[c]	507	350
Asbestosis[4]	---	201	---	427	---
All other causes	2547.27	2359	93[c]	2149	84[c]

1. Expected deaths based upon death rates 1967-1986 of the U.S. National Center for Health Statistics, for white males.

2. Ascertained after review of autopsy, surgical and clinical material. Where no such data were available, death certificate diagnosis was utilized except for mesothelioma. Cases were accepted for this diagnostic category only after Mount Sinai's histopathology review and confirmation.

3. Calculated for information only, since it utilized "best evidence vs. death certificate" diagnoses, not strictly comparable due to different quality of ascertainment and verification.

4. Rates are not available since these have been rare causes of death in the general population.

5. Includes cancer of stomach, esophagus, colon/rectum.

6. Includes cancer of stomach, esophagus, colon/rectum, liver, gall bladder and bile ducts.

Probability levels = $p<.05$ [b]$p<.01$ [c]$p<.001$

Table 3

Deaths among 17,800 asbestos insulation workers
in the United States and Canada
January 1, 1967 - December 31, 1986

Less common asbestos-associated cancers

		Observed deaths			
Cause of Death	Expected Deaths[1]	Death Certificate Number	(DC) Ratio	Best Evidence Number[2]	Ratio[3]
Cancer of Laryrux	10.57	17	1.61	18	1.70[a]
Cancer of Oro-pharynx	22.02	38	1.75[b]	48	2.18[a]
Cancer of Kidney	18.87	32	1.70[b]	37	1.96[a]
Cancer of Pancreas	39.52	92	2.33[a]	54	1.37[a]
Cancer of Esophagus	17.80	29	1.63[a]	30	1.68[a]
Cancer of Stomach	29.36	34	1.16	38	1.29
Cancer of Colon/rectum	88.49	125	1.41[c]	121	1.37[b]
Cancer of Gall bladder, bile ducts	5.37	13	2.42[b]	14	2.61[b]

1. Expected deaths based upon death rates 1967-1986 of the U.S. National Center for Health Statistics, for white males.
2. Ascertained after review of autopsy, surgical and clinical material. Where no such data were available, death certificate diagnosis was utilized.
3. Calculated for information only, since it utilized "best evidence" vs. "death certificate" diagnoses, not strictly comparable due to different quality of ascertainment and verification.

Prob. - Range -		
	<.001 - c	.001 but less than .009
	<.01 - b	.010 but less than .050
	<.05 - a	

Table 4

Deaths among 17,800 Asbestos Insulation Workers
in the United States and Canada
January 1, 1967 - December 31, 1986

Cancers Not Found With Increased Incidence

				Observed Deaths	
Cause of Death	Expected Deaths[1]	Death Certificate Number	(DC) Ratio	Best Evidence Number	(BE)[2] Ratio[3]
Cancer of bladder	20.77	17	0.82	22	1.06
Cancer of prostate	52.56	59	1.12	61	1.16
Leukemia	28.74	32	1.11	33	1.15
Lymphoma	43.24	33	0.76	39	0.90
Melanoma (skin)	12.65	11	0.87	9	0.71
Brain tumors (all)	26.35	40	1.52[a]	3	1.25
Cancer	22.55	29	1.29	7	1.20
Cancer of liver	11.06	31	2.80[a]	12	1.00

1. Expected deaths based upon death rates 1967-1986 of the U.S. National Center for Health Statistics, for white males.
2. Ascertained after review of autopsy, surgical and clinical material. Where no such date were available, death certificate was utilized.
3. Calculated for information only, since it utilized "best evidence" vs. death certificate diagnoses, not strictly comparable due to different qualify of ascertainment and verification.

Prob - Levels -	
	<.001 = c
	< .01 = b
	< .05 = a

Table 8

Deaths of gastro-intestinal cancer[4] among 17,800 asbestos insulation workers in the United States and Canada, 1967-1986

Duration from onset of employment			Observed and expected			
			Observed deaths			
			(OC)[1]		(BE)[2]	
Years from onset (years)	Person-years	Expected deaths	Number	Ratio	Number	Ratio
<15	61,655.4	2.34	1	0.43	1	0.43
15-19	52,709.5	5.72	5	0.87	6	1.05
20-24	57,595.4	12.54	25	1.99[a]	25	1.99[a]
25-29	50,518.7	20.75	29	1.40	28	1.35
30-34	37,165.8	25.71	31	1.21	32	1.24
35-39	20,340.0	21.90	25	1.14	32	1.46[a]
40-44	10,200.5	15.56	27	1.74[b]	25	1.61[a]
45-49	5,256.5	10.64	18	1.69[a]	14	1.32
50+	6,151.0	20.53	27	1.32[c]	26	1.27
	301,592.6	135.69	188	1.39[c]	189	1.39[c]

1. Expected deaths are based upon age and year specific death rates 1967-1986 of the U.S. National Center for Health Statistics, for white males ("DC").
2. Best evidence ("BE"). Ascertained after review of all available autopsy, surgical and clinical material. Where no such data were available, death certificate diagnosis was utilized.
3. Calculated for information only, since observed deaths are based on best evidence while expected deaths are those calculated from death certificate rates of the U.S. National Center for Health Statistics 1967-1986 for white males. The two are not strictly comparable since they reflect different quality an precision of ascertainment (death certificate diagnosis are not generally subjected to investigation and verification).
4. Includes cancer of stomach, esophagus, colon/rectum (and 2 cases of cancer of the small intestines).

Prob. Range - <.001 - c
<.01 - b
<.05 - a

Selikoff, I.J., "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place," Andrews Communications, Inc., p. 11, (1990).

19. Seidman and Selikoff 1990

In their 1990 article, "Decline in Death Rates Among Asbestos Insulation Workers 1967-1986 Associated with Diminution of Work Exposure to Asbestos," Drs. Seidman and Selikoff again reported on the mortality experience of the 17,800 American and Canadian insulation workers. Mortality figures as of 1986 were compared to those in 1972 and 1979 in Table 7 below. Notably, the SMR's for gastrointestinal cancers show a consistent decline over the years.

Table 7. Observed and Expected Deaths among 17,800 Asbestos Insulation Workers in the United States and Canada, 1967-1986: Deaths in Three Periods of Time, 1967-1972, 1973-1979, 1980-1986.

Observed DC / Cause of Death	Observed BE Expected	No.	SMR	No.	SMR
Expected and Observed Deaths, 1967-1972					
All causes	945.35	1395	148	139	148
All cancer	173.19	553	319	591	341
Lung cancer	55.39	255	460	286	516
Pleural mesothelioma	-	21	-	30	-
Peritoneal mesothelioma	-	14	-	63	-
G.I. cancer	32.82	57	174	62	189
G.I. cancer-extended	46.59	100	215	83	178
Non-infectious respiratory disease	31.85	111	349	132	414
Asbestosis	-	46	-	105	-
All other causes	740.31	731	99	672	91
Expected and observed deaths, 1973-1979					
All causes	1195.13	1749	146	1749	146
All cancer	259.48	740	285	803	309
Lung cancer	91.51	361	394	418	459
Pleural mesothelioma	-	27	-	61	-
Peritoneal mesothelioma	-	19	-	94	-
G.I. cancer	46.51	62	133	61	131
G.I. cancer-extended	65.65	112	171	86	133
Non-Infectious respiratory disease	47.06	167	355	172	365
Asbestosis	-	69	-	145	-
All other causes	888.59	842	95	774	87
Expected and observed deaths, 1980-1986					
All causes	1313.02	1807	138	1807	138
All cancer	328.74	834	254	901	274
Lung cancer	120.96	391	322	464	381
Pleural mesothelioma	-	41	-	82	-
Peritoneal mesothelioma	-	45	-	128	-
G.I. cancer	56.35	69	122	66	117
G.I. cancer-extended	79.42	112	141	99	125
Non-infectious respiratory disease	65.91	187	284	203	308
Asbestosis	-	86	-	177	-
All other cases	918.37	786	86	703	77

p = .05, p = .01 and p = .001 levels under the Poisson distributions with Program 13 in Rothman et al. Populations at risk are enumerated in Table 6 and include 301,592.6 person-years at risk 1967-1986.

Seidman, H. & Selikoff, I.J., "Decline in Death Rates Among Asbestos Insulation Workers 1967-1986 Associated with Diminution of Work Exposure to Asbestos," Annals of the New York Academy of Sciences, 1990, Vol. 609, p. 308.

20. Brown, Hoskins, Miller, and Mossman 1990

In 1990, Brown and Associates concluded that efforts to link other cancers to asbestos were poorly justified:

> "The health consequences of exposure to asbestos and other mineral fibres can include the excessive deposition of collagen (fibrosis) at various thoracic sites, tumours of the pleura or peritoneum (mesothelioma) and lung cancer. Attempts have been made to link asbestos exposure to tumours at other sites but these are problematic and poorly justified (Mossman & Gee, 1989)."

Brown, R.C., Hoskins, J.A., Miller, K., and Mossman, B.T., "Pathogenic Mechanisms of Asbestos and Other Mineral Fibres," Molecular Aspects of Medicine, Vol. 11, 1990, p. 326.

IV. ASBESTOS AND SPECIFIC CANCERS

A. PHARYNGEAL CANCER

1. Description and Etiology

The pharynx is the part of the alimentary canal which is located behind the nose, mouth, and larynx. (Gray's Anatomy, p. 889-890 (1974)). It is a musculomembranous tube that extends from the base of the skull to the lower border of the sixth cervical vertebra where it meets the esophagus. The four and one-half inches of the pharynx may be divided into the nasal, oral, or laryngeal. The nasal pharynx performs respiratory functions only. The oral pharynx serves as a passageway for food as well as air and the laryngeal pharynx serves as a passageway for food only. Id.

The mouth and pharynx are lined by a mucous membrane which is composed of the epithelium, a basement membrane, and the fibro-elastic lamina propria. The wall of the pharynx is composed of a mucous membrane, a muscle layer and a thin fibrous sheath that attaches the pharynx to the adjacent structures.

Only 3 percent of all cancers in the United States are cancers of the oral cavity. In 1989, it was estimated that there would be 31,000 new cases of oral cancer. American Cancer Society, Cancer Facts and Figures-1989, p. 11 (1989). The incidence of mouth cancer is twice as high in males as in females, and is

most frequently found in men over the age of 40. Oral cancer can affect any part of the oral cavity, including the lip, tongue, mouth, or throat. In 1989, it was estimated that there would be 8,650 deaths due to oral cancer. Id. at 9.

The five year survival rates for oral cancer vary substantially depending upon the site in the oral cavity. Rates range from 32 percent for patients with pharyngeal cancer, to 91 percent for patients with lip cancer. Overall the five year survival rate is approximately 51 percent. Id.

2. Risk Factors

Users of tobacco products including cigarettes, cigars, pipes, or smokeless tobacco are at an increased risk for developing oral cancer as are heavy alcohol drinkers.

The synergistic effect of alcohol and tobacco is well recognized. Many authors have concluded that the relative risk of contracting cancer is 2 and 1/2 times that expected if the effects of alcohol and tobacco were merely added together. Keane, et al., "Epidemiology of Head and Neck Cancers," The Laryngoscope, 1981, Vol. 99, pp. 2037-2045, 2041. The effects of alcohol and tobacco may account for 75% of the oral cancers of men in the United States. Table 1 demonstrates some of the agents that are allegedly associated with cancers of the oral cavity. Id. at 2042.

TABLE I.

Agents Associated with Cancer in the Head and Neck.

Agent	Circumstances	Anatomic Site
Aflatoxin	Food, dust	Nasal sinuses
Arsenic	Manufacturing, mining, medication, pesticides	Lung, pharynx
Asbestos	Manufacturing, mining, insulation, environment	Lung, larynx
Bis (Chloromethyl) ether	Chemical manufacturing	Lung
Chromium	Manufacturing	Lung, nasal sinuses
Ethanol	Diet	Pharynx, larynx
Mustard gas	Manufacturing	Lung, nasal sinuses, larynx, pharynx
Nickel	Manufacturing	Lung, nasal sinuses, larynx
Polycyclic hydrocarbons	Manufacturing, environment	Lung, nasal sinuses, larynx, pharynx
Quid	Chewing	Oropharynx
Radiation (ionizing)	Medical treatment, X-ray technique (mesothorium), dial painters	Nasal sinuses, pharynx, lip
Tobacco	Chewing, smoking	Pharynx, larynx, lung
Wood and leather dust	Manufacturing	Nasal sinuses
Oils and chemical, vinyl, chloride, hydrocarbons, nitrosamines, benzene, isopropyl oil, naphthylamine, aniline, dyes, carbon tetrachloride.	Manufacturing	Lung, nasal sinuses, larynx

Keane, et al., "Epidemiology of Head and Neck Cancers," The Laryngoscope, 1981, Vol. 99, 2042.

In their large case-control study of California and New Jersey residents, Blot and Associates examined the risk of oral and pharyngeal cancer in smokers and drinkers. They reported the following:

> A case-control study of oral and pharyngeal cancer conducted in four areas of the United States provided information on the tobacco and

alcohol use of 1,114 patients and 1,268 population-based controls. Because of the large study size, it could be shown that the risks of these cancers among nondrinkers increased with amount smoked, and conversely that the risks among nonsmokers increased with the level of alcohol intake. Among consumers of both products, risks of oropharyngeal cancer tended to combine more in a multiplicative than additive fashion and were increased more than 35-fold among those who consumed two or more packs of cigarettes and more than four alcoholic drinks/day.

Blot, W. J., McLaughlin, J.K., Winn, D.M., et al., "Smoking and Drinking in Relation to Oral and Pharyngeal Cancer," Journal of Cancer Research, 1988, Vol. 48, pp. 3282-3287, 3282.

Individuals with diets low in vitamins A and C as well as beta-carotene are at a substantial risk for pharyngeal cancer. McLaughlin, J.K., Gridley, G., Block, G., et al. "Dietary Factors in Oral and Pharyngeal Cancer," Journal of the National Cancer Institute, 1988, Vol. 80, pp. 1237-1243; Rossing, M.; Vaughan, T.L., McKnight, B., "Diet and Pharyngeal Cancer," International Journal of Cancer, 1989, Vol. 44, pp. 593-597.

Mustard gas production workers have been shown to be at an increased risk of contracting respiratory tract carcinomas, including cancers of the oral pharynx and nasal pharynx. Keane, et al., "Epidemiology of Head and Neck Cancer," The Laryngoscope, 1981, Vol. 91, pp. 2037-45. Also occupationally at risk are those working in nickel refining, woodcrafting and shoe making. Id. at 2038.

Workers exposed to formaldehyde, wood dust, nickel, chromium, and other occupational agents have been shown to be at an increased risk for cancer of the nasopharynx and nasal sinus cavities. Olsen, et al., "Occupational Formaldehyde Exposure and Increased Nasal Cancer Risk in Man," International Journal of Cancer, 1986, Vol. 34, pp. 639-644. Table III below lists substances that have allegedly been associated with an increased risk of cancer of the nasopharynx or sinuses with occupational exposure. Id. at 640.

TABLE III - CARCINOMAS OF THE SINONASAL CAVITIES AND NASOPHARYNX IN RELATION TO OCCUPATIONAL EXPOSURE

Exposure	Sex	Exposure frequency among controls(%)	Carcinomas of the Sinonasal cavities RR	95% C.L.	Nasopharynx RR	95% C.L.
Formaldehyde	M	4.2	2.8	1.8- 4.3	0.7	0.3- 1.7
	F	0.1	2.8	0.5-14.3	2.6	0.3-21.9
Wood dust	M	5.8	2.5	1.7- 3.7	0.4	0.2- 1.0
	F	0.0	--		--	
Leather dust	M	0.1	1.7	0.5- 6.3	00	
	F	0.0	1.8	0.2-17.2	--	
Nickel, chromium	M	7.2	1.2	0.8- 1.9	1.1	0.6- 2.0
	F	0.0	--		--	
Chlorophenois	M	1.9	1.4	0.6- 3.0	0.5	0.1- 2.1
	F	0.0	--		--	
Textile dust	M	1.9	0.7	0.2- 1.9	0.9	0.2- 2.6
	F	2.5	1.3	0.5- 3.5	1.5	0.4- 5.2
Man-made mineral fibers	M	3.7	0.9	0.5- 1.8	1.0	0.4- 2.2
	F	0.0	--		--	
Asbestos	M	2.3	1.5	0.7- 3.0	0.9	0.3- 2.6
	F	0.0	--		--	
Metal work	M	9.9	1.4	1.0- 1.5	1.3	0.8- 2.0
	F	0.0	--		2.7	0.3-22.4
Paint, lacquer and glue manufacture	M	8.4	2.1	1.4- 3.0	0.7	0.4- 1.3
	F	1.4	1.9	0.6- 5.8	0.9	0.1- 6.8
Plastic manufacture	M	1.2	1.1	0.4- 3.1	1.2	0.4- 4.2
	F	0.0	2.8	0.5-14.3	2.6	0.3-21.8
Silage manufacture	M	3.5	1.0	0.5- 1.9	0.4	0.1- 1.4
	F	0.0	--		--	

Olsen, et al., "Ocupational Formaldehyde Exposure and Increased Nasal Cancer Risk in Man," International Journal of Cancer, 1984, Vol. 34, pp. 639-644, 641.

3. Asbestos Exposure

In Dr. Lumley's proportional study of cancer registrations for dockyard workers, no significant excess of pharyngeal cancer was identified. Of the more than 1,300 dockyard workers employed between 1960 and 1969, 53 cases of cancer of the buccal cavity and pharynx were reported versus 51.3 expected yielding an insignificant SMR at the 103.3

level. Lumley, K.P.S, "A Proportional Study of Cancer Registrations of Dockyard Workers," British Journal of Industrial Medicine, 1976, Vol. 33, pp. 108-110.

In "Mortality Experience of Insulation Workers in the United States and Canada, 1943-1976," Drs. Selikoff, Hammond and Seidman reported only 1.7 deaths caused by cancers of the larynx, pharynx, and buccal cavity where 2.0 were expected. Selikoff, I.J., Hammond, E.C., Seidman, H., "Mortality Experience of Insulation Workers in the U.S. and Canada, 1943-1976," Annals of the New York Academy of Science, Vol. 330, pp. 91-116, 94.

The results of Dr. Enterline's study of 1,074 retirees from a U.S. asbestos company is consistent with previous studies showing a statistically insignificant excess of cancer deaths caused by pharyngeal cancer. Five cases were observed where 3.60 were expected (SMR=139). Enterline, P.E., Hartley, J., Henderson, V., "Asbestos and Cancer - a Cohort Followed up to Death," British Journal of Industrial Medicine, 1987, Vol. 44, pp. 396-401, 397.

In his recent report on the mortality of 17,800 asbestos insulation workers in the U.S. and Canada, Dr. Selikoff reported an increased risk for cancer of the oropharynx as compared to his 1979 report. Dr. Selikoff reported a relative risk of 1.73 for cancer of the oropharynx with 38 cases reported compared to 22.02 expected. Selikoff, I.J., "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place," Andrews Communications, Inc. (1990). Significantly, Dr. Selikoff's failure to control for alcohol or tobacco casts a dark shadow on these results given the important etiological role these factors play in carcinogenesis.

The epidemiological evidence concerning asbestos exposure and pharyngeal cancer is varied and conflicting. Despite Dr. Selikoff's recent report, studies which account for smoking and alcohol have failed to convincingly establish an association between asbestos exposure and pharyngeal cancer.

B. LARYNGEAL CANCER

1. Description and Etiology

The larynx is the organ of voice which lies between the trachea and the base of the tongue. (Gray's Anatomy, p. 955). Laryngeal cancer is relatively uncommon with peak incidence occurring during the seventh decade of life. Laryngeal tumors may be categorized into three groups depending on anatomical origin: supraglottic, glottic, and subglottic. See Schottenfeld, D., and Fraumeni, J.F., at pp. 554-55. These tumors occur in the United States at an approximate ratio of 40:59:1, respectively. Id. The most common form of laryngeal cancer is of the squamous cell type with the majority of these being moderately or well differentiated. (Cowles, 1983). Laryngeal cancer occurs predominantly in men. Of those diagnosed with laryngeal cancer in the United States, 60 percent of cases involve tumors still localized to the larynx, 25 percent are not diagnosed until the cancer has spread to nearby lymph nodes, and 15 percent are not diagnosed until the cancer has spread to more remote parts of the body. The prognosis for those with laryngeal cancer is favorable with 64 percent of the white males diagnosed between 1967 and 1973 reaching the five year survival rate. Survival rates for white males are slightly better than for white females and blacks. Id.

2. Alcohol and Tobacco

Drs. Chan and Gee reported on the importance of alcohol and tobacco use in the etiology of laryngeal cancer:

> There has been a gradual increase in laryngeal cancer rates in the United States over the last four decades. Part of the increase may be attributable to more accurate reporting of the disease or increased detection, but smoking and alcohol drinking have been consistently shown to be the two most important environmental factors for this neoplasm. The dose-response relationships which support causality between smoking, alcohol, and laryngeal cancer have been

> elegantly demonstrated by Wynder, et al and Rothman, et al. Flanders and Rothman also reported a synergistic effect between smoking and alcohol consumption for laryngeal cancer; the interaction being such that a one pack-a-day smoker who also consumes a moderate amount of alcohol (more than 6 ounces of liquor per day) has a greater than twenty-fold increased risk of developing laryngeal cancer.

Chan, C.K. and Gee, J.B., "Asbestos Exposure and Laryngeal Cancer: An Analysis of the Epidemiological Evidence", Journal of Occupational Medicine, 1988, Vol. 30, p.23.

David Edelman reported on the overwhelming effect of smoking on the incidence of laryngeal cancer.

> Smoking is associated with a high relative risk of laryngeal cancer. In the study of U.S. veterans, the risk of death from cancer of the larynx was 11.5 times higher for smokers and 4.8 times higher for ex-smokers compared to never smokers. In the American Cancer Society study of over one million men and women the mortality ratios for men with a history of cigarette smoking compared to those who never smoked regularly were 6.1 for men aged 45 to 64, and 9.0 for men aged 65 to 79.

Edelman, D., "Laryngeal Cancer and Occupational Exposure to Asbestos", International Archives of Occupational and Environmental Health, 1989, Vol. 61, p. 226.

There is strong epidemiological data to support the assertion that tobacco and alcohol are the primary risk factors for laryngeal cancer.

> Tobacco and alcohol are both major causes of laryngeal cancer and an excess on the order of 50 percent could possibly be due to above average consumption of either.

Doll, R., and Peto, R., "Asbestos - Effects on Health of Exposure to Asbestos," Health & Safety Commission, London: HMSO 1985.

3. Risk Factors

Risk factors identified in the literature for laryngeal cancer include exposure to nickel, mustard gas, strong alcohol, wood dust, irradiation, grain, and foundry materials.

Pederson, et al. reported nearly a six-fold increase in observed to expected deaths among workers at a Norwegian Nickel refinery. See Pederson E., Hogetveit A.L., Anderson, A., "Cancer of Respiratory Organs at a Nickel Refinery," Norway International Journal of Cancer, 1943, Vol. 12, pp. 32-41.

Wada et al. reported an increased mortality from respiratory tract cancer including laryngeal cancer, among Japanese workers manufacturing mustard gas between 1929 and 1945. See Wada S., Miya Nishi, M., Nishimoto, Y., et al., "Mustard Gas as a Cause of Respiratory Neoplasia in Man," Lancet, 1968, Vol. 1, pp.1161-1165.

Lynch et al. found a significant excess of laryngeal cancer among workers involved in the manufacture of ethanol in which high concentrations of dimethyl sulfate was used. See Lynch, J., Harris, N.M., Bird, M.G., et al., "An Association of Upper Respiratory Cancer with Exposure to Dimethyl Sulfate," Journal of Occupational Medicine, 1979, Vol. 21, pp. 333-341.

Wynder et al. found a strong association between exposure to wood dust and laryngeal cancer in a retrospective case control study of laryngeal cancer patients. Although their findings have not been confirmed by others, they reported a relative risk among non-smokers of 24 (4.9070 C.L. = 8-70). See Wynder, E.L., Covey, L.S., Mabuchi, K., et al., "Environmental Factors of Cancer of the Larynx - A Second Look," Cancer, 1976, Vol. 38, pp. 1591-1601.

Dietary factors also associated with laryngeal cancer include deficiencies in vitamins A and C. (Cann and Fried, (1984)).

4. Asbestos Exposure

A relationship with laryngeal cancer was suggested by a retrospective case control study in 1973. Drs. Stell and McGill studied 119 patients

diagnosed with squamous laryngeal carcinoma. Thirty-three patients reported significant asbestos exposure. The authors admitted the weaknesses of their study:

> Whilst the results quoted above suggest that there is an association between exposure to asbestos and laryngeal carcinoma, it has to be admitted that this conclusion is based on a retrospective study, with all the disadvantages of such a study. We would also like to point out that this report is based on a small number of male patients who may have been influenced by the prospect of compensation.

Stell, P.M. and McGill, T., "Exposure to Asbestos and Laryngeal Carcinoma," Journal of Laryngology and Otology, 1975, Vol. 89, pp. 513-517, 515.

In their study stratified for tobacco use, alcohol consumption, and asbestos exposure, Hinds et al. found no increased risk from asbestos exposure alone. To elucidate the importance of adjusting for smoking and alcohol, the unadjusted odds ratio for laryngeal cancer associated with asbestos exposure was somewhat high but statistically insignificant at the 1.76 level, however after adjustment the ratio became 1.0. In their discussion, the authors conclude:

> This study found, as have others, that the most readily identifiable risk factors for laryngeal cancer are tobacco and alcohol consumption. 9.20,21 The findings in this study, however, are not supportive of the hypothesis that asbestos exposure is an important risk factor for cancer of the larynx, although the RR of 1.75 found is consistent with a small risk associated with asbestos exposure. Both the studies of Stell and McGill 17 and Shettigara and Morgan 15 found very high relative risks for laryngeal cancer associated with asbestos exposure (RR=14.5 and ∞, respectively). It is difficult to understand why such a strong relationship would have been missed in the current study if it is a real one.

Hinds, M.W. and Thomas, D.B., O'Reilly, H.P., "Asbestos, Dental X-rays, Tobacco and Alcohol in the Epidemiology of Laryngeal Cancer," Cancer, 1979, Vol. 44, pp. 1114-1120.

Selikoff, et al., in 1979, reported a relative risk of 1.91 for laryngeal cancer in the cohort of 17,800 United States and Canadian insulation workers. Unfortunately, neither tobacco nor alcohol was considered. Selikoff, I.J., Hammond, E.C., Seidman, H., "Mortality Experience in Insulation Workers in United States and Canada 1943-1976," Annals of the New York Academy of Science, 1979, Vol. 330, pp. 91-116.

An increased risk of 3.16 was reported by Rubino, et al. in their mortality study of 900 Northern Italian chrysotile miners. Although all six of the cases were smokers, smoking was not considered. Notably, standardized mortality ratios of 2.53 and 3.13 were found for non-malignant respiratory diseases and cirrhosis of the liver respectively, thus clarifying the need for adjustment for both alcohol and tobacco. Rubino, G.F., Pivlatto, G., Newhouse, M.L., et al., "Mortality of Chrysotile Asbestos Workers at the Balangero Mine, Northern Italy," British Journal of Industrial Medicine, 1979, Vol. 36, pp. 187-194.

Burch, et al. conducted a case control study of laryngeal cancer in 204 newly diagnosed subjects and controls which were matched for age, sex, and residence. Burch, J.D., Howe, G.R., Miller, A.B., Semenciw, R., "Tobacco, Alcohol, Asbestos and Nickel in the Etiology of Cancer of the Larynx: A Case-Control Study," Journal of the National Cancer Institute, 1981, Vol. 67, pp. 1219-1224. Smoking history, alcohol use and asbestos exposure were the factors under study. A dose-response relationship with relative risks of 1.0 for non-smokers, 2.0 for those with life-time consumption of less than 150,000 cigarettes, 4.5 for those who smoked 150,000-299,000 cigarettes, and 5.4 for those who consumed 300,000 cigarettes or more was found. Consumption of alcohol was also examined, yielding relative risks from 1.3 for consumption of more than four drinks of spirits per day to 4.8 for consumption of more than four drinks of beer per day.

Finally, Burch and Associates examined asbestos exposure. Subjects were categorized as "exposed" or "unexposed" based both upon their personal opinion and that of an occupational epidemiologist. Twenty-three of 204 subjects and seven controls were classified by the occupational epidemiologist as exposed, yielding a relative risk of

2.3 after adjustment for smoking. Although an increased relative risk was found, this result is of little validity since the number of those "definitely exposed" was so small. Furthermore, no concrete information was provided as to duration or time since first exposure. The authoris discussed the inherent limitations of the case-control study as it relates to laryngeal cancer:

> ...the case-control study, is subject to three methodologic problems: the relative infrequency of larynx cancer and exposure to asbestos in the population, the difficulty in the assessment of whether or not an individual really has been exposed to asbestos when one relies on interview data, and the need to adequately control for the possible confounding effects of tobacco and alcohol. In view of these problems it is hardly suprising that RR estimates ranging from 1.4 to 13 have been obtained from case-control studies (3, 5, 8, 15).

Burch, J.D., Howe, G.R., Miller, A.B., Semenciw, R., "Tobacco, Alcohol, Asbestos and Nickel in the Etiology of Cancer of the Larynx: A Case-Control Study," Journal of the National Cancer Institute, 1981, Vol. 67, p. 1224.

Newhouse has conducted two studies yielding statistically significant relative risks of 5.41 and 3.70. Although numerically impressive, these results are of little value given the fact that only two and three cases of laryngeal cases were present. Furthermore, the combined effects of alcohol and tobacco were not considered even though the author admits that tobacco use is positively associated with laryngeal cancer. Newhouse, M.L., "A Study of the Mortality of Workers in an Asbestos Factory," British Journal of Industrial Medicine, 1969, Vol. 26, pp. 294-301; Newhouse, M.L., Berry, G., Wagner, J.C., "Mortality of Factory Workers in East London 1933-1980," British Journal of Industrial Medicine, 1985, Vol. 42, pp. 4-11.

Drs. Chan and Gee conducted a critical analysis of the studies allegedly establishing a causal relationship between asbestos exposure and laryngeal cancer in 1988. Concluding that the available epidemiological data does not support a causal association between asbestos exposure and laryngeal

cancer, Chan and Gee suggest that the leading studies claiming such a link are biased to the extent they did not take into account the smoking and alcohol habits of their subjects. Chan and Gee suggest that:

> ... much of the evidence derives from epidemiologic studies which have simply examined the relation between asbestos and laryngeal cancer without any regard to other known potent carcinogenic factors, specifically cigarette smoking and ethanol consumption, and second that the evidence implicating asbestos is minimal or absent.
>
> . . .
>
> ... In sharp contrast to other incontrovertible hazards of asbestos,[1,2] the foregoing evidence inculpating asbestos in laryngeal cancer is weak or nonexistent.[3-13, 21-34] With a few exceptions,[9-11, 27-33] discussed above, the SMRs for laryngeal cancer in asbestos workers are all small.[3-8, 23-26]
>
> . . .
>
> If only 10% of an asbestos worker population were to smoke more than one pack a day or to smoke one pack a day and drink 6 oz. of ethanol a day, then the SMR for laryngeal cancers in the ***whole*** population would approach three times that of a nonsmoking, nondrinking population. (emphasis added)

Chan, C.K. and Gee, J.B., "Asbestos Exposure and Laryngeal Cancer: An Analysis of the Epidemiologic Evidence," Journal of Occupational Medicine, 1988, Vol. 30, pp. 23-27, 23,26.

Dr. Raymond Parks reported on laryngeal carcinoma, stating:

> Carcinoma of the larynx is known to be linked with cigarette smoking but an association between asbestos exposure and an increased incidence of this tumour which appears to develop ten years earlier than in patients with no known asbestos exposure was reported by Stell and

McGill (1973 and 1975). Other studies have suggested that the association with asbestos, which is largely confined to smokers, is stronger than the association with smoking alone, (Libshitz, et al., 1974; Morgan and Shettigara, 1976). However, in 4463 deaths among 11,379 chrysotile production workers followed from 1926 to 1975 there was no excess due to laryngeal carcinoma - 21 cases in all (McDonald et al., 1980). And no evidence of a relationship between the tumour and asbestos exposure was found in an unselected group of 305 male and 206 female patients attending a London Hospital (Newhouse, Gregory and Shannon, 1979); in 47 males with laryngeal cancers in Washington State (Hinds, Thomas and O'Reilly, 1979); and in 60 cases investigated in Italy (Bianchi et al., 1978). The importance of the combination of alcohol with smoking and development of the tumour has been emphasized by McMichael (1978) who also noted ethnic associations.

At present, therefore, it is incorrect to regard asbestos exposure as a proven cause of this uncommon tumour.

Parks, W.R., "Silicates and Lung Disease," Chapter 9, Occupational Lung Disorders, 2nd Edition, 1982, p. 294, 295.

Of 11,379 miners exposed to chrysotile fibers in Quebec, Canada, McDonald, et al., found no excess deaths from laryngeal cancer (RR 1.07). McDonald, J.C., Liddell, F.D.K., Gibbs, G.W., et al., "Dust Exposure and Mortality in Chrysotile Mining 1910-1975," British Journal of Industrial Medicine, 1980, Vol. 37, pp. 11-24. These results were confirmed by Hodgson and Jones whose review of over 30,000 asbestos insulation workers in 1981 found no excess deaths due to laryngeal cancer. Hodgson, J.T.; Jones, R.D., "Mortality of Asbestos Workers in England and Wales, 1971-1971," British Journal of Industrial Medicine, 1986, Vol. 43; pp. 158-164.

While tumors have been reported in the larynx in some cohorts of asbestos workers, other etiologies such as smoking and alcohol confound the determination of epidemiologic data. Mossman,

B.T., Bignon, J., Corn, M. Seaton, A., and Gee, J.B.L., "Asbestos: Scientific Developments and Implications for Public Policy," Science, Vol. 247, p. 295-96.

Significantly, **no statistically significant increased risks have been identified of those studies which have controlled for alcohol and tobacco.** In his study entitled "Laryngeal Cancer and Occupational Exposure to Asbestos," Edelman reviewed data derived from 13 cohort and eight case-control studies, and concluded that none of them established an increased risk of laryngeal cancer for asbestos workers.

> In 1973 Stell and McGill first suggested that occupational exposure to asbestos may be associated with a higher risk of laryngeal cancer.
>
> . . . .
>
> A 1980 review of the aetiology of laryngeal cancer concluded there was a positive association with asbestos exposure. However, the results of studies published since 1980 do not support this point of view. The apparent contradictory data between asbestos exposure and laryngeal cancer might be related to how other risk factors for laryngeal cancer (principally smoking and alcohol consumption) were taken into consideration in the data analyses. Some studies totally ignored these risk factors while others made adjustments to the risk estimates.
>
> . . .
>
> Overall, the results from cohort studies do not indicate any higher risk of laryngeal cancer mortality for asbestos-exposed workers.
>
> . . .
>
> None of the studies published since 1979 have found a significantly higher risk of laryngeal cancer among persons with occupational asbestos exposure. In these studies the relative risk estimates ranged from 0.3 to 1.8 and the SMRs ranged from 0.56 to 1.74. These findings do not point to an association between laryn-

geal cancer and occupational exposure to asbestos. The finding of some investigators of a higher risk of laryngeal cancer for asbestos workers must be attributed to some aspects of the methodologies used, and to the failure of the investigators to account adequately for alcohol and tobacco consumption: two risk factors for laryngeal cancer that have been demonstrated in many studies.

Edelman, D., "Laryngeal Cancer and Occupational Exposure to Asbestos", International Archives Occupational Environmental Health, 1989, Vol. 61, p. 225-226.

Drs. Churg and Green also confirm that there is no pathological means to determine if laryngeal cancer, among others, is caused by asbestos. Given the common occurrence of such cancer in the nonexposed population, there is no scientific way for a pathologist to link a specific case of laryngeal cancer to asbestos exposure. Churg, A. and Green, F., Pathology of Occupational Lung Disease, p. 319, (1988).

In "The Third Wave of Asbestos Disease - Exposure to Asbestos in Place," Selikoff's results support the assertions expressed by other researchers that asbestos does not place an individual at an increased risk of developing laryngeal cancer. For the recent follow up period, Selikoff reported 17 deaths due to laryngeal cancer where only 10.57 were expected, yielding a statistically insignificant relative risk of 1.61. Selikoff, I.J., "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place," 1990. However, this risk might be articially high since neither alcohol nor tobacco use was controlled for. Furthermore, the studies which did control for tobacco and alcohol support the position that asbestos exposure is not an important factor in the development of laryngeal cancer.

In 1990, Dr. F.D.K. Liddell commented on the varying results of the epidemiologic studies which have examined asbestos exposure and laryngeal cancer in an editorial published in the British Journal of Medicine:

To summarize the findings: (1) those from the case-referent studies are mutua-

lly inconsistent; (2) those from the cohort studies, while not demonstrably inconsistent, do not indicate a major excess of laryngeal cancer mortality in cohorts of asbestos workers; and (3) exposure-response relations were unobtainable or equivocal. No experimental evidence has been proffered. Estimates of the RR of cancer of the larynx obtained from the various surveys are so divergent that it is impossible to find a merged value without violating established epidemiological principles. The disease has seldom been found among non-smoking asbestos workers and there is no evidence as to whether these few cases were also non-drinkers.

Thus it is my opinion that the evidence on the link between exposure to asbestos and laryngeal cancer definitely fails to satisfy the criteria for causation set by Bradford Hill. Furthermore, even if asbestos cannot be disregarded as one of the subsidiary causes of laryngeal cancer the risk of such cancer after exposure to asbestos (relative to its asbence) is lower than that for lung cancer; and as the absolute risk of laryngeal cancer is much less than that of lung cancer, the absolute risk attributable to asbestos must be extremely small. Finally, excesses appear quite unlikely in relation to exposure to chrysotile, although this fibre was and is by far the most common form of asbestos.

The Industrial Injuries Advisory Council (UK) has recently recommended that, on the balance of the evidence, cancer of the larynx should not be added to the schedule of prescribed diseases in respect of occupations involving exposure to asbestos.

Liddell, F.D.K., "Laryngeal Cancer and Asbestos," British Journal of Medicine, 1990, Vol. 47, pp. 290-291.

Of the prospective epidemiological studies undertaken which claim statistically significant relative risks for asbestos exposure and laryngeal

cancer, all are flawed in that either alcohol and/or tobacco use was not controlled for or the number of cases reported on was too small to be of any representative value. The studies which did control for tobacco and alcohol support the position that asbestos exposure is not an important factor in the development of laryngeal cancer.

C. ESOPHAGEAL CANCER

1. Description and Etiology.

The esophagus starts in the neck as a downward continuation of the pharynx. The esophagus extends downward from the neck through the mediastina of the thorax and joins the cardia of the stomach at the level of the tenth thoracic vertebra. Gray's Anatomy, pp. 891-92. When viewed from the front, the esophagus assumes the form of a gentle "s" curve. The length of the esophagus can vary, but in the average individual it is approximately 24 centimeters or, ten inches, long. The average resting width of the esophagus is approximately two centimeters. Id.

The incidence of esophageal cancer varies greatly among countries. In China, the occurrence of esophageal cancer is about 50 per 100,000 men and is responsible for 18 percent of all cancer deaths. Esophageal cancer is less frequent in the United States, with an incidence of 10 per 100,000 men which translates into about 8,000 - 9,000 new cases per year and about 8,000 deaths each year. Esophageal cancer occurs almost three times more frequently in males than females. Although the etiology of esophageal carcinoma is far from well defined, certain pre-disposing factors and conditions have been identified. Smoking and alcohol ingestion are identified risk factors, as is the drinking of hot tea. Known pre-disposing conditions include a history of previous squamous cell carcinoma of the aerodigestive tract (particularly the head and neck area); the presence of a Barrett's, or columnar, epithelium within the distal esophagus; a history of lye ingestion; and esophageal achalasia. The common element of these predisposing factors is chronic irritation of the esophageal epithelium.

2. Alcohol and Tobacco

Heavy tobacco and alcohol use has been shown to increase the risk for esophageal cancer. In fact a well defined dose-response relationship exists for both of these factors. In North America and Western Europe, 90 percent or more of the risk for esophageal cancer can be attributed to these factors alone. Different types of alcohol have been shown to lead to different risks as well. Wynder & Bross found a higher risk for heavy whiskey drinkers than for heavy beer drinkers among men smoking between 15-34 cigarettes per day. Wynder, E.L. and Bross, I.J., "A Study of Etiological Factors in Cancers of the Esophagus," Cancer, 1961, Vol. 14, pp. 389-413.

La Vecchia and Negri considered the role of alcohol in non-smokers and tobacco in non-drinkers in their 1988 study of individuals in northern Italy. Of the 250 patients interviewed with confirmed esophageal cancer who were under the age of seventy-five, 38 were classified as non-smokers and 30 as non-drinkers. They found no difference in risk between non-drinkers and moderate (more than four drinks per day) drinkers, however the risk increased from 2.1 to 3.6 for those consuming more than eight drinks per day. A statistically significant association was also found in non-drinkers who smoked. The risk estimates were 2.0 for smokers of less than 15 cigarettes, 3.9 for those that smoked 15-24 cigarettes and 6.2 for smokers of 25 or more cigarettes per day. LaVecchia, C. and Negri, E., "The Role of Alcohol in Oesophageal Cancer in Non-Smokers, and of Tobacco in Non-Drinkers," International Journal of Cancer, 1989, Vol. 43, pp. 784-786.

3. Dietary Factors

As with other gastrointestinal cancers, diet plays a large role in the development of esophageal cancer. Despite the methodological problems associated with tracking dietary habits over time through use of a questionnaire, various foods, vitamins and trace elements have been correlated with esophageal cancer. Some have proposed that the ingestion of hot food and drink sensitizes the esophagus to carcinogenic exposure. However there is no firm evidence to support this hypothesis. For example, in the Soviet Union, native Northern

and Eastern Siberians have high esophageal cancer incidence and are also reported to be heavy drinkers of strong hot tea. Kolicheva, N.I. "Epidemiology of Esophagus Cancer in the USSR," Joint USA/USSR Monograph on Cancer Epidemiology in the USA and USSR, 1980.

Nicotinic acid, and trace elements of zinc, molybdenum, and magnesium are all reported to have a beneficial effect, while copper is reported to increase risk for esophageal cancer. Vitamin A deficiency has been shown to impair the structure of the esophageal epithelium. Further, vitamin A supplementation in animals has been shown to inhibit carcinogenesis. Low riboflavin levels have also been associated with increased risk of esophageal cancer in different parts of the world.

There is some evidence that ionizing radiation and ingestion of the bracken fern are associated with an increased risk for esophageal cancer as well. Hirayama, T., "Diet and Cancer," Nutritional Cancer, 1979, Vol. 1, pp. 67-81. Also suspected of increasing risk of esophageal cancer are vitamin and mineral deficiencies including zinc, riboflavin, thiamin, pyridoxine, vitamin C, and perhaps iron. See Schottenfeld and Fraumeni at 613-614. Consumption of hard, crusty breads and very hot tea are also related to an increased risk of esophageal cancer. This combination can irritate the esophageal mucosa and is thought to predispose the esophagus for cancer over long periods of time. Swaroop, V., Damle, S.R., et al., "Nutrition and Esophageal Cancer," Seminars in Surgical Oncology, 1989, Vol. 5, pp. 370-372.

Animal protein, green vegetables, fresh fruits, dairy products, butter, margarine, and oils containing polyunsaturated fats have been found to be associated with a low risk for esophageal cancer. On the other hand, pork, wheat, corn, maize, and dried salted fish have been associated with an increased risk for esophageal cancer. See Id.

4. Asbestos Exposure

Drs. Selikoff, Churg and Hammond first suggested that esophageal cancer may be associated with asbestos exposure in their 1964 study. They found 29 deaths which were attributed to cancer of the esophagus, stomach, colon, or rectum, where only 9.7 were expected. Selikoff, I.J., Churg, J.,

and Hammond, E.C., "Asbestos Exposure and Neoplasia," Journal of the American Medical Society, 1964, Vol. 188, pp. 106-112. However, subsequent studies have failed to replicate these findings.

In 1987, Yu et al., conducted a study of confirmed cases of esophageal cancer in Los Angeles County. Cases were identified through a local cancer surveillance program which recorded all microscopically verified cases as well as those mentioned on death certificates. Controls were selected from the cases' neighborhood. Of the 488 cases identified, 275 agreed to participate in the study. In addition to questions regarding dietary and tobacco habits, the subjects were interviewed regarding workplace exposure to dusts. While there was a significant excess among cases of exposure to metal dust (42 cases: 29 controls = 2.2 R.R.), no association was found between occupational exposure to asbestos and esophageal cancer risk (18 cases: 25 controls = .6 R.R.). Noticeably, Yu, et al., identified a particularly strong association between beryllium exposure and esophageal cancer (12 cases: 2 controls = 6.0 R.R.). The results of this study may be attacked since no information was available as to the date of last exposure and duration of exposure, or the amount of exposure. However, these results are consistent with other studies which have also failed to confirm an association between asbestos exposure and esophageal cancer. Yu, A.C., Garabrant, P.H., Peters, J.M., and Mack, T.M., "Tobacco, Alcohol, Diet, Occupation, and Carcinoma of the Esophagus," Cancer Research, (1988), Vol. 48, pp. 3843-3848.

Dr. Enterline's study of 1,074 white male asbestos company retirees did not find a statistically significant excess of esophageal cancer. A slightly high, but statistically insignificant SMR of 135.6 was computed for esophageal cancer as four were observed when 2.95 were expected. Although exact fiber levels could only be estimated, the fact that the subjects in Enterline's study were exposed before threshold limit values were lowered in the 1960's, coupled with the fact that follow-up began after age 65, and the average exposure period was 25 years, lend some reliability to Dr. Enterline's findings.

Dr. Acheson et al., reported on cancer incidence among English men working in an amosite

asbestos plant. Of the almost 6,000 men who were employed between 1947 and 1979, Acheson et al., reported no statistically significant excess cancer mortality with the exception of five deaths which were due to mesothelioma. In fact, an SMR of one (1.0) was recorded for esophageal cancer in the asbestos workers, where an SMR of 1.61 was calculated for the control group. Exact information on exposure level and smoking history was not available. The results of the Acheson et al.'s study have been set out in Table 5 below.

TABLE 5 Observed deaths, expected deaths and SMRs from cancer by site amongst asbestos and other workers

	Asbestos workers (68922)+			Other workers (16609)+		
Cancer of:--	Obs	Exp	SMR	Obs	Exp	SMR
Oesophagus (150)	2	2.0	100	1	0.6	161
Stomach (151)	7	7.5	94	4	2.5	159
Colon (153)	6	4.4	137	2	1.4	142
Rectum (154)	4	3.2	124	0	1.1	0
Pancreas (157)	3	3.1	96	0	1.0	0
Lung (162,163)^	61+	29.1	210**	10	9.4	106
Skin (172,173)	1	1.0	102	0	0.3	0
Prostate (185)	2	2.1	94	2	0.9	218
Testis (186)	0	1.1	0	1	0.3	377
Bladder (188)	2	2.2	89	1	0.8	124
Other Urinary (189)	2	1.4	139	0	0.4	0
Brain etc.(191,192)	5	3.0	165	0	0.8	
Hodgkin's disease (201)	1	1.6	64	0	0.4	0
Leukaemia (204-208)	4	2.6	154	0	0.7	0
Other cancers	9++	10.0	90	3	2.9	103
All malignant neoplasms (140-209)	109	74.4	147**	24	23.5	102

+ 4 of the 61 deaths were from mesothelioma of the pleura.
++1 of the 9 deaths was from mesothelioma of the peritoneum.
* significant at 5% level.
**significant at 1% level.
^ the SMR for lung cancer for the District in which the factory is situated was 107 during 1968-78.

Acheson, E.D., Gardner, M.J., Winter, P.D., and Bennett, C., "Cancer in a Factory Using Amosite Asbestos," International Journal of Epidemiology, 1984, Vol. 13, pp. 3-10, 6.

Drs. Hodgson and Jones tracked a small decrease in the mortality experience of esophageal cancer in workers in England and Wales exposed to asbestos before the threshold limit values were lowered in 1969. Of those workers employed more than twenty years, only four (4) cases of esophageal cancer were observed when five (5) were expected.

> The present study shows no excess from cancer at any of the four main alimentary tract sites examined (oesophagus, stomach, colon, rectum), either overall or in association with increasing exposure to asbestos nor among insulation workers, who showed heavy excesses of the established asbestos related diseases. The present results therefore weigh against the hypothesis that exposure to asbestos is responsible for an increase in the incidence of cancer of the alimentary tract.

Hodgson, J.T. and Jones, R.D., "Mortality of Asbestos Workers in England and Wales 1971-81," British Journal of Industrial Medicine, 1986, Vol. 43, pp. 158-164.

Despite his initial findings that asbestos exposure may increase the risk of developing esophageal cancer, Dr. Selikoff in "The Third Wave of Asbestos Disease - Exposure to Asbestos in Place," reported a relative risk of only 1.63 for esophageal cancer among the 17,800 asbestos insulation workers tracked since 1967. This represents a slight decline in relative risk from earlier studies. Once again, smoking and alcohol were not examined in persons developing esophageal cancer to control for its effect on incidence rates.

D. STOMACH CANCER

1. Description and Etiology

The stomach is a reservoir of the digestive tract in which food is soaked in gastric juices, and then released spasmodically into the duodenum. See Gray's Anatomy, pp. 905-911. The form and size of the stomach can vary considerably depending upon the position of the body and degree of filling. The stomach is entirely covered by a peritoneum. The lining of the stomach is a reddish gray mucous membrane composed of a single surface layer of epithelial cells. The muscles of the stomach wall consist of smooth muscle fibers that are arranged in three layers. Id.

Deaths due to stomach cancer have decreased dramatically over the last fifty years in the United States. In fact, in 1930 stomach cancer was the leading cause of death among U.S. males. The American Cancer Society projected that approximately 13,900 people died from stomach cancer in 1989, representing a decrease in excess of 50 percent since 1930. American Cancer Society, "Cancer Facts & Figures," 1989, p. 29.

2. Risk Factors

Biological factors associated with stomach cancer include genetic history, anemia, and gastric ulcer. Graham and Lilienfeld conducted a family aggregation study and concluded that family members of individuals with gastric cancer are two to three times more likely to develop stomach cancer than the average individual. Graham, S. and Lilienfeld, A.M., "Genetic Studies of Gastric Cancer in Humans: An Appraisal," Cancer, 1958, Vol. 11, pp. 945-958. Other environmental factors studied in association with stomach cancer include: socioeconomic status, tobacco and alcohol use, radiation exposure, diet, and exposure to nitrate and related compounds. Tables 88.1 and 88.2, below, contain a list of other factors which are thought to play a role in the development of gastric cancer.

TABLE 88.1

Dietary and endogenous factors implicated in the etiology of gastric cancer.

Highly spiced, salted, and pickled foods
Polycyclic hydrocarbons, especially those generated by high-temperature pyrolysis of animal fat and aromatic amino acids in grilled and barbecued meats
Inorganic dusts (miners and potters)
High consumption of animal fats
High salt consumption (osmotic damage to the gastric mucosa)
Protein malnutrition (may lead to achlorhydria)
Viral infections (may damage the gastric mucosa and cause temporary achlorhydria)
Excess alcohol consumption
Tobacco smoking
Dietary nitrites
Refluxed bile acids (especially after gastric surgery)
Bacterial overgrowth in the stomach
Selenium deficiency

TABLE 88.2

Recognized risk factors in the development of gastric carcinoma

Gastric polyps
Atrophic gastritis
Type III intestinal metaplasia
Dysplasia
Previous gastric surgery
Giant rugal hypertrophy (Menetrier's disease)
Genetic factors
Blood group A
Familial hypogammaglobulinemia

Moosa, A.R., Schimpff, S.C., Robson, M.C., The Comprehensive Textbook of Oncology, Chapter 88, "Tumors of the Stomach," 1991, Vol. 1, pp. 802-882, 862-863.

3. Asbestos Exposure

As with esophageal cancer, the epidemiological studies which have examined the risk of stomach cancer in asbestos exposed individuals are varied. In their study published in 1987, Sanden et al., reported on the mortality experience of 365 Swedish shipyard workers. Death certification was used to determine cause of death and personnel records were reviewed for occupational classification. More than twenty years elapsed since first exposure for all subjects and no statistically significant excess of gastrointestinal cancer was identified among the subjects (eight cases observed versus 14.2 expected). Of those workers who were classified as heavily exposed, only one died of stomach cancer, while 1.3 were expected. The results of this study have been reprinted below in Tables 2 and 3.

Table 2. Cancer morbidity in 1978-1983 in shipyard workers

Site All	Obs.	Exp.	95% C.I.
All (140-209)(c)	54(b)	66.2	0.61-1.1
Lung (162)	11	9.8	0.56-2.0
Pleural mesothelioma (163)	4	_(a)	____
Peritoneal mesothelioma (158)	0	_(a)	____
Gastrointestinal tract (150-158)	11*	22.2	0.25-0.89
Stomach (151)	3	3.4	0.18-2.6
Colon/rectum (152-154)	3	7.8	0.08-1.1
Urinary bladder (188)	6	4.5	0.49-2.9
Kidney (189)	2	3.3	0.07-2.2
Prostate (185)	10	8.5	0.57-2.2

*P < 0.05
(a) There is no incidence data for calculating expected values
(b) In addition to the sites mentioned there were four cases of pancreatic cancer and one case each of lymphoma and leukemia
(c) Figures in parentheses, IDC number 8th revision

Table 3. Cancer morbidity in shipyard workers where at least 20 years have elapsed since onset of asbestos exposure

Site	Heavy or very heavy exposure to asbestos		All exposure to asbestos(a)	
	Obs.	Exp.	Obs.	Exp.
All	49	54.5	16	25.6
Lung	10	8.2	3	3.9
Mesothelioma	4	_(b)	3	_(b)
Gastrointestinal	8	14.2	5	6.7
stomach	3	2.8	1	1.3
rectum	3	6.6	2	3.1
Urinary bladder	6	3.8	2	1.8
Kidney	1	2.7	0	1.3
Prostate	9	7.4	4	3.5

(a) According to answers in the questionnaire of the individuals
(b) Data lacking for calculation of expected values

Sanden, A. and Jarvholm, B., "Cancer Morbidity in Swedish Shipyard Workers 1978-1983", International Archives of Occupational Environmental Health, 1987, Vol. 59, p. 458.

Dr. Acheson and associates studied the mortality experience of 5,969 men employed at an amosite asbestos factory from 1947 to 1979, and found an excess risk for all cancer, but no statistically significant increase in stomach cancer was identified. Seven cases were observed as compared to 7.5 expected. Acheson, E.D., Gardner, M.J., Winter, P.D., and Bennett, C., "Cancer in a Factory Using Amosite Asbestos," International Journal of Epidemiology, 1984, Vol. 13, pp. 3-10, 6.

Dr. Lumley examined cancer registrations of dockyard workers at The Royal Naval Base at Devonport, Plymouth, England. Prior to the implementation of strict exposure controls in the late 60's, these workers were exposed to crocidolite, amosite, and chrysotile asbestos fibers.

Of the 4,998 cancer cases registered between 1960 to 1969, 1,377 or 27.5% of these cases were dockyard workers. Lumley reported a small excess of gastrointestinal cancers (SMR 101.8). One hundred seventy-nine cases of stomach cancer were observed where only 157.1 were expected. The excess in overall gastrointestinal cancers was largely due to the excess in stomach cancer cases since no excesses were noted for esophageal, intestinal or colo-rectal cancer. Addressing the high increased incidence of deaths due to stomach cancer, Lumley notes that this could be due to misdiagnosis. This would also explain the total lack of peritoneal mesothelioma cases reported. One important limitation of Lumley's study is the unavailability of exposure duration information for all subjects. Despite this limitation, the results Lumley noted were consistent with regional cancer trends in England and Wales. See Lumley, K.D.S., "A Proportional Study of Cancer Registrations of Dockyard Workers," British Journal of Industrial Medicine, 1976, Vol. 33, pp. 108-114.

In a retrospective study of over 12,000 shipyard workers, Tola et al., observed only 63 cases of stomach cancer, as compared to 78.8 expected (SIR 80) among shipyard workers. They found only 42 cases versus 47.5 expected (SIR 88) among machine shop workers. Tola, S., Kalliomaki, P.L., Pukkala, S. and Korkala, M.L., "Incidence of Cancer Among Welders, Platers, Machinists and Pipe Fitters in Shipyards and Machine Shops," British Journal of Industrial Medicine, 1988, Vol. 45, pp. 209-218, 212-213.

As discussed previously, Drs. Morgan, Foliart, and Wong reported statistically significant summary SMRs for stomach and gastrointestinal tract cancer based on best evidence. When reanalyzed according to death certificate diagnosis, the SMRs were not statistically significant. Morgan, R.O., Foliart, D.E., and Wong, O., "Asbestos and Gastrointestinal Cancer," Western Journal of Medicine, 1985, Vol. 143, pp. 61-65.

Drs. Hodgson and Jones tracked the mortality experience of asbestos workers in England and Wales. Of the over 30,000 workers examined, 27 cases of stomach cancer were observed where 27 were expected among the pre-regulation workers. Of the post-regulation subjects, a slight decrease in stomach cancer was noted with five observed versus 6.1 expected. The authors acknowledge the excesses of gastrointestinal cancers found in the early studies undertaken by Selikoff, Newhouse and Enter-

line, however, they endorse Doll and Peto's explanation that these excesses were likely due to misdiagnosis of mesotheliomas. Hodgson, R.T., and Jones, R.D., "Mortality of Asbestos Workers in England and Wales, 1971-1981," British Journal of Industrial Medicine, 1986, Vol. 43, pp. 158-164. Since no excess of deaths due to stomach cancer was noted among that group presumably exposed to the highest levels of asbestos, Hodgson and Jones' results are consistent with the results of Sanden et al., Acheson et al., and Lumley, that exposure to asbestos does not significantly increase the risk of developing stomach cancer. Dr. Selikoff's 1990 report entitled, "The Third Wave of Asbestos Disease - Exposure to Asbestos in Place, " also found the mortality experience of 17,800 asbestos insulation workers in the recent follow up period yielded 34 stomach cancer deaths when 29.36 were expected for an insignificant relative risk of 1.16.

E. SMALL-INTESTINE CANCER

1. Description and Etiology

The small intestine is one of the least cancer prone organs of the body. Although it contains some of the body's most rapidly proliferating cells, its surrounding organs, the stomach and colon, are common cancer sites, and it comes into direct contact with any dietary carcinogens which happen to be ingested, only about 2,000 cases of cancer of the small intestine occur per year. See Shottenfeld and Fraumeni at 692.

Of the three components of the small intestine, the duodenum, jejunum, and ileum, the duodenum is the most susceptible to cancer. Of the various cancer cells, duodenal adenocarcinoma is most common and is the type presumed when not specified. Id. at 694.

The risk of small bowel cancer is essentially nil in both sexes until age 30, at which time the risk steadily rises with a steep increase in risk after the fifth decade. The disease strikes males more often than females and the mortality rate of the disease parallels its incidence. Id. at 693.

2. Risk Factors

Risk factors for small bowel cancer include regional enteritis (Crohn's Disease), Peutz-Jeghers syndrome, familial polyposis, Gardner's syndrome, parasitic infestation, immunodeficiency, and celiac disease. Id. at 694-698.

3. Asbestos Exposure

The relatively infrequent incidence of cancer of the small intestine coupled with the fact that the majority of epidemiological studies examining the link between asbestos exposure and gastrointestinal cancer did not break down results into specific sites has resulted in a lack of published scientific literature addressing a meaningful association.

F. COLO-RECTAL CANCER

1. Description and Etiology

The colon and rectum meet at the rectosigmoid junction and it is oftentimes hard to differentiate cancer at this site as either colon or rectal cancer. A cancerous lesion in this area may be labeled colon cancer by the pathologist or rectal cancer by the surgeon. Therefore, the majority of epidemiological studies which report on colon and rectal cancer give combined mortality or incidence rates for "colo-rectal" cancer.

Carcinoma of the colon and rectum are two of the most common malignant lesions. Bruckstein, A.H., "Update on Colorectal Cancer, Risk Factors, Diagnosis, and Treatment," Postgraduate Medicine, Vol. 86, 1989, p. 83. The incidence of colon cancer among men and women is approximately the same. However, the incidence of rectal cancer is higher in men than it is in women of all ages. In 1989, it was estimated that 151,000 new cases of colon or rectal cancer would be discovered--107,000 colon and 44,000 rectal cancer cases. American Cancer Society, Cancer Fact and Figures-1989, 9 (1989). It was also estimated that 61,300 people would die from colon cancer in 1989, second to deaths attributable to lung cancer. Id. The American Cancer Society statistics for 1990 estimate that 15 percent of all cancers, approximately 155,000 cases, will develop in the colo-rectum. The disease will result in 11 percent of all cancer deaths in both sexes, and 13 percent of all cancer deaths in women. Moosa, A.R., Schimpff, S.C., Robson, M.C., "The Comprehensive Textbook of Oncology," Chapter 91, "Tumors of the Colon and Rectum: Clinical Features and Surgical Management," 1991, Vol. 1, p. 904.

Treatment for cancer of the colon or rectum includes surgery, sometimes combined with radiation therapy, and chemotherapy. Boyle, et al., "Descriptive Epidemiology of Colorectal Cancer," International Journal of Cancer, 1985, Vol. 36, pp. 9-18. The incidence of colon and rectal cancer increases with age, starting after 40. The American Cancer Society, Cancer Facts & Figures, 19 (1989). More than 94 percent of all colorectal cancers occur after the age of 50. Id. If colon or rectal cancer is detected and treated in the early or localized stage, the five year survival rate is 87 percent for colon cancer and 79 percent for rectal cancer. See Boyle at at 9-18. If the cancer is permitted to spread to

other parts of the body, the five year survival rate is reduced to 40 percent for colon cancer and 31 percent for rectal cancer. Id.

2. Risk Factors

Heredity and diet can be important risk factors for the development of colorectal cancer. Individuals at risk for colon cancer include those with a personal or family history of polyps in the colon or rectum, or inflammatory bowel disease. American Cancer Society, Cancer Fact and Figures-1989, 9 (1989).

Dietary factors are considered to be among the most important environmental risk factors for cancer of the colon, ranking second only to smoking. Zaridze, "Environmental Etiology of Large-Bowel Cancer," Journal of the National Cancer Institute, 1983, Vol. 70, p. 389. Diets high in meat and animal protein consumption are strongly correlated with incidence of colo-rectal cancer. Armstrong and Doll, "Environmental Factors and Cancer Incidence and Mortality in Different Countries with Special Reference to Dietary Practices," 1975, International Journal of Cancer, Vol. 36, pp. 9-18,15. Persons with diets of low fiber content are also thought to be at an increased risk of colon cancer. Lowenfels, et al., "Diet and Cancer," Cancer, 1985, Vol. 36, pp. 9-18, 15. Diets high in fiber and which include vegetables are associated with a low risk of colo-rectal cancer. Boyle, et al., "Descriptive Epidemiology of Colorectal Cancer," 1985, International Journal of Cancer, 1985, Vol. 36, pp. 9-18, 15. Some evidence suggests that beer drinking increases the risk of rectal cancer. Zaridze at 389.

One study showed that individuals with sedentary occupations had almost three times the risk of cancer of the colon than those with active occupations. Garabrant, et al., "Job Activity and Colon Cancer Risk," American Journal of Epidemiology, 1984, Vol. 119, pp. 1005-1014, 1010. Telegraph, telephone, and power lineman, serviceman, and installers experience an excess risk of cancer of the large intestine (excluding rectum). Dubrow and Wegman, "Setting Priorities for Occupational Cancer Research and Control: Synthesis of the Results of Occupational Disease Surveillance Studies," Journal of the National Cancer Institute, 1983, Vol. 71, pp. 1123-1142, 1137. Metal molders and tool and dye makers also experience a high rate of incidence of colo-rectal cancer. Id.

Studies have shown a strict correlation between the presence of adenomas (polyps) and an increased incidence of colo-rectal cancer. Polyps larger than 2 centimeters show a malignant transformation in 34.7 percent of cases. Id.

> POLYPS--Three types of polyps are implicated in colon cancer: tubular, villous, and villoglandular . . . . The incidence of invasive carcinoma clearly differs among these three types. In Morson's study of 2,506 adenomas, invasive carcinoma was present in 40.7% of villous adenomas, 22.5% of villoglandular adenomas, and 4.8% of tubular adenomas. Size of the polypoid lesion is important; the malignancy rate is less than 2% in polyps smaller than 1 cm and as high as 46% in those larger than 2 cm. Polyp type and size are not independent variables, however, 76% of tubular adenomas are smaller than 1 cm, and 60% of villous adenomas are larger than 2 cm. Thus, larger polyps are much more likely to be villous and to be associated with a relatively high incidence of invasive malignancy.

Bruckstein, A.H., "Update on Colorectal Cancer," Postgraduate Medicine, 1989, Vol. 86, p. 84.

As the polyps grow, the risk of cancer increases. Morson, "Evolution of Cancer of the Colon and Rectum," Cancer, 846 (Supp. 1974). Clinical observations demonstrate that it takes at least five years for a polyp to evolve into a cancer. Muto, et al., "The Evolution of Cancer of the Colon and Rectum," Cancer, 2262 (1975). It has also been demonstrated that patients who have had one intestinal cancer removed are at an increased risk of developing an entirely new primary cancer in any remaining large intestine. Id.

3. Asbestos Exposure

Although Enterline, et al. reported an excess of gastrointestinal cancer cases among 1,074 male asbestos company retirees, their study demonstrated that this increased risk was largely due to a statistically significant excess in stomach cancer. There was no increase in the number of large intestine cancer cases with 14 cases observed, when 14.24 were expected.

Enterline, P.E., Hartley J. and Henderson V., "Asbestos and Cancer: A Cohort Followed Up to Death," British Journal of Industrial Medicine, 1987, Vol. 44, pp. 396-401. Enterline's results are consistent with those of Lumley, Tola and Doll and Peto.

Although Lumley reported a small excess of gastro-intestinal cases among English shipyard workers, he attributed most of those to an excess in cancers of the stomach and pancreas. Lumley found no excesses for cancers of the esophagus, small intestine, colon or rectum. Lumley, K.P.S., "A Proportional Study of Cancer Registrations of Dockyard Workers," British Journal of Industrial Medicine, 1976, Vol. 33, pp. 108-114.

In their 1979 study of asbestos insulation workers, Drs. Selikoff, Hammond, and Seidman reported that asbestos exposure increased the risk of colo-rectal cancer. However, they limited their results to insulation workers and declined to comment on the degree of this alleged association.

In the large retrospective cohort study conducted by Tola et al., no excess of colo-rectal cancer was identified for the more than 12,000 shipyard and machine shop workers studied. Of the shipyard workers, only 35 cases of colo-rectal cancer were observed compared to 44.1 expected and 28 cases were observed among machine shop workers compared with 28.1 expected.

Table 3 Observed (Obs) and expected (Exp) numbers, standardized incidence ratios (SIRs) and 95% confidence limits (95% CL) of various cancer sites among shipyard workers

Cancer type (ICD No.)	Obs	Exp	SIR	95% CL
Stomach (151)	63	78.8	80	61-102
Rectum and colon (153-154)	35	44.1	79	55-110
Nose (160)	1	2.7	37	1-206
Larynx (161)	24	20.0	120	77-179
Lung (162-163. excl Mesothelioma)	227	192.1	118	103-135
Prostrate (177)	48	49.2	98	72-129
Urinary bladder (181)	21	22.9	92	57-140
Skin (191)	10	11.5	87	42-160
Hodgkin's disease and lymphomas (200-202)	16	18.2	88	50-143
Leukaemia (204)	19	16.6	114	69-179
Total	611	629.4	97	90-105

Table 5 Observed (Obs) and expected (Exp) numbers, SRIs and 95% CL of various cancer sites among machine shop workers

Cancer type (ICD No.)	Obs	Exp	SIR	95% CL
Stomach (151)	42	47.5	88	64-120
Rectum and colon (153-154)	28	28.1	100	66-144
Nose (160)	2	1.3	154	19-556
Larynx (161)	8	11.6	69	30-136
Lung (162-163. excl Mesothelioma)	110	118.8	93	76-112
Prostrate (177)	39	30.9	126	90-173
Urinary bladder (181)	19	14.4	132	79-206
Skin (191)	11	7.8	141	70-252
Hodgkin's disease and lymphomas (200-202)	8	11.4	72	31-142
Leukaemia (204)	9	9.8	92	42-174
Total	376	388.3	97	87-107

Tola, S., Kalliomaki, P.L., Pukkala, S. and Korkala, M.L., "Incidence of Cancer Among Welders, Platers, Machinists and Pipe Fitters in Shipyards and Machine Shops," British Journal of Industrial Medicine, 1988, Vol. 45, pp. 209-218, 212-213.

In their 1985 article, Drs. Morgan, Foliart, and Wong reported that the statistical data was inconclusive and that further research was required before asbestos could be documented as increasing an individual's risk for colo-rectal cancer.

In their 1985 study, Doll and Peto reviewed the epidemiological data addressing gastrointestinal cancer incidence and asbestos exposure. They concluded there were no grounds for believing that gastrointestinal cancers are likely to be caused by exposure to asbestos. They criticized Selikoff's 1982 study claiming that the excess mortality due to gastrointestinal cancer was due "largely or wholly" to misdiagnosis of lung cancer and mesothelioma of the pleura or peritoneum. Doll, R. and Peto, J., "Asbestos - Effects on Health of Exposure to Asbestos," Health & Safety Commission, Her Majesty's Stationary Office, 1985.

In further support of the assertion that asbestos exposure does not pose a statistically significant risk for colo-rectal cancer stands the results of the studies undertaken by Hodgson and Jones, and Sanden et al.. Both noted significant deficits of colo-rectal cancer among asbestos workers. In their national study of British asbestos workers, Hodgson and Jones reported a deficit

of colon cancer for subjects exposed prior and subsequent to the enactment of the 1969 exposure regulation, with only six cases observed compared to 16.7 expected. (See Tables 2 and 3, infra. at 54-55.) Sanden, et al. also found a decreased incidence of gastrointestinal cancer incidence in the 365 deceased Swedish shipyard workers he studied retrospectively. Sanden reported only 8 deaths caused by gastrointestinal cancer compared to 14.2 expected with only 3 colo-rectal cancer deaths with 7.8 expected.

The great abundance of epidemiological data examining the effect of asbestos exposure for risk of colorectal cancer has led to the publication of various articles which attempt to review and reconcile the sometimes varying results. Dr. William Weiss reviewed 21 cohort studies of asbestos exposed workers for a possible association between asbestos exposure and colorectal cancer. Acknowledging that earlier studies favored a relationship between asbestos and gastrointestinal cancer, Weiss noted that recent studies have failed to replicate or support this hypothesis. Weiss tabulated all published data derived from cohort studies which reported on colo-rectal cancer. Significantly, no dose response relationship was found nor was any increased risk for colo-rectal cancer identified. Of the 13 cohorts reviewed, only 254 cases of colo-rectal cancer were observed as compared to 282.6 expected. Although the varying methodologies of the cohorts makes comparisons somewhat difficult, Weiss' conclusions are as follows:

> Reports in the literature on 21 cohorts of workers exposed to asbestos were reviewed and analyzed to determine whether there is a causal association between asbestos and colorectal cancer. ... The latest report up to 1988 was used for each cohort. The summary standardized morbidity or mortality ratio for all 21 cohorts was 0.97 ($P > 0.05$), and there was no dose-response relationship in the two studies with such data. The evidence does not meet the established criteria for making a judgment that there is a causal relationship between asbestos and colorectal cancer. The latest report up to 1988 was used for each cohort.

. . .

... The descriptive epidemiology of colorectal cancer includes the observation that its incidence in United States increased in men over the past four decades only in those aged 65 years and older when the incidence actually decreased among those aged less than 45 years. Overall mortality rates declined from 1950 to 1980. These facts are not consistent with the marked increase in asbestos consumption in the United States from 1940 to 1970, given the long latency period for colorectal cancer, if it is postulated that asbestos made a substantial contribution to this type of cancer in the form of occupational exposure.

. . .

Among insulators, the relative risk for gastrointestinal cancer (esophagus, stomach, and colon-rectum) was 1.58 (16)). However, the relative risk was just as high 7.5 years after the onset of exposure to asbestos as it was later [Nicholson (52), Figure 1; note that in this reference the legends for Figures 1 and 2 were interchanged]. The pattern was quite different from the pattern in lung cancer relative risk (Nicholson, Figure 2), which rose to a peak in the fourth decade after onset of exposure and declined thereafter. The data for gastrointestinal cancer suggest an induction-latency period of less than 10 years with no increase after that, an idea which is biologically implausible for solid tumors and the known increase of colorectal cancer incidence with increasing age.

These observations show a lack of coherence for the hypothesis that asbestos causes colorectal cancer.

The evidence reviewed in this section indicates that the criteria for causality are not met. The association is inconsistent, weak, nonspecific, and incoherent. Only the temporality of the association, when present, is frequently correct. There is no evidence to determine whether the association, in the few cohorts where there appears to be one, decreased after the cessation of exposure.

Finally, there is no support for the hypothesis of causality from animal experiments in which asbestos has been administered orally (53,54). Condie (53) reviewed 11 animal experiments and concluded that ingested asbestos fibers did not cause any organic-specific carcinogenic effects.

Weiss, W.,"Asbestos and Colorectal Cancer," Gastroenterology, 1990, Vol. 99, p. 883.

Tables 2 and 4 from Dr. Weiss' review have been reprinted below:

Table 2.

Relative Risk of Colorectal Cancer in Inception Cohorts of Asbestos Workers

Reference No.	Cancer cases: Observed No.	Cancer cases: Expected No.	O/E	P	Power	Comment
18	79	101.3	0.78	<0.05	0.99	No dose-response
19	16	18.5	0.86	>0.05	0.47	
20	10	7.6	1.32	>0.05	0.20	Young cohort but O/E for lung cancer was 2.1
21	15	20.9	0.72	>0.05	0.56	
22	13	16.7	0.78	>0.05	0.44	No elevated risk with longer latency or longer exposure
23	4	1.5	2.67	>0.05	0.08	
24	11	5.9	1.86	>0.05	0.20	Low exposure, no increase in lung cancer O/E
25	11	15.4	0.71	>0.05	0.42	High turnover, 82% worked less than 5 yr
26	22	11.9	1.85	>0.02	0.35	
27	21	23.3	0.90	>0.05	0.56	No dose-response relationship, studied in one plant
28	3	3.4	0.88	>0.05	0.11	
29	35	44.1	0.80	>0.05	0.75	No increase in lung cancer O/E
30	14	12.3	1.14	>0.05	0.36	
Total	254	282.8	0.90	>0.05	1.00	

Table 4.

Relative Risk of Colorectal Cancer in
Cross-Sectional Cohorts of Asbestos Workers

Reference No.	Cancer cases: Observed No.	Cancer cases: Expected No.	O/E	P	Power	Comment
31	5	2.9	1.75	>0.05	0.09	1 Case of mesothelioma
16	54	34.0	1.59	<0.02	0.73	
32	34	24.4	1.39	>0.05	0.60	
33	14	27.4	0.51	<0.01	0.61	
34 I	5	6.3	0.79	>0.05	0.19	
II	3	1.4	2.15	>0.05	0.07	
35	23	19.9	1.16	>0.05	0.52	
36	3	7.8	0.38	>0.05	0.22	
Total	141	124.1	1.14	>0.05	1.00	

William Weiss, "Asbestos and Colorectal Cancer," Gastroenterology, 1990, Vol. 99, No. 3, P. 880.

G. RECTAL CANCER

1. Description and Etiology

2. Risk Factors

3. Asbestos Exposure

Because many of the studies discussed previously under the colon cancer section included rectal cancer, there are only a few additional studies which have specifically addressed the incidence or mortality of the asbestos exposed individual from rectal cancer. Specifically, Enterline identified nine deaths compared to 5.66 expected (SMR=159.0). This SMR was similar to the results found by Acheson, et al who examined the mortality experience of 5,969 amosite asbestos workers. Of those exposed between 1947 and 1979, six had died of rectal cancer as compared to 4.4 expected (SMR=137). Significantly, the SMR for rectal cancer in non-exposed workers was even higher at 142.

In their 1986 study, Drs. Hodgson and Jones observed ten cases of rectal cancer among pre-regulation asbestos exposed individuals where 12.9 were expected (SMR=77). Further, Drs. Sanden and Jarvholm reported only three cases of rectal cancer among Swedish shipyard workers while 6.6 were expected. (SMR=45)

Because there are so few studies specifically reporting on rectal cancer incidence, and since the associations found by Enterline, Acheson, and Sanden's studies are statistically insignificant, one is forced to rely on the results of the studies previously discussed which reported on the incidence of colo-rectal cancer.

Although in their earlier studies, Dr. Selikoff and others hypothesized that asbestos exposure might increase one's risk for rectal cancer, follow-up of the large cohort of asbestos workers reported on colon and rectal cancer together making any determination regarding rectal cancer alone impossible.

H. PANCREATIC CANCER

1. Description and Etiology

The pancreas is a gland whose shape resembles a human tongue and is similar in texture to a bunch of grapes. Gray's Anatomy, p. 945. It is similar in structure to the salivary glands and is located across the back wall of the abdomen. Id. The pancreas produces pancreatic juices which pass into the duodenum and play an important role in digestion. Additionally, the pancreas produces the hormones insulin and glucagon which, in conjunction with other hormones, regulate carbohydrate metabolism. Tabers Cyclopedic Medical Dictionary, F.S. Davis Co., 1989, p. 1309-1310.

While it is one of the most fearsome cancers, little is known about the etiology or prevention of pancreatic cancer which is the fifth leading cause of cancer deaths in the United States. In 1989, there were an estimated 27,000 new cases of pancreatic cancer in the U.S. American Cancer Society, Cancer Facts and Figures-1989, 14 (1989). Once diagnosed, the patient has a less than 20% chance of surviving a year. About 27,000 Americans die from pancreatic cancer every year. The most common pancreatic tumors are composed of exocrine adenocarcinoma cells.

Diagnosis of pancreatic cancer can be quite troublesome due in part to its location and the high morbidity associated with biopsy. Only a small proportion of pancreatic cancer cases may be verified histologically. See Schottenfeld and Fraumeni at 639. Furthermore, pancreatic cancer may be clinically indistinguishable from diseases of the liver, bilary tract, or duodenum. Because of these diagnostic difficulties, review of pancreatic cancer cases is very likely to turn up tumors which have originated in the ampulla, stomach, biliary tract, small intestine, ovary or are of unknown origin. Id. at 641. The extent of diagnostic error has been illustrated by Dr. Leach who examined the proportion of autopsy verified cases which were properly diagnosed before death in Montreal in 1950. Id. Of 39 cases reported, only 55 percent were accurately diagnosed. Of the 139 cases reported in Boston between 1955 and 1965, proper diagnosis occurred in only 47.5 percent of the cases. Id.

Age is considered one of the most reliable indicators of pancreatic cancer. After age 30 in both males and females, incidence rates increase linearly. Thus, individuals in their 80's experience a 40 times greater risk than those in their 40's. Pancreatic cancer is twice as common in males than females. Id. at 643.

2. Risk Factors

Biological risk factors for pancreatic cancer include chronic pancreatitis, diabetes, leukemia, asthma, cholecystitis, and cirrhosis of the liver. Id. at 652-653. Among the occupations believed to be at risk are aluminum and coke workers, rubber workers, and workers exposed to radiation. Higher incidence rates have also been identified for managers, administrators, metal workers, produce workers, timber workers, stationery engineers, dentists, chemists and electrical engineers. Obviously, there is no one common element on this list and experts have postulated that the common thread is likely to be something non-work related.

In a recent case-control study conducted in a high-risk area of Louisiana between 1979 and 1983 by Falk and Associates, the relationship between occupational exposures and pancreatic cancer was examined. After adjustment for smoking and diet, white-collar occupations showed consistently elevated incidences. Although asbestos exposure was not studied, it is interesting to note that no significant relative risks were found for those working in settings where asbestos was most likely present (shipbuilding, construction, plasterer). The results of this study have been set out in Table II below.

TABLE II. Odds Ratios for Pancreatic Cancer According to Ever-Employment in Occupational and Industrial Categories Among Men in Louisiana Pancreatic Cancer Study.*

Exposure	Cases. Controls	Odds Ratio All	Cajun	Non-Cajun
Industry				
Sugar Cane Farming	6.12	1.16	0.69	2.14
Agriculture	59.68	0.82	1.03	0.63
Oil/gas extraction	18.33	0.38*	0.14*	1.07
Construction	56.58	1.06	1.54	0.78
Manufacturing		1.25	2.93	0.59
Food	21.16			
Lumber	14.16	0.87	0.53	1.03
Paper	5.5	1.06	----	3.24
Fabricated metal	4.4	1.06	0.91	1.26
Machinery	4.5	0.85	0.60	1.25
Chemical processing	14.14	0.94	1.38	0.97
Petroleum refining	7.15	0.51	0.37	0.61
Transportation	41.46	1.20	0.85	1.59
Trade	69.65	1.46	2.06*	1.06
Government	81.70	1.59*	2.00	1.20
Personal services	39.47	0.93	0.98	0.69
Shipbuilding	12.13	1.24	1.09	0.93
Occupation				
White collar worker	120.119	1.34	1.89	0.85
Professional/manager	59.53	1.50	2.17	1.23
Sales/clerk	46.37	1.69*	1.69	1.47
Service	61.65	1.05	1.46	0.80
Farmer	69.75	0.95	0.98	0.98
Food/tobacco processor	7.10	0.76	3.73	0.40
Chemical processor	4.6	0.70	----	1.69
Mechanic/machine repairer	12.12	1.13	1.09	1.07
Wood machine worker	10.10	1.12	0.35	2.09
Metal fabricator	4.10	0.52	0.22	0.61
Welder/cutter	5.6	0.88	0.90	0.62
Electric assembler/installer/repairer	8.5	2.20	0.90	3.24
Painter/plasterer	4.4	1.06	2.77	0.41
Excavator/grader/paver	7.9	0.87	0.90	0.83
Construction worker	48.58	0.92	0.86	0.99
Structural worker	8.8	0.95	0.76	2.53
Truck driver	20.19	1.66	2.68	1.41
Transportation worker (excluding truck driver)	20.19	1.04	0.84	0.98
Package/material handler	17.17	1.61	0.90	2.06
Miner	7.130	.70	0.53	0.61

*Odds ratios adjusted for age, type of respondent, race, cigarette use, income, pork and fruit intake, and residence. For those categories in which fewer than 7 cases and 7 controls worked, unadjusted odds ratios were calculated.
*Statistically significant at $p = 0.05$.

Falk, R.T., Pickle, L.W., Fontham, E.T., et al., "Occupation and Pancreatic Cancer Risk in Louisiana," American Journal of Industrial Medicine, 1990, Vol. 18, pp. 565-576, 569.

In their population based case-control study of Swedish pancreatic cancer cases, Norrell and Associates identified an increased risk for those frequently consuming fried or grilled meat and margarine or fat. Conversely, consumption of vegetables high in betacarotene and fruits high in vitamin C was found to be inversely related to pancreatic cancer. Norrell, S.E., Ahlbom, A., Erwuld, R., et al., "Diet and Pancreatic Cancer: A Case-Control Study," American Journal of Epidemiology, 1986, Vol. 124, pp. 894-902, 900-901. Similar results were reported by Drs. Farrow and Davis in 1990, when they conducted a population based case-control study in western Washington. One hundred forty-eight men diagnosed with pancreatic cancer between July 1982 and June 1986 were interviewed by telephone and later filled out a food frequency questionnaire. The results indicate that pancreatic cancer risk increased with increasing protein intake, especially in those over age 65. Contrary to other studies, however, no association was identified between intake of fat, cholesterol, or vitamins A and C. Farrow, D.C. and Davis, S., "Diet and the Risk of Pancreatic Cancer in Men," American Journal of Epidemiology, 1990, Vol. 132, pp. 423-431, 427.

3. Tobacco and Alcohol

Tobacco and alcohol are also related to pancreatic cancer. Smokers exhibit an increased risk (between 1.6 - 3.9) for developing carcinoma of the pancreas compared to non-smokers. See Schottenfeld and Fraumeni at 658. Alcohol combined with a high fat diet has been found to be directly related to the development of chronic calcifying pancreatitis, the form of pancreatitis most strongly suspected of constituting a significant risk for pancreatic cancer. Id. at 659.

4. Asbestos Exposure

In 1986, Dr. Lumley reported on cancer registrations for Plymouth dockyard workers. Forty-six cases of pancreatic cancer were reported, while 42.2 were expected, yielding a statistically insignificant SMR of 109.0. Lumley, K.P.S., "A Proportional Study of Cancer Registrations of Dockyard Workers," British Journal of Industrial Medicine, 1976, Vol. 33, pp. 108-114.

Selikoff and Seidman examined the mortality experience of U.S. and Canadian asbestos workers for pancreatic cancer. Of those deceased workers having 20

or more years of exposure, pancreatic cancer was listed on death certificates as the cause of death in 49 cases while only 17.5 were expected. However, upon further review, these results were not confirmed.

> Analysis of the deaths indicated, however, that such conclusions could not be supported by more detailed information. After review of all deaths, it was ascertained that there were only 23 deaths of cancer of the pancreas (22 so categorized on death certificate, and 1 listed as myocardial infarction). On the other hand, there were 27 instances in which deaths had been listed on death certificates as due to cancer of the pancreas but where further study had shown other causes. Cancer of the lung accounted for 4 deaths, peritoneal mesothelioma for 16, cancer of the colon for 2 and disseminated carcinomatosis, primary site not ascertained, for 5.

Table 4

Deaths among 17,800 asbestos insulation workers
in the United States and Canada
January 1, 1967 - December 31, 1986
Number of Men 17,800
Man-Years of Observation 166,853

		Observed		Ratio o/e	
Underlying Cause of Death	Expected	(BE)	(DC)	(BE)	(DC)
Total deaths, all causes	1658.9	2271	2271	1.37	1.37
Cancer, all sites	319.7	995	922	3.11	2.88
Deaths of less common malignant neoplasias					
Pancreas	17.5	23	49	1.32	2.81
Liver, biliary passages	7.2	5	19	0.70	2.65
Bladder	9.1	9	7	0.99	0.77
Testes	1.9	2	1	----	----
Prostate	20.4	30	28	1.47	1.37
Leukemia	13.1	15	15	1.15	1.15
Lymphoma	20.1	19	16	0.95	0.80
Skin	6.6	12	8	1.82	1.22
Brain	10.4	14	17	1.35	1.63

* Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976.

(BE) Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC) Number of deaths as recorded from death certificate information only.

Selikoff, I.J. and Seidman, H., "Cancer of the Pancreas Among Asbestos Insulation Workers," 1981, Cancer, Vol. 42, pp. 1469-1473.

In Selikoff's more recent report on the large cohort of asbestos workers, 54 deaths attributed to pancreatic cancer based on best evidence were reported, as compared to 39.52 expected (RR=1.37). When computing mortality based on death certificates alone, 92 deaths were reported. Thus, the diagnostic inaccuracy associated with pancreatic cancer experienced by Drs. Selikoff and Seidman in their 1981 report on pancreatic cancer reappears in the 1991 report making meaningful interpretation problematic.

In Dr. Acheson and associates' study of cancer in amosite asbestos factory workers, only three pancreatic cancer deaths were observed as compared to 3.1 expected. Acheson, E.D., Gardner, M.J., Winter, P.D., Bennett, C., "Cancer in a Factory Using Amosite Asbestos," International Journal of Epidemiology, 1984, Vol. 13, pp. 3-10, 9. These results were corroborated by Enterline and others who reported in 1987 on a cohort of retired asbestos workers. Enterline, Hartley, and Henderson reported eight cases of pancreatic cancer while 7.37 were expected (SMR=108.6). Enterline, P.E., Hartley J. and Henderson V., "Asbestos and Cancer: A Cohort Followed Up to Death," British Journal of Industrial Medicine, 1987, Vol. 44, pp. 396-401.

Although Sanden, et al. reported an unexpectedly high number of pancreatic cancer cases among the deceased shipyard workers they examined, the overall SMOR (Standardized Mortality Odds Ratio) for gastrointestinal cancer was not statistically significant and the authors' postulated that the high number of pancreatic cancer cases identified were probably misclassified cases of malignant mesothelioma. Sanden, A., Jarvholm, B., "Cancer Morbidity in Swedish Shipyard Workers 1978-1983," International Archives of Occupational Environmental Health, 1987, Vol. 59, p. 461.

In conclusion, the evidence associating asbestos with pancreatic cancer is weak and does not support the assertion that asbestos exposure increases one's risk for pancreatic cancer.

I. PROSTATE CANCER

1. Description and Etiology

In 1990, prostate cancer was expected to be the most common cancer diagnosed in U.S. males and the second leading cause of death in U.S. males. Twenty thousand new cases are diagnosed each year. One in ten men will develop prostate cancer in his lifetime. It primarily attacks men aged 65 and older. Carter, B.S., Carter, H.B., Isaacs, J.T., "Epidemiologic Evidence Regarding Predisposing Factors to Prostate Cancer," The Prostate, 1990, Vol. 16, pp. 187-197, 187. Cook et al., explain that prostate cancer appears late in life and incidence then increases with age more rapidly than with any other cancer. From this information they hypothesized that prostate cancer might be due to carcinogenic factors which are absent early in life and/or have a long latency period. It is estimated that the period between first exposure and clinical onset is greater than 32 years. Cook, P.J., Doll, R., and Fellingham, S.A., "A Mathematical Model for the Age Distribution of Cancer in Man," International Journal of Cancer, 1968, Vol. 4, pp. 93-112.

There are four general hypotheses concerning the etiology of prostate cancer: (a) a genetic predisposition; (b) endogenous hormonal influences; (c) exposure to chemicals or dietary factors; and, (d) venereal transmission of an infectious agent. No single hypothesis provides a satisfactory explanation for most cases. See Schottenfeld and Fraumeni at 941-945; See also Carter, B.S., Carter, H.B., and Isaccs, J.T., "Epidemiologic Evidence Regarding Predisposing Factors to Prostate Cancer," The Prostate, 1990, Vol. 16, pp. 187-197.

2. Risk Factors

Of the dietary factors, there is some evidence that diets high in animal fat, saturated fat, and animal protein increase one's risk for prostate cancer. See Carter, et al., at 191. Occupations believed to be associated with an increased risk for prostate cancer include rubber workers, bookkeepers, shipping and receiving clerks, newspaper printers, motor vehicle dealers, ministers, farmers, plumbers, and coal miners. As with pancreatic cancer, it is hard to identify one common thread among these varied occupations. Checkoway, H., DiFerdinando, G., Holika, B.S., and Mickey, D.D., "Medical, Life-Style, and Occupational Risk Factors for

Prostate Cancer," The Prostate, 1987, Vol. 10, pp. 79-88.

3. Asbestos Exposure

Some researchers have labeled asbestos exposure as a risk factor for prostate cancer. There is little evidence to support such a contention. In their 1980 study of mortality in workers in two U.S. shipyards, Drs. Beaumont and Weiss observed 32 deaths attributed to prostatic cancer, yielding an SMR of 1.10. Beaumont, J.J. and Weiss, N.S., "Mortality of Welders, Shipfitters, and Other Metal Trades Workers in Boilermakers Local No. 104, AFL-CIO," American Journal of Epidemiology, 1980, Vol. 112, pp. 775-786. Of those workers whose mortality experience was examined by Enterline, et al., seventeen deaths caused by prostate cancer were observed while 18.17 were expected (SMR=93.6). Enterline, P.E., Hartley J. and Henderson V., "Asbestos and Cancer: A Cohort Followed Up to Death," British Journal of Industrial Medicine, 1987, Vol. 44, pp. 396-401. Similar results were found by Acheson and Gardner who observed two deaths from prostate cancer among asbestos workers while 2.1 were expected. Acheson, E.D., Gardner, M. J. and Winter, P.D., and Bennett, C., "Cancer in a Factory Using Amosite Asbestos," International Journal of Epidemiology, 1984, Vol. 13, pp. 3-10.

Drs. Sanden and Jarvholm also reported a small, but statistically insignificant, number of deaths due to prostatic cancer. Of those shipyard workers where at least 20 years have elapsed since first exposure nine deaths were observed, where 7.2 were expected (RR=1.22). Sanden, A. and Jarvholm, B., "Cancer Morbidity in Swedish Shipyard Workers 1978-1983," International Archives of Occupational and Environmental Health, 1987, Vol. 59, pp. 4-12. Tola, et al, observed a small increased incidence of prostate cancer among machine shop workers (39 observed, 31 expected), but not in shipyard workers (48 observed, 49.2 expected). Tola, S., Kalliomaki, P.L., Pukkala, E., Asp, S. and Korkala, M.L., "Incidence of Cancer Among Welders, Platers, Machinists and Pipe Fitters in Shipyards and Machine Shops," British Journal of Industrial Medicine, 1988, Vol. 45, pp. 209-218.

Dr. Selikoff in, "The Third Wave of Asbestos Disease - Exposure to Asbestos in Place," placed prostate cancer on his list of cancers not found with increased incidence in the 17,800 asbestos insulation workers he studied. There is no convincing evidence that occupational exposure to asbestos is a risk factor for the development of prostate cancer.

J. KIDNEY CANCER

1. Description & Etiology

Humans have two kidneys which are located in the back of the abdomen. Their purpose is to separate certain materials from the blood which, when mixed with water, are extracted by the kidneys (urine). Gray's Anatomy, p. 985. Each kidney is about four inches long, two inches wide, and one inch thick. Id.

Kidney cancer, also called renal carcinoma and hypernephroma occurs primarily in men at a male/female ratio of about 3:1. Peak incidence occurs during the sixth and seventh decades, although it has been known to strike in the second and third. Both incidence of, and mortality from, renal carcinoma have been steadily increasing for both black and white males over the last few decades. Moosa, A.R., Schimpff, S.C., Robson, M.C., "The Comprehensive Textbook of Oncology," Vol. 2, pp. 1055-1066, 1055.

2. Risk Factors

Among the environmental risk factors thought to be associated with an increased risk of renal cancer are beer and coffee, leaded drinking water, and cholesterol. A familial propensity for renal carcinoma has also been identified. See Schottenfeld and Fraumeni at 928-930.

The most convincing epidemiologic evidence implicates smoking and cadmium exposure. In their case-control study of 96 patients with cancer of the renal pelvis and ureter, Jensen, et al., identified increased risks for those employed in the chemical, petrochemical, and plastics industries. See Jensen, O.M., Knudsen, J.B., McLaughlin, J.K., Sorenson, B.L., "The Copenhagen Case-Control Study of Renal Pelvis and Ureter Cancer: Role of Smoking and Occupational Exposures," International Journal of Cancer, 1988, Vol. 41, pp. 557-561, 557.

The results of the Copenhagen study with respect to occupational exposure have been reprinted below in Table V.

TABLE V - OCCUPATIONS AND OCCUPATIONAL EXPOSURES AND RELATIVE RISKS OF RENAL PELVIS AND URETER CANCER IN DENMARK. 1979-82.

Occupation/exposure	Sex	Exposed: Cases	Exposed: Controls	RR[1]	95% CI
Chemical, petrochemical, plastics industries, gasoline	M+F	14	14	4.0	(1.6-9.8)
Coke, Coal	M	8	7	4.0	(1.2-13.6)
Asphalt, Tar	M	9	6	5.5	(1.6-19.6)
Gasworks, installation	M	2	3	2.7	(0.3-23.4)
Dye-stuffs industry, dyeing	M+F	6	9	2.1	(0.6-7.0)
Rubber industry	M+F	4	7	1.6	(0.4-6.7)
Leather, tanning	M+F	7	11	2.2	(0.7-6.7)
Painter, paint manufacture	M+F	10	19	1.8	(0.7-4.6)
Iron/metal industry, blacksmith	M	17	41	1.4	(0.7-2.9)
Wood industry, woodwork	M	4	14	0.8	(0.2-2.7)
Textile industry	M+F	8	27	0.9	(0.4-2.4)
Hair-dressing	F	2	2	3.0	(0.3-33.0)
Cook, kitchen aid	M+F	7	25	0.7	(0.2-1.8)
Health, care sector	M+F	4	24	0.4	(0.1-1.4)
Office work	M+F	19	61	1.0	(0.5-1.9)

[1] Relative to persons not in industry/not exposed. Adjusted for sex (when both sexes included) and lifetime tobacco consumption.

In Table II, the relative risks for different smoking habits are present. Significantly increased RR are seen for exclusive smokers of cigarettes and for mixed smokers who had also smoked cigarettes regularly. For other smoking habits, numbers are too small to yield stable risk-estimates.

In view of the diversity of smoking habits (Table I) and the limited size of the study, all types of smoking ere combined into lifetime tobacco use. Table III shows a highly significant trend in relative risk for both men ($p<0.001$) and women ($p=0.004$) with amount of tobacco consumed over a lifetime. Men with a lifetime tobacco consumption of 80 or more pack-years have an almost 8-fold increase in risk compared to men with a consumption of less than 10 pack-years. For corresponding levels of consumption, the relative risks for men and women were quite similar.

Jensen, O.M., Knudsen, J.B., McLaughlin, J.K., and Sorenson, B.L., "The Copenhagen Case - Control Study of Renal, Pelvis and Ureter Cancer: Role of Smoking and Occupational Exposures", International Journal of Cancer, 1988, Vol 41, pp. 557-561, 559.

Jensen and Associates also examined smoking habits among renal pelvis and ureter cancer subjects and found smoking to be an important risk factor.

TABLE II - SMOKING HABITS AND RELATIVE RISK OF RENAL PELVIS AND URETER CANCER IN DENMARK, 1978-82

Smoking habit	Cases	Controls	RR[1]	95% CI
Never Smoked	8	57	1.0	(R)[2]
Pipe only	1	10	2.2	(0.1-97)
Cigar only	4	24	1.3	(0.3-6.1)
Cigarette only	32	91	2.6	(1.0-6.7)
Mixed, cigarettes	48	99	3.8	(1.3-11.5)
Mixed, no cigarettes	3	7	6.5	(0.4-21.2)

[1] Adjusted for sex and age (-64 years, 65+ years).-[2](R) is the reference category.

Table III - LIFETIME TOBACCO CONSUMPTION AND RELATIVE RISK OF RENAL PELVIS AND URETER CANCER IN DENMARK, 1979-82

Lifetime Tobacco Consumption (Pack-Years)	Male				Female				Male or Female	
	Case	Control	RR[2]	95% CL	Case	Control	RR[2]	95% CL	RR[3]	95% CL
0-90	3	33	1.0	(R)[4]	8	48	1.0	(R)[2]	1.0	(R)[2]
0-39	13	63	2.2	(0.6-8.2)	16	42	2.2	(0.9-5.8)	2.2	(0.97-5.2)
40-79	25	55	5.0	(1.5-16.6)	12	18	4.0	(1.4-11.1)	4.4	(1.9-10.7)
80+	19	29	7.9	(1.9-39.1)	--	--	---	----	7.9	(1.9-39.1)
Test	--	--	---	p<0.001	--	--	---	p=0.004	---	p<0.001

[1] Cigarette or pack-year equivalents for all types of tobacco (see text).
[2] Adjusted for age.
[3] Adjusted for age and sex.
[4] (R) is the reference group.

The present investigation corroborates the role of smoking in the development of tumors of the renal pelvis and ureter, and the clear dose-effect of lifetime tobacco consumption (Table III) provides further evidence of the causal role of smoking in the etiology of these tumors. The effect is related to cigarette smoking, but detailed assessment of the risk in persons who smoked exclusively cigars or pipes is hampered by the limited number of observations. Compared with out parallel investigation of bladder cancer in the same population and time period (Jensen et al., 1987a), this study suggests that the relative risk associated with heavy smoking is 2.5

times greater for renal pelvis-ureter cancer than for bladder cancer (Fig. 1).

Our present investigation points unequivocally to tobacco smoking as the most important risk factor for renal pelvis and ureter cancer in Denmark.

Jensen, O.M., Knudsen, J.B., McLaughlin, J.K., and Sorenson, B.L., "The Copenhagen Case - Control Study of Renal, Pelvis and Ureter Cancer: Role of Smoking and Occupational Exposures", International Journal of Cancer, 1988, Vol 41, pp. 557-561, 559.

3. Asbestos Exposure

Drs. Selikoff, Seidman and Hammond reported an increased risk of renal cancer in their 1979 mortality study of U.S. insulation workers. Selikoff and colleagues reported a relative risk of 2.23 using death certification with 18 deaths due to kidney cancer observed versus 8.1 expected. Selikoff, I.J., Hammond, E.C., Seidman, H., "Mortality Experience of Insulation Workers in the United States and Canada, 1943 - 1976," Annals New York Academy of Sciences, 1979, Vol. 330, pp. 91-116, 103.

Also reporting a statistically significant risk for kidney cancer are Enterline and associates. Of the 1,074 retired asbestos workers, seven deaths caused by kidney cancer were observed compared to 2.54 expected (SMR-275.8).

Although numerically impressive, neither Selikoff, Seidman and Hammond, nor Enterline, et al. adjusted for tobacco or alcohol use. Despite the increased risk identified by Selikoff, Hammond and Seidman, and Enterline, et al., other studies and authors have failed to replicate their results. Drs. Beaumont and Weiss reported 11 deaths due to renal cancer among U.S. shipyard workers resulting in a SMR of 1.14. Beaumont, J.J. and Weiss, N.S., "Mortality of Welders, Shipfitters, and Other Metal Trades Workers in Boilermakers Local No. 104, AFL-CIO," American Journal of Epidemiology, 1980, Vol. 112, pp. 775-786.In their 1987 study, Drs. Sanden and Jarvholm likewise reported a small number of deaths caused by kidney cancer among a group of Swedish shipyard workers (2 obs., 3.3 exp.). Sanden, A. and Jarvholm, B., "Cancer Morbidity in Swedish Shipyard Workers 1978-1983," International Archives of Occupational and Environmental Health, 1987, Vol. 59, pp. 4-12.

In "ASBESTOS - Effects on Health of Exposure to Asbestos," Richard Doll and Julian Peto reported:

> In their study of the mortality of insulation workers, Selikoff, Hammond, and Seidman (1979) concluded that the men had experienced an increased risk of renal cancer as a result of their employment. In addition to the risks of lung and gastro-intestinal cancer referred to above. Eighteen deaths were attributed to renal cancer against 8.1 expected, including 15 against 7.0 expected 20 years or more after first employment. Only two other studies have reported separately on this type of cancer. In one, Acheson et al (1984) observed two deaths against 1.4 expected in men making asbestos insulation board while, in the other, we observed one death against 4.29 expected in textile workers (or one against 2.72 expected 20 years or more after first employment: Peto et al (1985). In the absence of any positive experimental evidence these data alone do not, in our opinion, justify the belief that asbestos can cause this type of disease.

Doll, R., Peto, J., "ASBESTOS - Effects on Health of Exposure to Asbestos," Health and Safety Commission, Her Majesty's Stationary Office, 1985, p. 7.

Dr. Malcolm Maclure contacted 1,190 individuals with renal adenocarcinoma. Their names were taken from the records of 37 Boston-area hospitals between 1981 and 1984. Of the 518 cases interviewed, 141 reported past asbestos exposure. Dr. Maclure attempted to control for known and hypothesized risk factors such as smoking, kidney stones, hypertension, income, and education, and reported an exposure odds ratio of 1.6. Maclure, M., "Asbestos and Renal Adenocarcinoma: A Case-Control Study." Environmental Research, 1987, Vol. 42, pp. 353-361. Dr. Maclure's study is susceptible to attack since exact information as to first exposure, type of exposure, and duration of exposure was unavailable.

In his recent report on the cohort of asbestos insulation workers, Selikoff reported 32 deaths caused by kidney cancer when 18.87 were expected (RR 1.70). Although of marginal significance statistically, this relative risk represents a decrease from that reported in 1979 (RR=2.23). Selikoff, I.J., "The Third Wave of Asbestos Disease - Exposure to Asbestos in Place," 1990.

K. LYMPHOMA

1. Description and Etiology

Lymphoma is defined as a growth of new tissue in the lymphatic system and includes Hodgkin's Disease, lymphatic leukemia, and reticuloses. Taber's Cyclopedic Medical Dictionary, 16th Ed. (1989). The lymphatic system runs throughout the human body and carries lymph fluid which is filtered by lymph ducts, freeing the lymph fluid of foreign matter, especially bacteria. Absorption of material is most active in the alimentary canal, with digestive material passing into the blood stream through the vessels of the portal circulation. Id. Lymphomas are relatively uncommon in the United States, with only about 15,000 new cases estimated each year. Schottenfield & Fraumeni at 757. Approximately 4.9 per 100,000 white males will die of lymphoma this year.

2. Risk Factors

Among the risk factors associated with an increased risk for lymphoma are a past history of rheumatoid arthritis, exposure to pesticides, and possibly benzene and other solvents. Additionally, there is a strong familial association with this disease. See Schottenfeld and Fraumeni at 759, 767-771.

An increased, but unconfirmed, risk of lymphoma in patients with rheumatoid arthritis was identified by Isomaki et al., in 1979. Isomaki, H., Hakulinen, P., Joutsenlahti, U., Lancet, 1979, page 392. The mortality experience of 173 men who worked in a pesticide factory and died between 1940 and 1972 exhibited an excess of Hodgkin's and other lymphomas. A prospective study of the same workers undertaken between 1940 and 1973 exhibited a relative risk of 3.85. Ott, M.G., Holden, B.D., Gordon, H.G., Archives of Environmental Health, 1974, Volume 29, pages 250 - 255. Benzene exposure is also suspected to be a risk factor for the development of lymphoma, however, the epidemiological data on the association is inconsistent.

In their study published in the British Journal of Cancer in 1981, Hardell, et al. examined the relationship between various solvents and lymphoma:

> Summary. - A number of men with malignant lymphoma of the histiocytic type and previous exposure to phenoxy acids or chlorophenols were observed and reported in 1979. A matched case-control study has therefore been performed with

cases of malignant lymphoma (Hodgkin's disease and non-Hodgkin lymphoma). This study included 169 cases and 338 controls. The results indicate that exposure to phenoxy acids, chlorophenols, and organic solvents may be a causative factor in malignant lymphoma. Combined exposure of these chemicals seemed to increase the risk. Exposure to various other agents was not obviously different in cases and in controls.

Hardell, L., Eriksson, M., Lenner, P., and Lundgren, E., "Malignant Lymphoma and Exposure to Chemicals, Especially Organic Solvents, Chloroprenols and Phenoxy Acids: A Case-Control Study." British Journal of Cancer, 1981, Vol. 43, pp. 169-176, 169.

An excess of lymphoma was reported among sales and clerical personnel, postal workers, insurance and real estate brokers, engineers, stationary engineers, several types of electrical workers, mechanics, machinists, primary metal workers, and farmers. Some of these groups may reflect socio-economic or general environmental factors, while others likely involve chemical or physical exposures in the workplace. See Schottenfeld and Fraumeni at 770.

Like the other cancers surveyed in this paper, it is unlikely that there is one common exposure underlying these varied occupations. Therefore, the increased risk may be attributed to some common environmental or lifestyle exposure.

3. Asbestos Exposure

In their mortality study of 1,074 retirees from a United States asbestos company, Dr. Enterline, et al. observed nine deaths attributed to all lymphatic and haematopoietic tissue whereas 10.76 were expected. Breaking those numbers into specific types of lymphoma, they observed two cases of lymphosarcoma where 2.24 were expected, no cases of Hodgkin's disease where 0.72 cases were expected, and three cases of leukemia and aleukaemia where 5.36 were expected. However, four deaths were attributed to other lymphatic causes, whereas 2.54 were expected, yielding an SMR of 163.9. Enterline, E., Hartley, J., and Henderson, V., "Asbestos and Cancer: A Cohort Followed up to Death," British Journal of Industrial Medicine, 1987, Vol. 44, pp. 396-401, 397.

Tola and Associates examined the incidence of both Hodgkin's disease and lymphomas among the 12,693 ship-

yard and machine shop workers studied in 1988. The results of their study have been set forth previously at pages 104-105. Notably, no increase for Hodgkin's disease or lymphoma was noted in either the shipyard workers or machine shop workers studied.

In their 1985 report on the health effects of asbestos exposure, Drs. Doll and Peto report the following:

> A very rare type of cancer - large cell lymphoma of the oral cavity and gastrointestinal tract - was also found to be related to occupational exposure to asbestos in a case-control study in California (Ross, et al. 1982). Of the 28 affected patients, 17 had some evidence of substantial exposure against 6 of 28 controls matched for age, sex, and race, who were living in the same neighborhood. This superficially surprising finding is given credence by the report of 2 deaths from lymphosarcoma of the small intestine in 2 small cohort studies of asbestos workers, which, like large cell lymphoma of the oral cavity and gastrointestinal tract, is normally an extremely rare disease (See Ross, et al. 1982 for references). The association is not supported by experience in Sweden, Bengsteon, et al., 1982; Olsson and Brandt, 1983), nor by Selikoff, et al.'s (1979) massive study of insulation workers in North America (Table 3-3), that the later grouped all lymphomas together in large cell lymphomas limited primarily to the oral cavity and gastrointestinal tract for only 5% of the total. On these data, it is not now possible to reach any conclusion, but the possibility that these rare tumors can be produced by exposure to asbestos needs to be kept in mind.

Doll, R. and Peto, J., "Asbestos - Effects on Health of Exposure to Asbestos," Health and Safety Commission, Her Majesty's Stationary Office, 1985, p. 7.

In "The Third Wave of Asbestos Disease - Exposure to Asbestos in Place," Selikoff includes lymphoma in his list of cancers for which no increased incidence was identified.

> Of both practical and theoretical interest, these experiences did not demonstrate an increased incidence in a variety of other

cancers (urinary, bladder, prostate, leukemia, lymphoma, melanoma, brain tumors, primary cancer of the liver) (Table 4). Theoretical interest, because some thought has been given to the possibility that a carcinogenic agent such as asbestos would be likely to produce cancer in whatever organ it was found. At least in the present investigation, this was not the case.

Table 4

Deaths among 17,800 asbestos insulation workers in the United States and Canada January 1, 1967 - December 31, 1986

Cancers not found with increased incidence

		Observed deaths			
Cause of Death	Expected Deaths[1]	Death Certificate Number	(DC) Ratio	Best Evidence Number	(BE)[2] Ratio[3]
Cancer of bladder	20.77	17	0.82	22	1.06
Cancer of prostate	52.56	59	1.12	61	1.16
Leukemia	28.74	32	1.11	33	1.15
Lymphoma	43.24	33	0.76	39	0.90
Melanoma (skin)	12.65	11	0.87	9	0.71
Brain Tumors (All)	26.35	40	1.52[a]	3	1.25
Cancer	22.55	29	1.29	7	1.20
Cancer of Liver	11.06	31	2.80[c]	12	1.00

1. Expected deaths based upon death rates 1967-1986 of the U.S. National Center for Health Statistics, for white males.
2. Ascertained after review of autopsy, surgical and clinical material. Where no such data were available, death certificate diagnosis was utilized.
3. Calculated for information only, since it utilized "best evidence" vs. "death certificate" diagnoses, not strictly comparable due to different quality of ascertainment and verification.

Prob. - Level - <.001 - c
<.01 - b
<.05 - a

I.J. Selikoff, "The Third Wave of Asbestos Disease - Asbestos in Place."

Although some assert asbestos exposure increases one's risk for developing lymphomas, the epidemiologic data cited herein fails to support such an assertion.

V. EPIDEMIOLOGICAL EVIDENCE IN THE COURTROOM

A. Introduction

As illustrated, the results of epidemiological studies are often varied, inconclusive, and inconsistent. Yet, juries composed of six or twelve laypeople are required to deliberate and evaluate the evidence presented about such studies and to render a verdict. It is quite likely that the verdict will depend on the personality of the medical witness and speculation. This was recognized by the 5th Circuit Court of Appeals in a 1989 opinion, in a Bendectin case:

> " . . . juries are asked to resolve [these] questions, upon which even our brightest medical minds disagree, in order to resolve the case at hand and decide whether the Plaintiff is entitled to recovery, and in so doing must necessarily resort to speculation."

Brock v. Merrell Dow Pharmaceuticals, Inc., 874 F.2d 307, 309 (5th Cir. 1989).

B. Burden of Proof

In traditional products liability cases, the Plaintiff must demonstrate that a specific Defendant's conduct was more likely than not a substantial factor in bringing about the Plaintiff's injury. The long latency periods associated with most asbestos related diseases together with the ubiquitous nature of asbestos complicates the proximate cause requirement in asbestos litigation. Thus, the courts have relaxed traditional evidentiary requirements and have begun to accept epidemiological data despite the fact it relates to groups rather than to specific individuals. This limitation should be driven home to the jury at every opportunity. The existence of a correlation or association does not necessarily mean that exposure to asbestos caused plaintiff's disease. As this paper illustrates, the importance of other risk factors, especially alcohol and tobacco use cannot be emphasized enough. Likewise, Plaintiff must prove that a specific defendant's products were present at the work place and that plaintiff had sufficient exposure to such products to cause disease.

C. Risks

As is often the case with complex medical testimony, use of epidemiologic data in the courtroom presents a serious risk of confusing and overwhelming the jury. The jury might confuse the epidemiological data as establishing causation as

opposed to its true function, which is to examine incidence rates. Some courts have embraced this limitation:

> Because of its statistical foundations, epidemiology is useful in recognizing increased rates of affliction in different groups of individuals, rather than to identify the cause of a disease in a particular individual. At most, an epidemiologist can calculate the likelihood that an individual will contract a particular disease.

In Re: John Maiorana, 1991, WL53654 (S.D.N.Y.).

> The epidemiologist's investigation is carried on by comparing the disease experience of a population exposed to the factor with other populations not so exposed. Such studies do not attempt to determine the impact of these factors upon particular individuals. Their statistical import may be considered with other proofs in toxic tort litigation to help determine the suspected substance's effect on individuals.

Landrigan v. Celotex Corp., 243 N.J. Super. 449 (App. Div. 1990).

> Here, as in Landrigan, plaintiff's medical expert relied upon epidemiological studies and the absence of certain known risk factors to opine that plaintiff's illness was caused by asbestos fibers. As we explained in Landrigan, however, epidemiological studies serve only the purpose of determining whether exposure to asbestos fibers is a risk factor in the etiology of colon cancer."

Caterinicchio v. Pittsburgh Corning Corp, et al., ____ N.J. Super. _____ (App. Div. _____, (1990).

Finally, there is the risk associated with the mystique of statistical data. When the relative risk of a methodologically complex study is quantified, the lay juror is more likely to recall the bottom line than the intricate methodological errors which may have interacted to create an inflated risk.

> Commentators have noted that the mysterious nature of statistical arguments which can create an aura of certainty makes them at once impenetrable by the layman and impressive to him and creates a continuing risk that he will give such arguments a credence they may not deserve and weight they cannot logically claim.

Michael Dore, A Commentary on the Use of Epidemiological Evidence in Demonstrating Cause-in-Fact, Harvard Environmental Law Review, pp. 429-448, 437 (1983).

D. Minimizing Risks

Given its propensity to confuse and overwhelm, the use of epidemiologic evidence can be tempered through a well-planned and thorough cross-examination. However, this is not the lawyer's only tool. Lawyers should not forget that they have some measure of control over the evidence by way of motions in limine. In Brock, the Fifth Circuit acknowledged that under the traditional approach to scientific evidence, court's do not peer beneath the reasoning of medical experts to question their reasoning. However, given the critical medical issues presented in mass toxic tort cases, "courts must critically evaluate the reasoning process by which the experts connect data to their conclusions. . ." Brock, 874 F.2d at 310.

In Richardson by Richardson v. Richardson-Merrell, Inc., 857 F.2d 823 (D.C. Cir. 1988), the court discussed the importance of medical testimony in another Bendectin case.

> . . . [e]xpert witnesses are indispensable in a case such as this. But that is not to say that the court's hands are inexorably tied, or that it must accept uncritically any sort of opinion espoused by an expert merely because his credentials render him qualified to testify.

See Richardson v. Richardson at 829. The court then proceeded to look behind the conclusion of plaintiff's expert and found his reasoning inadequate. Id. at 829.

The Fifth Circuit recently affirmed an order of the District Court granting summary judgment in favor of the defendant manufacturers in a toxic-tort case. In Christophersen v. Allied-Signal Corp., the District Court rejected plaintiff's expert testimony that since exposure to nickel and cadmium is associated with small cell carcinoma of the lung, it is likely that plaintiff's small cell colon cancer was also caused by workplace exposure to nickel and cadmium. Christophersen v. Allied-Signal, ____ F.2d ___, _ (5th Cir. 1991). The Court of Appeals rejected plaintiff's expert's opinion as methodologically unsound. While plaintiff's expert testified that the primary methods by which theories of causation are developed are through epidemiological, animal, or in vitro studies, plaintiff's expert testified he relied on none of these to form his opinion. Furthermore, the court concluded that the District Court was

correct in rejecting the expert's conclusion as based on grossly inaccurate or critically incomplete "dosage" and duration data. Apparently in rendering his opinion, plaintiff's expert relied upon a factually deficient affidavit of a co-worker for information pertaining to duration and amount of exposure. Such information about exposure is typically relied upon by experts when forming opinions on causation.

A well-written motion in limine and supporting brief pointing out the limitations of a specific study may result in exclusion on the grounds that the specific study is not methodologically sound and/or medically accepted. Expert opinion must be based on the type of information reasonably relied upon by other experts in the field. Lynch v. Merrill National Laboratories, 646 F. Supp. 856 (D. Mass. 1986), aff'd, 830 F.2d 1190 (1st Cir. 1987). However, the Fifth Circuit has held that an expert's opinion need not be generally accepted in the scientific community before it can be sufficiently reliable to support a jury finding. Osburn v. Anchor Laboratories, 825 F.2d 908 (5th Cir. 1987). Rather, the court stated, that what is necessary is that the expert arrived at his opinion by relying on methods that other experts in his field would reasonably rely upon in forming their own opinions. Id. at 915.

Courts frequently assess the validity of epidemiological studies in reviewing health, safety, and environmental standards promulgated by federal regulatory agencies. Therefore, they should do the same in toxic tort litigation to insure that they admit only reliable epidemiological evidence and guide the jury toward its proper use.

Besides evaluating specific epidemiologic data to insure the study was methodologically sound and performed by a competent, highly regarded investigator, the court must also insure that testimony is elicited from a qualified witness. In general, an expert need only such "knowledge, skill, experience, training or education in the field to make it appear that his opinion will probably aid the trier in his search for truth." Fed.R.Evid. §702.

"It is time to take hold of expert testimony in federal trials." With this admonition, the Fifth Circuit sent a message to trial judges to resist the temptation to admit all alleged expert testimony with the attitude that the jury will "apply the weight such testimony deserves". Instead, the qualifications of proffered experts must be closely scrutinized. In In Re Air Crash Disaster, supra, the court stated:

> ... we recognize the temptation to answer objections to receipt of expert testimony with the shorthand remark that the jury will give it 'the

weight it deserves'.... Trial judges must be sensitive to the qualifications of persons claiming to be experts.... Many experts are members of the academic community who supplement their teaching salaries with consulting work. We know from our judicial experience that many such able persons present studies and express opinions they may not be willing to express in an article submitted to a refereed journal or in other contexts subject to peer review. We think that is one important signal, along with many others, that ought to be considered in deciding whether to accept expert testimony. Second, the professional expert is now commonplace. That a person spends substantially all of his time consulting with attorneys and testifying is not a disqualification. But experts whose opinions are available to the highest bidder have no place before a jury, and with the imprimatur of the trial judge's decision that he is an "expert".

In sum, we adhere to the deferential standard for review of decisions regarding the admission of testimony by experts. Nevertheless, we take this occasion to caution that the standard leaves appellate judges with a considerable task. We will turn to that task with a sharp eye, particularly in those instances, hopefully few, where the record makes it evident that the decision to receive expert testimony was simply tossed off to the jury under a 'let it all in' philosophy. Our message to our able trial colleagues: It is time to take hold of expert testimony in federal trials.

In Re Air Crash Disaster at New Orleans, La. -- Eymand v. Pan American World Airways, 795 F.2d 1230, 1234 (5th Cir. 1986).

Prior to deliberation the judge should carefully instruct the jury on the proper use of epidemiologic data as well as its limitations. Only after the jury has been thoroughly instructed should they be sent to deliberate.

VI. CONCLUSION

Epidemiological data cannot establish causation in an individual case. The most it can do is establish an association, the validity and strength of which depends upon numerous factors about which the lay juror must be informed. The jury should receive a short course on the general principles of epidemiology so that they have a better understanding of the methodological complexities of the studies. The cancer risks of the general population may be emphasized to establish proper perspective. Additionally, exposure to other known risk factors, especially alcohol and tobacco, should be introduced.

When presented with a plaintiff claiming that a non-lung related cancer is caused by asbestos exposure, the relevant studies should be presented to the jury. With the exception of mesothelioma and lung cancer in the presence of smoking and asbestosis, the epidemiological data fails to establish that asbestos exposure increases the risk for developing cancer.

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