

V

# 資料編

講義・講演、読影・症例研究 使用スライド

〈スライド〉


日本におけるじん肺及び石綿関連疾患等の職業性疾病の発生状況



Trends of occupational diseases such as pneumoconiosis and asbestos-related diseases in Japan

MS Yuka Takashima  
Workers' Medical Care Division of Medical Services Department,  
Japan Labour Health and Welfare Organization

1-01




Japan Labour Health and Welfare Organization  
In 2009

Number of staffs	13,986
Rosai Hospitals	30 hospitals
Number of beds	13,301
Number of outpatients	28,484 persons /day
Number of inpatients	10,466 persons /day
Rosai Nursing School	9
Prefectural Occupational Health Promotion Center	41
Rosai Rehabilitation Workshops	5




1-02

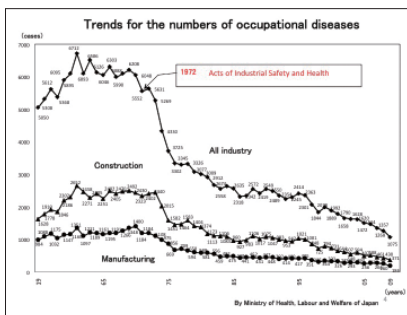
Total population and number of workers in Japan, 2009



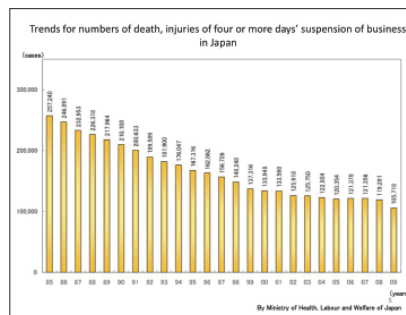
Total population	127,510,000
Number of workers	62,820,000
Primary sector of industry	2,620,000
Secondary sector of industry	15,930,000
Tertiary sector of industry	43,660,000

By Ministry of Internal Affairs and Communications of Japan 2009

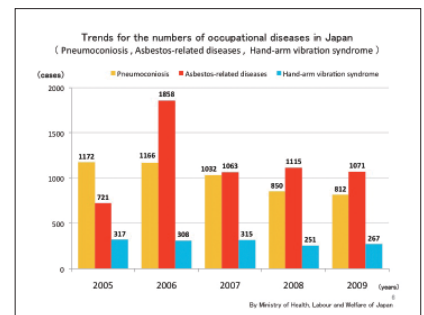
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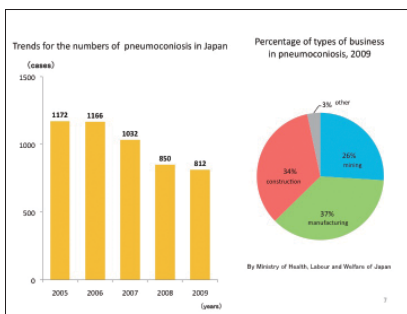
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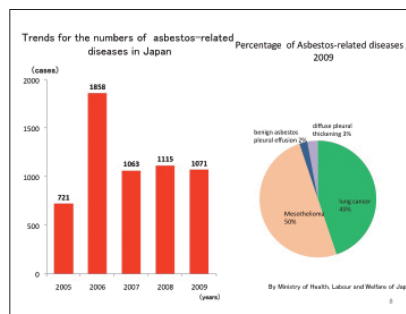
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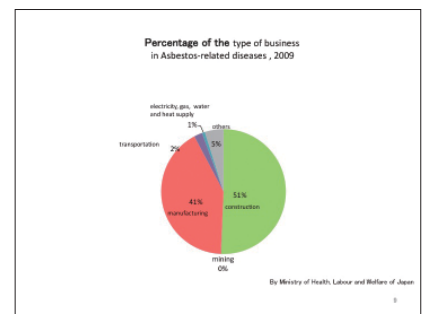
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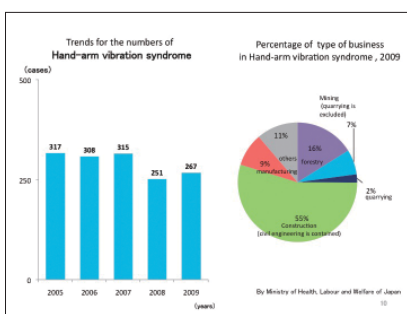
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1-10

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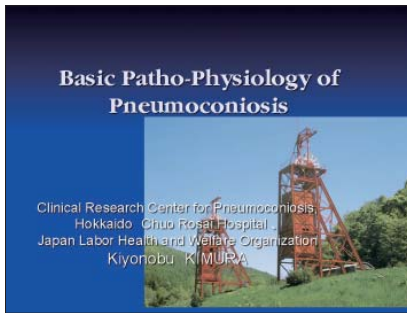


2010.10.15  
Debriefing session of workshop in Mongolia held in Japan

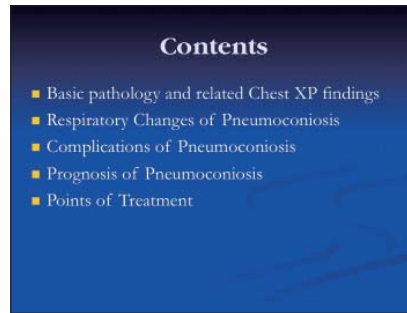
Japan Labour Health and Welfare Organization TEL:+81-44-556-9867 Web: <http://www.rofuku.go.jp>

1-11

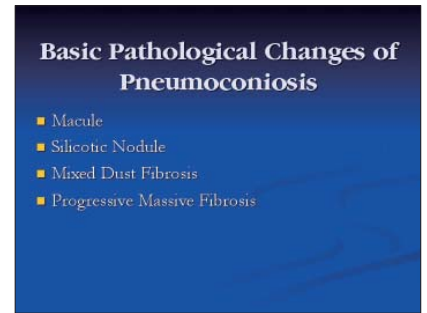
〈スライド〉  
じん肺の基本的病態生理



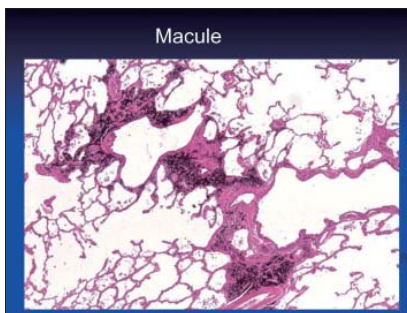
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2-02



2-03



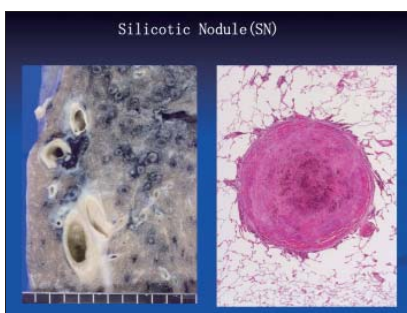
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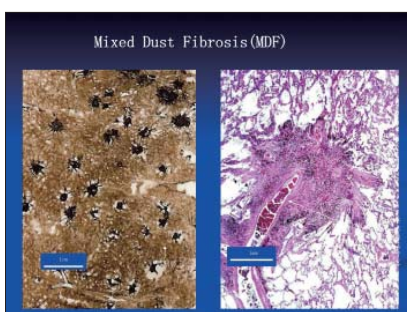
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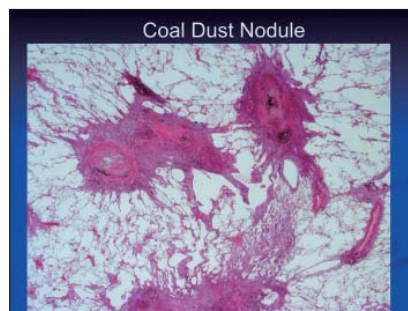
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2-10



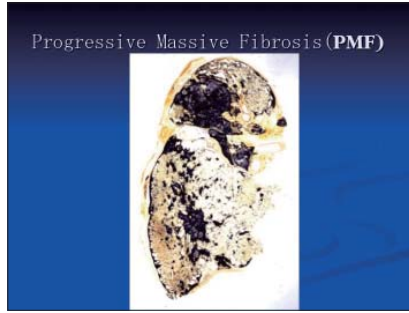
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2-13

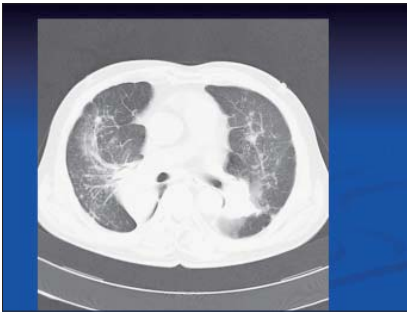


Progressive Massive Fibrosis (PMF)

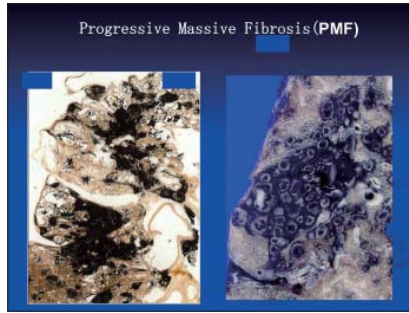
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2-15



2-16



Progressive Massive Fibrosis (PMF)

2-17



2-18

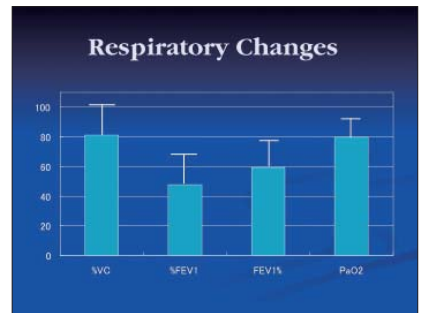


2-19

### Respiratory Changes

- Subjects: 527 compensated pneumoconiosis patients
- Occupations: Coal worker: 53.9%, Metal miners: 15.2%
- Age: 72.7 ± 6.6

2-20

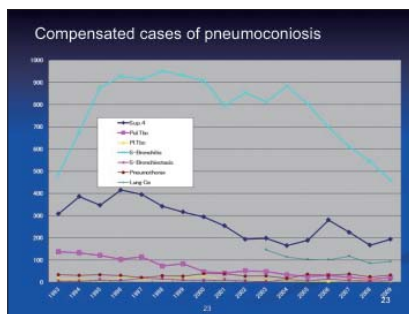


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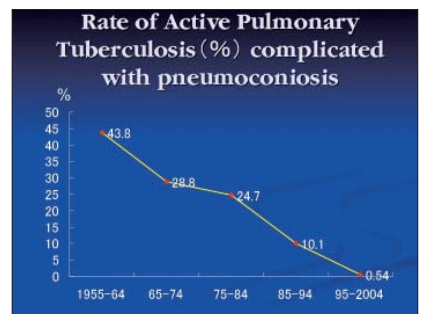
### Complication of pneumoconiosis

- 1) Pulmonary Tbc
- 2) Pleuritis Tbc
- 3) Secondary pneumothorax
- 4) Secondary bronchitis
- 5) Secondary bronchiectasis
- 6) Lung cancer

2-22



2-23

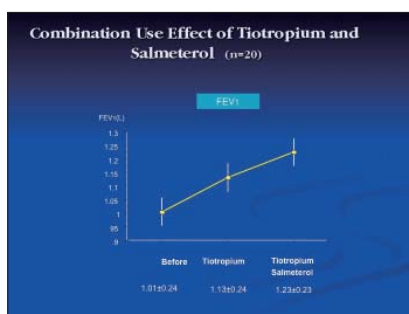


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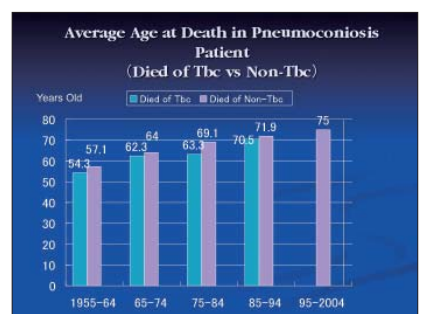
### Points of Treatment

- Control of Infection (Pul. Tuberculosis and other kinds of respiratory infection)
- Management for low respiratory function
- Early diagnosis of lung cancer

2-25



2-26



2-27

## Name of Co-Workers

Yoshinori OHTSUKA, Ikuo NAKANO,  
Kenzo OKAMOTO, Koichi ITABASHI,  
Takeshi IGARASHI, Rika SATO,  
Atsushi MORIOKA, Shinji NIGAWARA,  
Eiji NIGAWARA, Hiroshi KAJI,  
Masahiro AWAKA, Hiroki Honda,  
Mayumi SHIBUYA, and Yumiko SATO.

2-28

Thank you for your  
attention

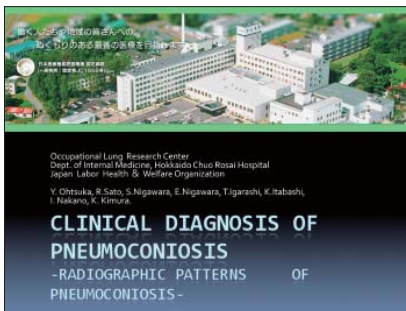
2-29

## I. 講義・講演編

## 03

〈スライド〉

## じん肺の臨床診断とX線パターン—炭鉱夫じん肺



3-01

## Clinical diagnosis of pneumoconiosis

1. Diagnosis of pneumoconiosis
2. Classification of pneumoconiosis

3-02

## 1. Diagnosis of pneumoconiosis

3-03

## 1. Diagnosis of pneumoconiosis

1. Chest radiograph consistent with the features of pneumoconiosis
2. Work history that is sufficient in exposure and latency to result in pneumoconiosis
3. Absence of other illness that may mimic pneumoconiosis

3-04

## 1. Diagnosis of pneumoconiosis

1. Chest radiograph consistent with the features of pneumoconiosis
2. Work history that is sufficient in exposure and latency to result in pneumoconiosis
3. Absence of other illness that may mimic pneumoconiosis

3-05



3-06



3-07

## Radiographic patterns of pneumoconiosis

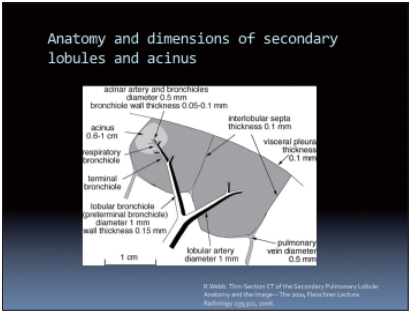
1. Small rounded opacities (<1cm)
2. Predominantly upper lung fields
3. Large opacities, symmetrically

3-08

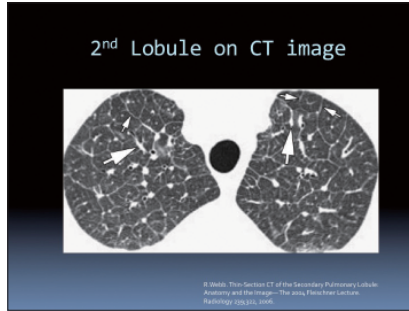
## 1. Diagnosis of pneumoconiosis

1. Chest radiograph consistent with the features of pneumoconiosis
2. Work history that is sufficient in exposure and latency to result in pneumoconiosis
3. Absence of other illness that may mimic pneumoconiosis

3-09



3-10



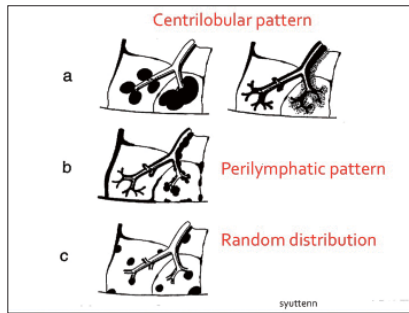
3-11



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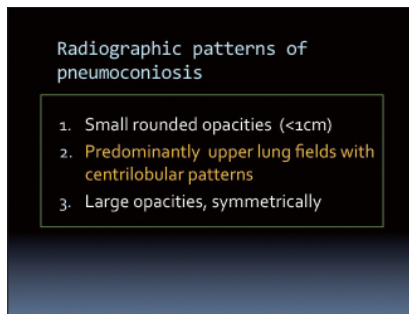
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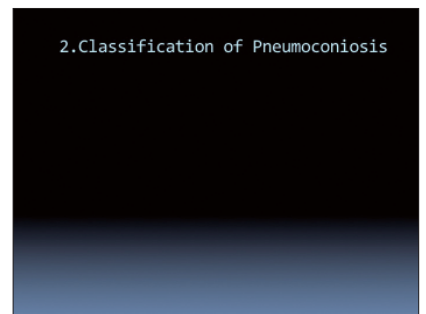
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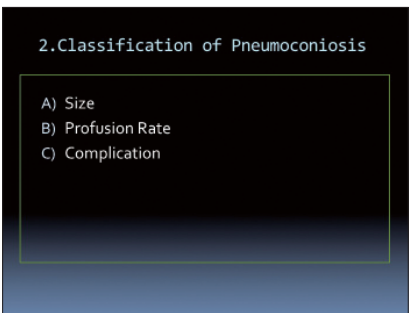
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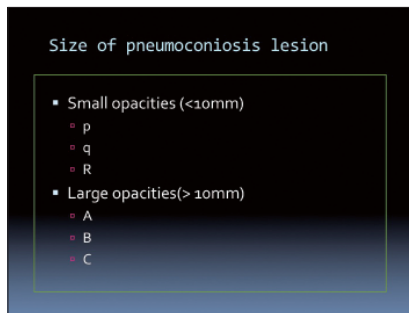
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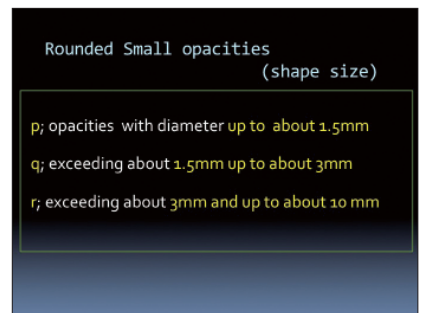
3-21



3-22



3-23



3-24

Large Opacities

4A; 10mm < large opacity < 50mm

4B; 50mm < large opacity < the area of the right upper zone

4C; the area of the right upper zone < large opacity

3-25

Profusion Rate:PR

PR= density of small opacities

The category of profusion is based on standard radiographs.

3-26

Profusion Rate

Increasing Profusion Rate →

Categories 0 1 2 3

Subcategories 0/- 0/0 0/1 1/0 1/1 1/2 2/1 2/2 2/3 3/2 3/3 3/+

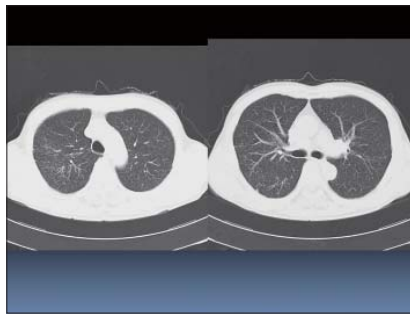
3-27

Case 1  
68 years old Male  
mining, drilling 22years

3-28



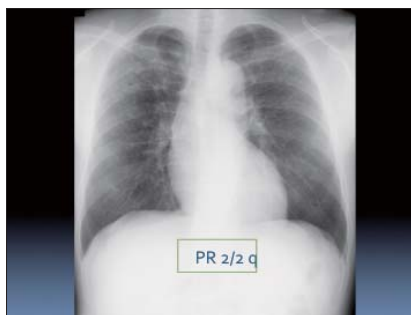
3-29



3-30

Case 2  
49 years old Male  
survey, blasting in coalmine shaft for 21 years

3-31



3-32



3-33

Case 3  
71 years old Male  
drilling in coalmine for 32 years

3-34



3-35



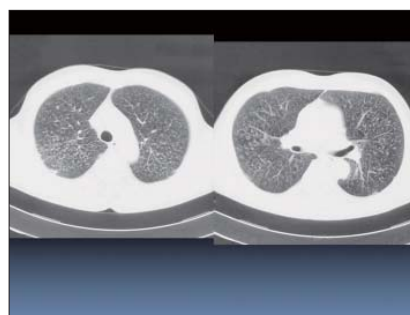
3-36

Case 4  
66 years old Male  
drilling, coal mining for 37 years

3-37



3-38



3-39

Case 5

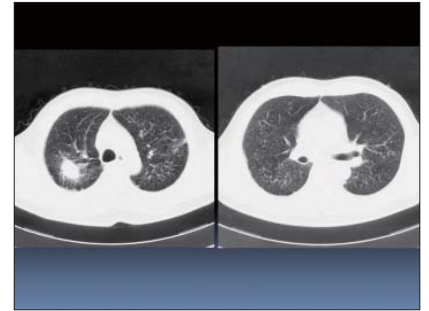
65 years old Male

drilling, mining, wheeling  
30 years

3-40



3-41



3-42

Case 6

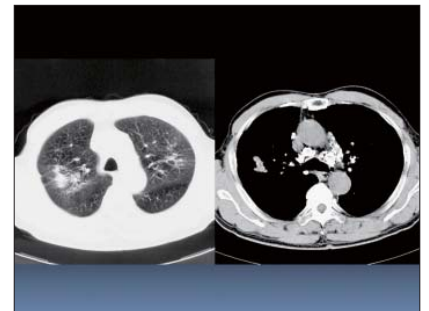
73 years old Male

drilling, mining 19 years

3-43



3-44



3-45

Case 7

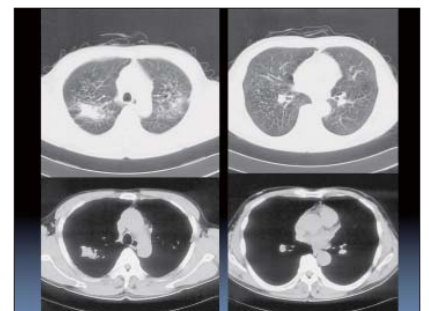
63 years old Male

survey, working in coal mine  
shaft for 26 years

3-46



3-47



3-48

Case 8

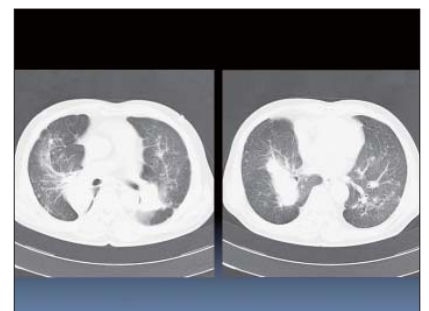
65 years old Male

drilling 25 years

3-49



3-50



3-51

Thank you for your  
attention.

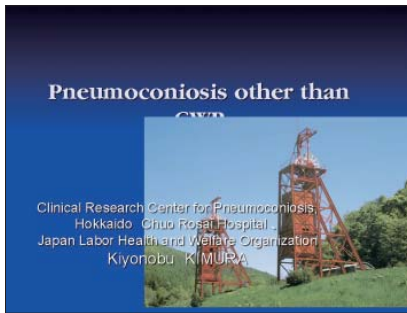
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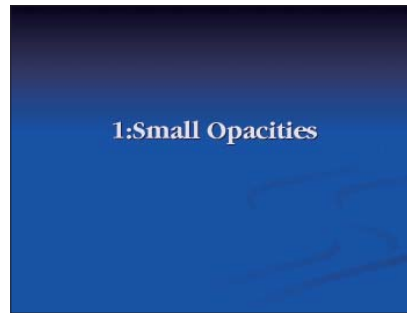
## I. 講義・講演編

## 04

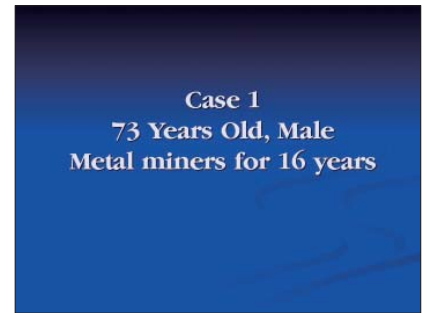
〈スライド〉  
その他のじん肺



4-01



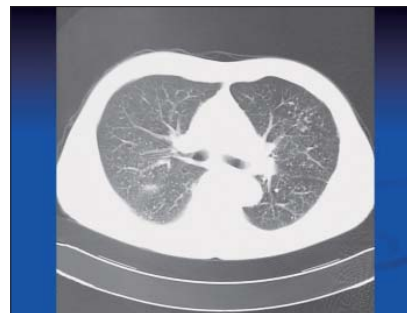
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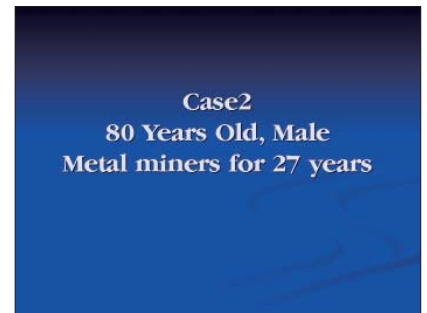
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4-04



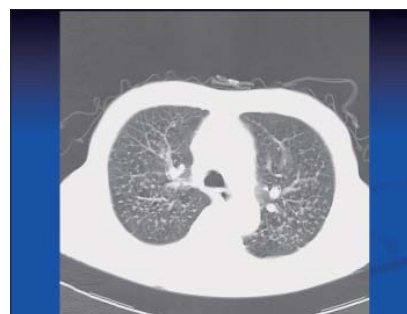
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4-06



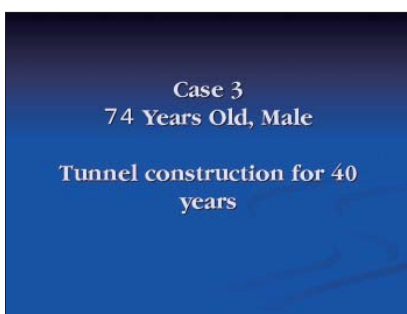
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4-11



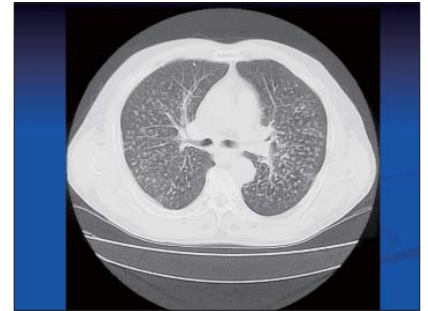
4-12

**Case 4**  
64 Years Old, Male  
Tunnel construction for 31  
years

4-13



4-14



4-15

**Case 5**  
75 Years Old, Male  
Ceramic Industry for 9 years

4-16



4-17



4-18

**Case 6**  
64 Years old, Male  
Arc and Gas Welder for 20  
years

4-19



4-20



4-21

**Case 7**  
55 Years old, Male  
Electric Welder for 20 years

4-22



4-23



4-24

**Case 8**  
43 Years old, Female  
Polish worker of hard metal for 15  
years.

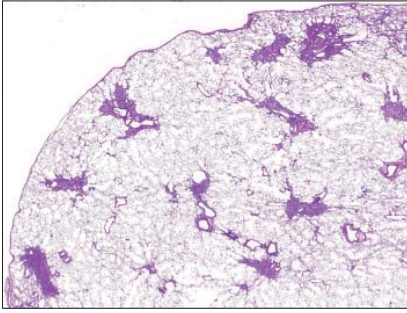
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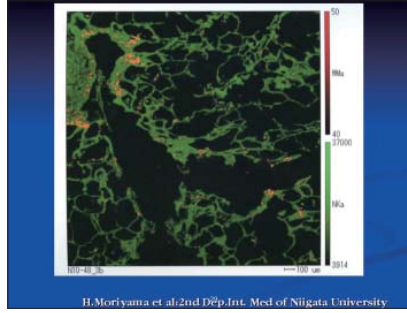
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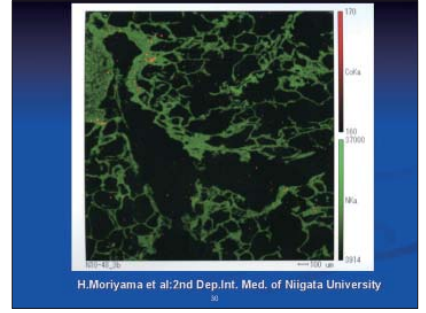
4-27



4-28



4-29



4-30

2: Large Opacities

4-31

Case 8  
77 Years Old, Male  
Tunnel construction for 25 years

4-32



4-33



4-34

Case 9  
68 Years Old, Male  
Ceramic Industry for 41 years

4-35



4-36



4-37

Case 10  
47 Years Old, Male  
Dental technician for 29 Years

4-38



4-39



4-40

**Key Facts of Imaging Findings of Small Opacities**  
①Dissemination of micronodules(<10mm)in centrilobular and subpleural distribution  
②More profuse in dorsal portion aspect of upper lobes, right side more severely involved than left

4-41

**Key Facts of Imaging Findings of Large Opacities**  
①Usually bilateral in upper lobes and superior segments of lower lobes.  
②Typically more common in dorsal aspect of lung.  
③Right hemithorax earlier and PMF larger than left hemithorax.

4-42

### Name of Co-Workers

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Kenzo OKAMOTO, Koichi ITABASHI,  
Takeshi IGARASHI, Rika SATO,  
Atsushi MORIOKA, Shinji NIGAWARA,  
Eiji NIGAWARA, Hiroshi KAJI,  
Masahiro AWAKA, Hiroki Honda,  
Mayumi SHIBUYA, and Yumiko SATO.

4-43

Thank you for your  
attention

4-44

## I. 講義・講演編

# 06

### 〈スライド〉 石綿肺の診断

## Asbestosis

Japan Organization of Labour, Health  
and Welfare

Vice-director Okayama Rosai Hospital  
Takumi Kishimoto, MD, PhD

6-01

### Kinds of asbestos

name of mine	name of asbestos	structure of mine
Serpentines		
Chrysotile	Chrysotile (white asbestos)	$Mg_3Si_2O_5(OH)_4$
Amphiboles		
Grüne-amphi.	Amesite (brown asbestos)	$(Mg, Fe)_3Si_4O_{10}(OH)_2$
Riebeck-amphi.	Crocidolite (blue asbestos)	$Na_2Fe_3^{2+}Fe_3^{3+}Si_8O_{22}(OH)_2$
Anthophyllite	Anthophyllite asbestos	$Mg_3Si_4O_{10}(OH)_2$
Tremolite	Tremolite asbestos	$Ca_2Mg_5Si_8O_{22}(OH)_2$
Actinolite	Actinolite asbestos	$Ca_2(Mg, Fe)_5Si_8O_{22}(OH)_2$

6-02

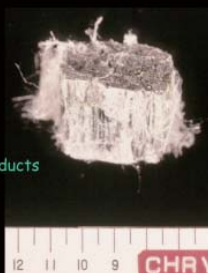
### Characteristic of asbestos

- Spinning and weaving
- Anti-friction
- Anti-corrosion
- Anti-heat
- Soundproofing
- Anti-drug (acid, alkaline)
- Insulating
- Affinity
- Economy

6-03

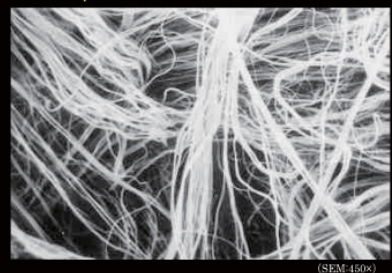
### chrysotile (White asbestos)

- Serpentine
- Curling fibers
- 95% of Japanese products
- Rare formation of asbestos bodies



6-04

### Chrysotile from South Africa

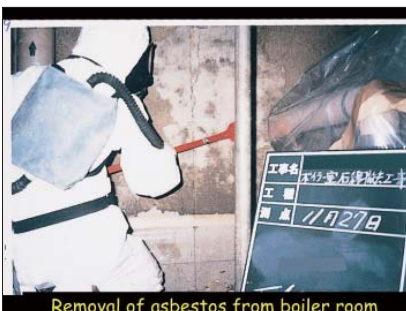


6-05

### Asbestos spinning factory



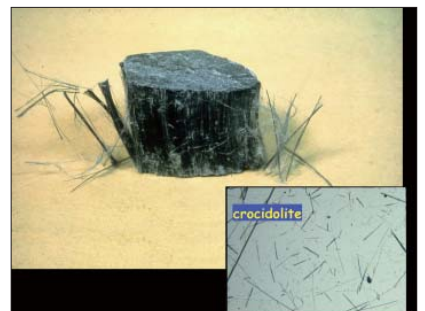
6-06



6-07



6-08



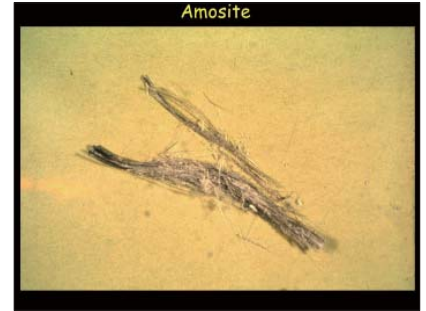
6-09



6-10



6-11



6-12



6-13

### Kinds of asbestos exposure

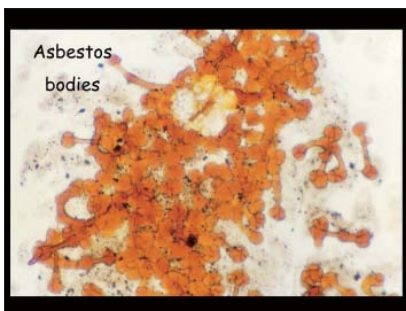
- Occupational asbestos exposure
  - (A) Direct occupational exposure
  - (B) Indirect occupational exposure
  - (C) Exposure in agriculture (asbestos in the soil)
- Para-occupational asbestos exposure
  - (A) Para-occup. Familiar exp. (Working clothes, asbestos bag et al)
  - (B) Para-occup. Exp. (asbestos boards)
- Environmental exposure
  - True environmental exposure

6-14

### Medical evidence for asbestos exposure

Asbestos bodies  
Pleural plaques

6-15



6-16



6-17

### Density of asbestos bodies in the lung - Estimation of the level of asbestos exposure-

No. of asbestos bodies (No./dry lung tissue 1g)	Level of asbestos exposure
<1,000	Level of citizen (neglective of occup. exposure)
1,000~5,000	Highly susp. of occup. exposure
>5,000	Level for the twice of Lung cancer Definite of occup. exposure

This criteria can not estimate chrysotile exposure

6-18

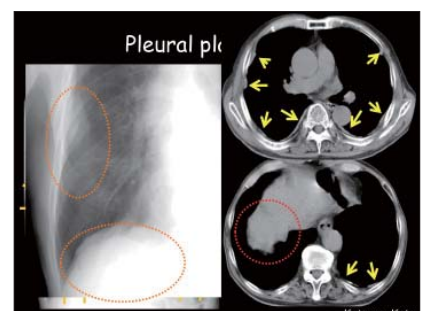
### Pleural plaques

6-19

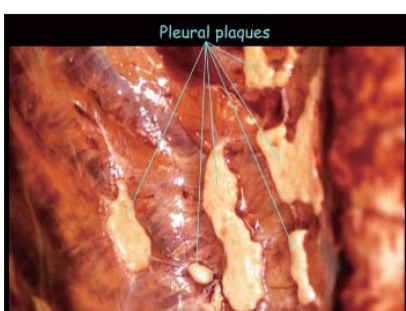
### What is pleural plaques ?

- Patch of pleura or limited pleural thickening, very good indicator for asbestos exposure
- Pleural plaques are caused by asbestos exposure in Japan
- Pleural plaques are detected in not only high dense exposed people but also low dense exposed people
- Pleural plaques appear after 15 to 30 years from the first exposed to asbestos and calcified plaques appear at least 20 years
- Pleural plaques exhibit uneven plates showing creamy color

6-20



6-21



6-22

### Asbestos-related diseases

- Asbestosis
- Asbestos-related lung cancer
- Mesothelioma (pleura, peritoneum, pericardium, tunica vaginalis)
- Benign asbestos pleurisy
- Diffuse pleural thickening

6-23

### Diagnosis of asbestosis

- Occupational asbestos exposure
- Irregular opacities in the lower lung field in chest X-ray
- Impairment of lung capacity by pulmonary function test
- Fine crackle audible in the lower lung field at inhalation
- Elimination of other similar diseases and excepting asbestos induced diseases

\* Asbestosis usually induced by high dense asbestos exposure. Therefore, minute occupational histories and HRCT examinations are essential.

6-24

### Case 1

62 years, male

He had a history of asbestos spraying for 4 years from eighteen years for part time job. Since then, he is white color and no histories of asbestos exposure.

He was diagnosed asbestosis in 2006 for the screening of chest x-ray. He got respiratory failure after 2 years of diagnosis. Further more, he had lung cancer in left lung field and died of lung cancer in 2009.

Number of asbestos bodies in the lung was 36,345/g

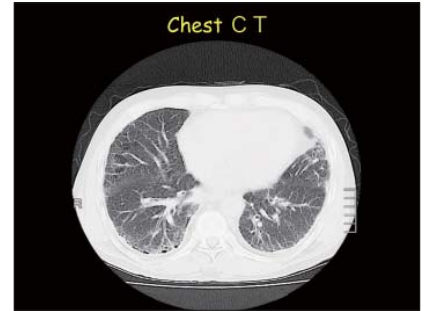
6-25

### Chest x-ray for case 1



6-26

### Chest C T



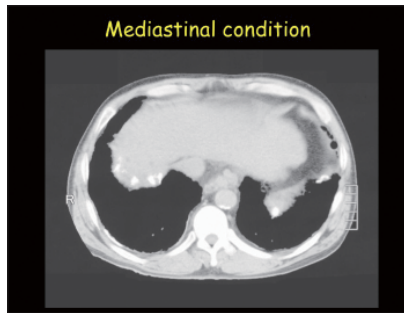
6-27

### HRCT



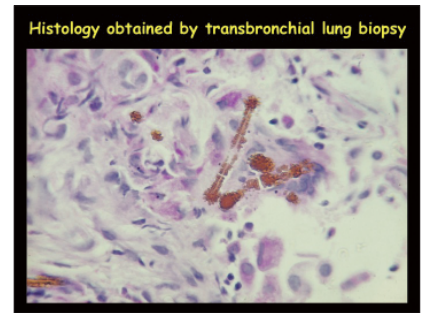
6-28

### Mediastinal condition



6-29

### Histology obtained by transbronchial lung biopsy



6-30

### Case 2



67 years, male  
Asbestos sprayer  
for 18 years

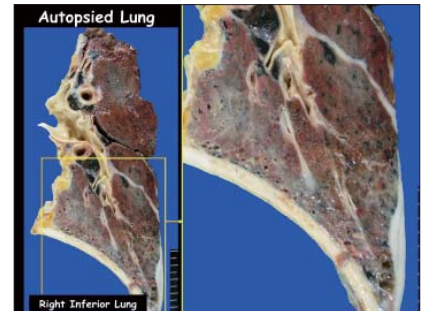
6-31

### Chest CT

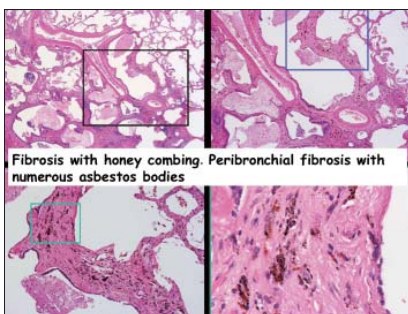


6-32

### Autopsied Lung

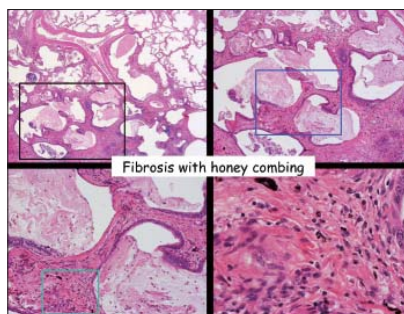


6-33



Fibrosis with honeycombing. Peribronchial fibrosis with numerous asbestos bodies

6-34

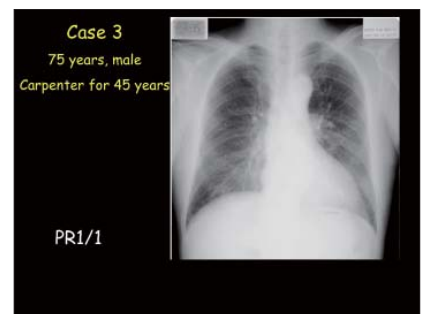


Fibrosis with honeycombing

6-35

### Case 3

75 years, male  
Carpenter for 45 years



PR1/1

6-36

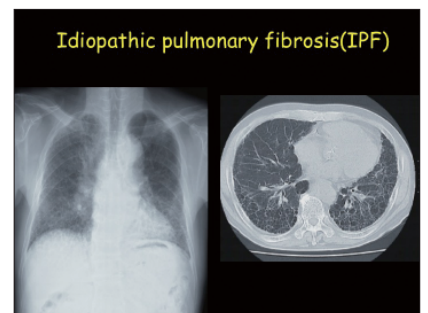


6-37



6-38

### Idiopathic pulmonary fibrosis(IPF)

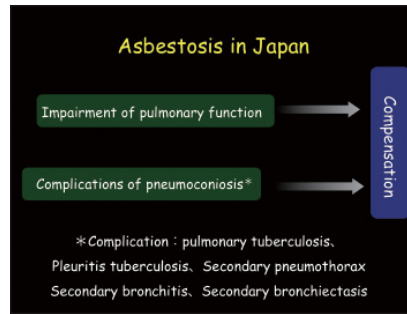


6-39

### Problems for the diagnosis of asbestosis

- There are some cases of asbestosis who can not be differentiated from idiopathic interstitial pneumonia
- A cases of Interstitial pneumonia with pleural plaques is not always asbestosis
- Asbestosis appeared by high dense asbestos exposure with more than 25fibers/mL · year.
- The pathological findings (lung fibrosis with more than 2 asbestos bodies/cm2) are not always consistent with the radiological findings.
- From the ILO classification, profusion rates of more than 1/1 are diagnosed asbestosis, but some radiologists diagnosed asbestosis by the findings of CT scanning.

6-40



6-41

### Practice for reading films for asbestosis

Age	gender	occupational history	exposed term (years)
1) 86 years	male	insulator	31
2) 71 years	male	asbestos sprayer	12
3) 75 years	male	construction worker	29
4) 79 years	male	dismantling	20

6-42

### Test trial: reading chest X-ray of pneumoconiosis including asbestosis September 17 th,2011

Age	Gender	Occupational history	working period (years)
5) 73 years	male	insulator	40
6) 66 years	male	asbestos sprayer	12

6-43

### Practice for reading films of Mesothelioma September 17 th,2011

6-44

### Practice for reading films for mesothelioma

Age	gender	occupational history	exposed term (years)
1) 54 years	male	Asbestos products	3
2) 84 years	male	Jap.naval shipyards	4
3) 74 years	male	carpenter in shipyards	10
4) 61 years	male	interior decoration	38
5) 57 years	male	wiring	27
6) 61 years	male	shipbuilding	37
7) 70 years	male	insulator	37
8) 69 years	male	pipng worker	43

6-45

I. 講義・講演編

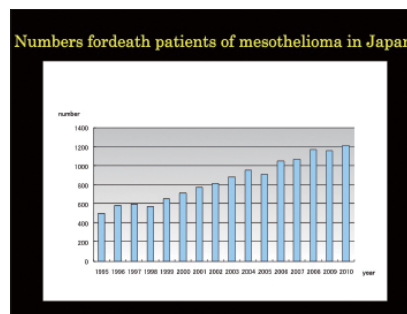
09

〈スライド〉  
悪性中皮腫の診断

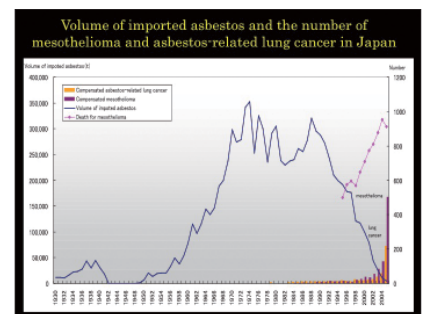
### Diagnosis of malignant mesothelioma

Japan Organization of Labor, Health and Welfare  
Vice Director of Okayama Rosai Hospital  
Takumi Kishimoto, MD,PhD

9-01



9-02

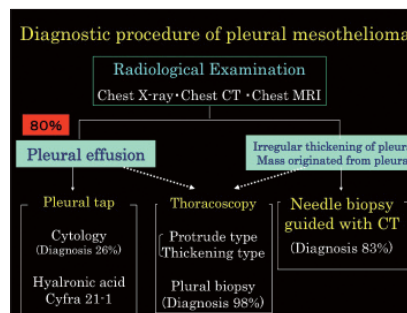


9-03

### Chief complaints of mesothelioma

Pleura : dyspnea, chest pain, cough, fever  
Peritoneum : abdominal pain or distension  
Pericardium : arrhythmia, dyspnea  
Tunica vaginalis : Tumor or pain from inguinal to testis

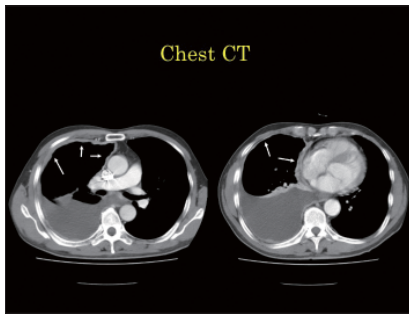
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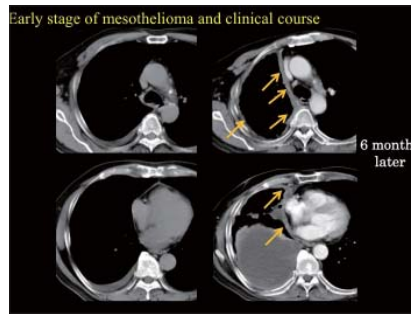
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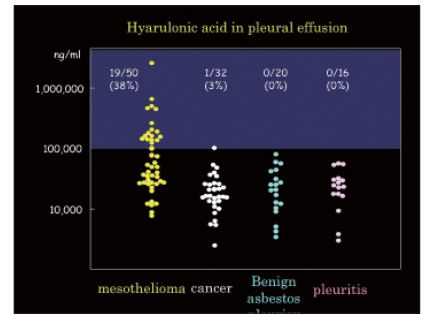
9-06



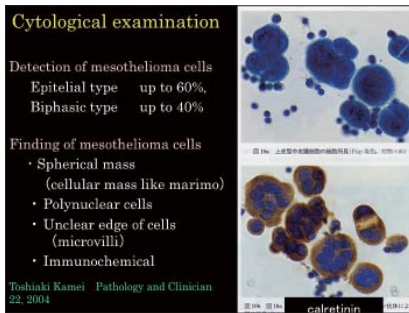
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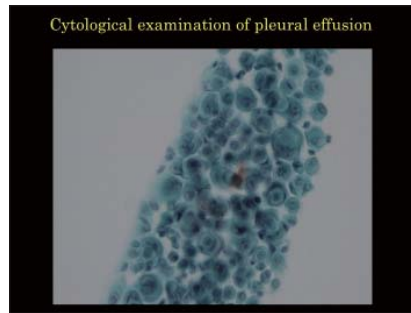
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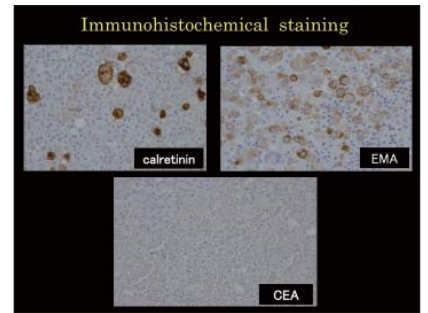
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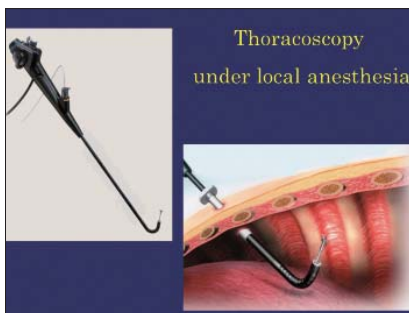
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9-11



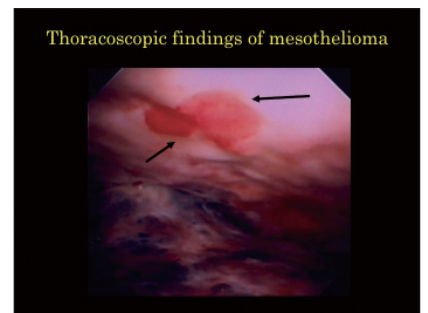
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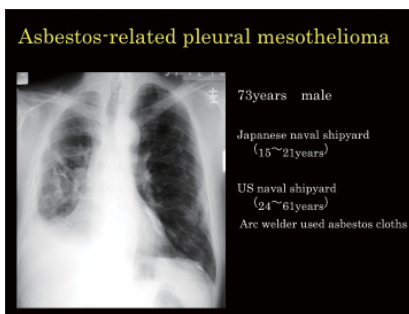
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9-14



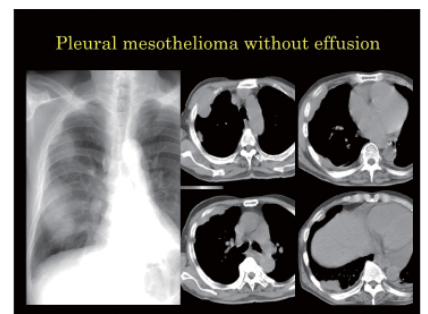
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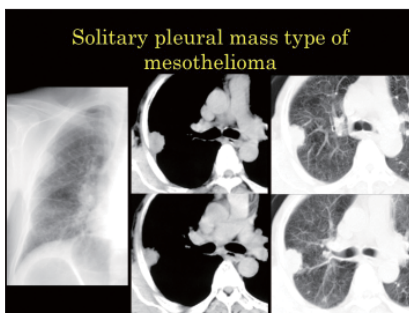
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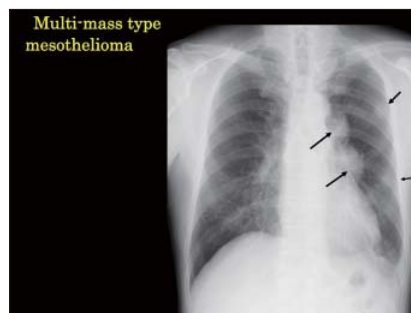
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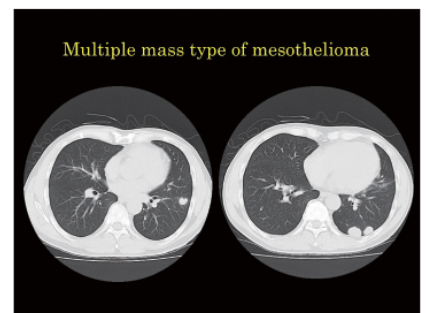
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9-19

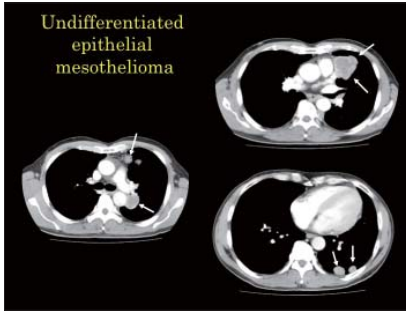


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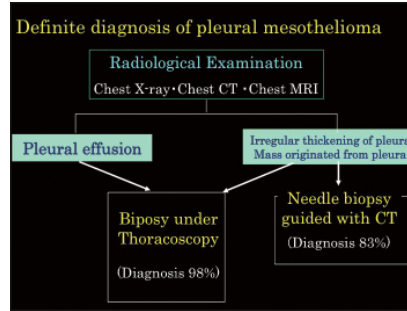


9-21

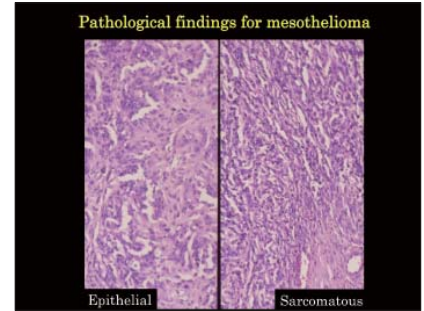




9-22



9-23

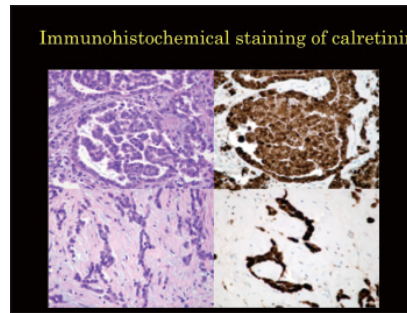


9-24

**Differential diagnosis by immunohistochemical method (Epithelial type)**

marker	mesothelioma (n=60)	Lung (n=60)
Calretinin	100%	8%
Cytokeratin 5/6	100%	0%
WT1	93%	0%
D2-40	96%	27%
Mesothelin	100%	36%
N-cadherin	73%	36%
HBME-1	85%	69%
CD44s	73%	49%
MOC-31	8%	100%
E-cadherin	40%	88%
BGP-4 (LAWISY)	7%	9%
TTF-1	0%	71%
CEA	0%	88%
B72.3 (TA0-72)	0%	8%
Leu-M1 (CD18)	0%	7%
Ordonez NG and Kushitani		
Ber-EP4	18%	100%
EMA	93%	100%
Vimentin	50%	35%

9-25



9-26

**Differential Diagnosis by immunohistochemical staining**

Positive Marker	Negative marker
<b>Epithelial type</b>	
calretinin, D2-40	CEA, TTF-1
WT-1, CK5/6	MOC-31, LeuM1
thrombomodulin	Ber-EP4
<b>Sarcomatous type</b>	
AE1/AE3, CAM5.2	desmin, s-100
calretinin, EMA	smooth muscle actin

9-27

**Differential Diagnosis**

**Pleural mesothelioma**  
Lung cancer,  
Metastatic pleural tumor (Kidney et al)  
Tumor of thoracic wall  
Mediastinal tumor  
Fibrotic pleuritis

**Peritoneal mesothelioma**  
Ovarian cancer  
Peritoneal cancer

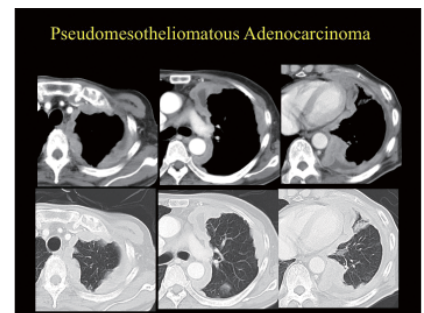
9-28

**Most important differential diagnosis**

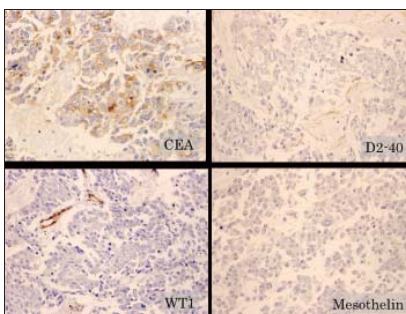
1) Pseudomesotheliomatous adenocarcinoma VS Pleural mesothelioma

2) Fibrotic pleuritis VS early stage of mesothelioma

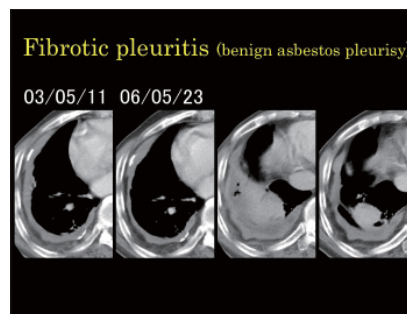
9-29



9-30



9-31



9-32

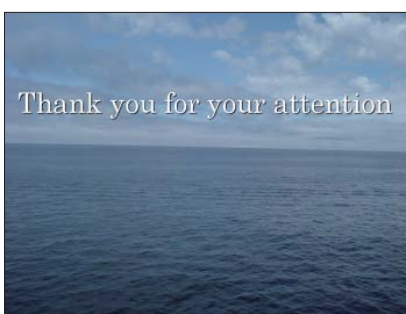
**Summary**

For the definite diagnosis of mesothelioma, needle guided biopsy under CT, video-assisted thoracoscopy or thoracoscopy under local anesthesia is required.

Tissue samples should be evaluated by immunohistochemical staining including at least 4 different antibodies.

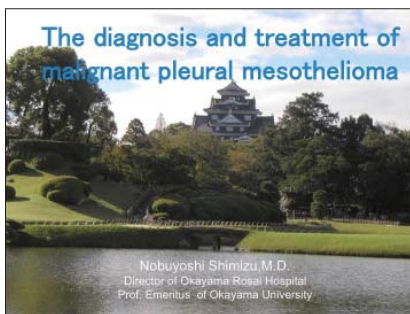
Positive diagnosis for epithelial type of mesothelioma is considered when at least 2 positive and 2 negative staining results are obtained.

9-33

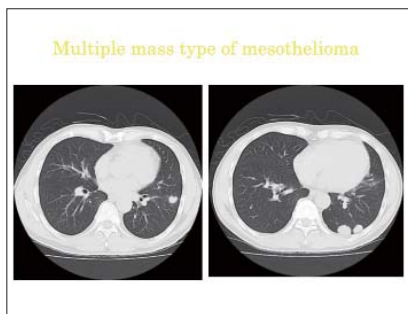


9-34

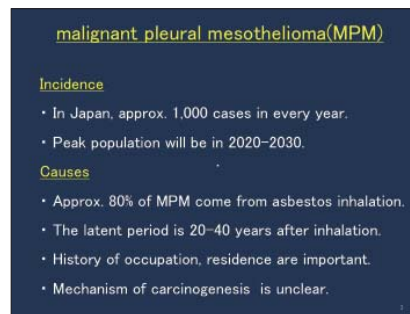
〈スライド〉  
胸膜中皮腫の治療



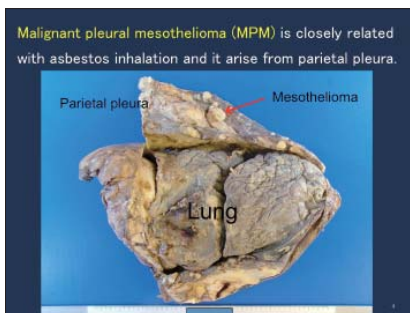
10-01



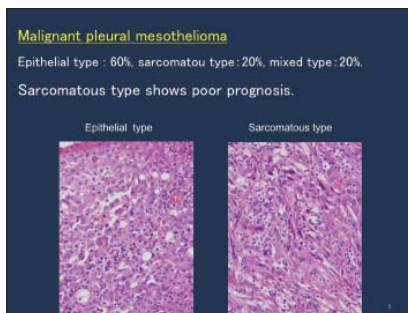
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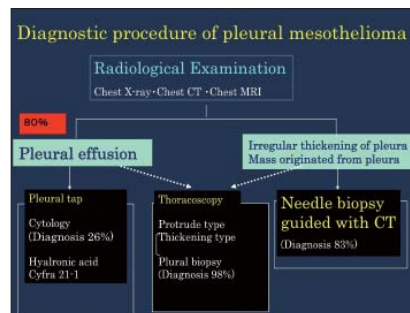
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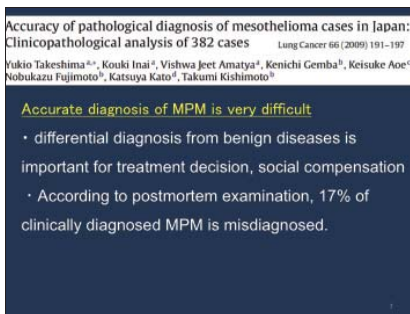
10-04



10-05



10-06



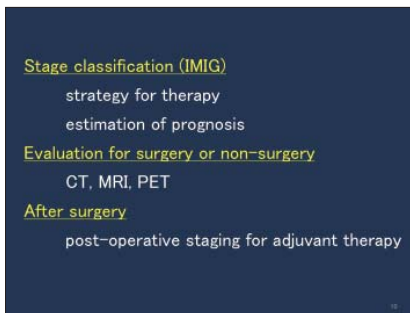
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10-08



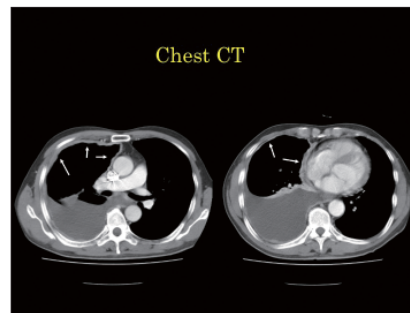
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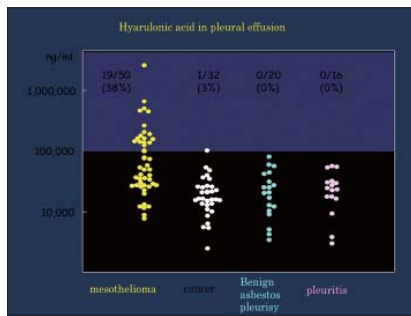
10-10



10-11



10-12



10-13

### Cytological examination

Detection of mesothelioma cells

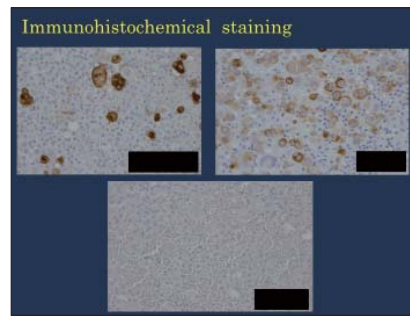
- Epithelial type up to 60%
- Biphasic type up to 40%

Finding of mesothelioma cells

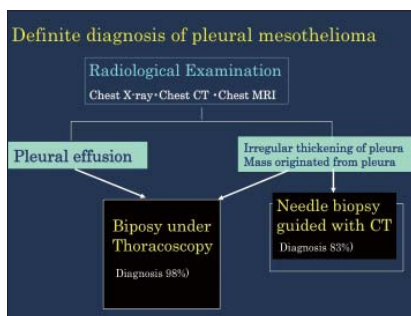
- Spherical mass (cellular mass like marimo)
- Polynuclear cells
- Unclear edge of cells (microvilli)
- Immunochemical

Toshiaki Kamei Pathology and Clinician 22, 2004

10-14



10-15



10-16

### Differential diagnosis by immunohistochemical method (Epithelial type)

marker	mesothelioma (n=90)	Lung (n=28)
Calretinin	100%	8%
Cytokeratin 5/6	100%	2%
WT1	93%	0%
D2-40	96%	27%
Mesothelin	100%	38%
N-cadherin	73%	30%
HBME-1	85%	68%
CD44s	73%	48%
MCIC-31	8%	100%
E-cadherin	40%	88%
Biom (Levity)	7%	96%
TP53	0%	74%
CEA	0%	88%
BT2.3 (TAG-72)	0%	84%
Leu-M1 (CD15)	0%	72%
Ber-EP4	18%	100%
EMA	93%	100%
Vimentin	95%	38%

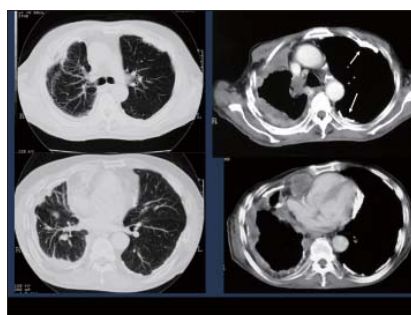
Ordones NG and Kushiitani

10-17

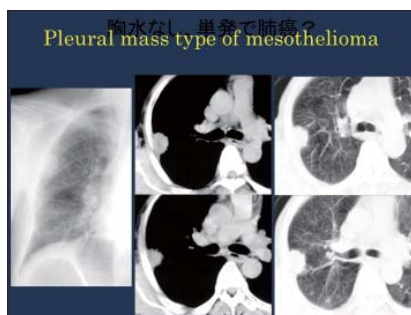
### Asbestos-related pleural mesothelioma

73years male  
Japanese naval shipyard (15~21years)  
US naval shipyard (24~61years)  
Arc welder used asbestos cloths

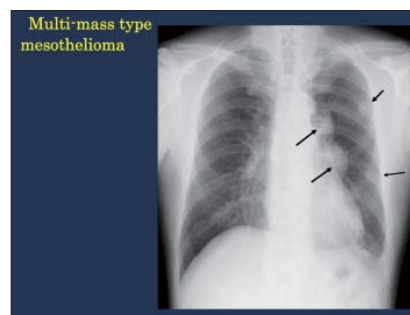
10-18



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10-21



10-22

- ### Treatment for mesothelioma
- 1)Surgery: Extrapleural pneumonectomy (EPP) (effective for the early cases up to Stage II)
  - 2)Chemotherapy CDDP+Pemetrexed(ALIMTA)
  - 3)Radiotherapy not effective
  - 4) Trimodality (Surgery,chemotherapy,radiation)  
*Some institutions have more than 5 years survival cases*

10-23

- ### Surgery for pleural mesothelioma
- ① Extrapleural pneumonectomy  
Extrapleural pneumo-pleurectomy  
partial resection of diaphragm and pericardium
  - ② pleurectomy/decortication  
(survival term is almost same as extrapleural pneumonectomy in Europe)  
extraction of pleura and tumor mass without pneumonectomy
  - ③ Pleurectomy  
Extraction of parietal pleural mass and pleura

10-24

### Extrapleural pneumonectomy, EPP

complete resection of tumor tissue,  
Indication : c-Stage: T1-3, N0, 1, (2), M0

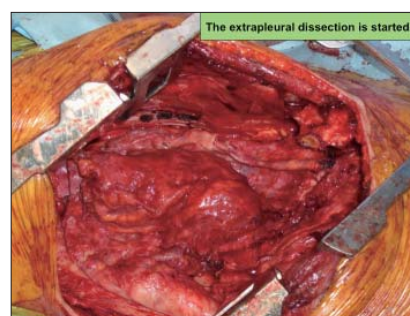
Resection  
parietal pleura  
visceral pleura & whole lung  
diaphragm

Reconstruction  
diaphragm  
pericardium

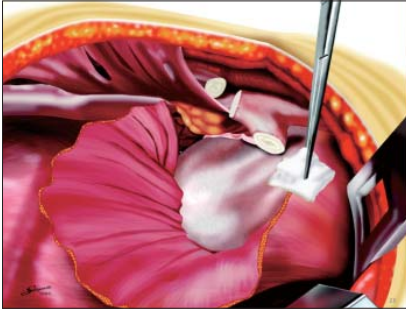
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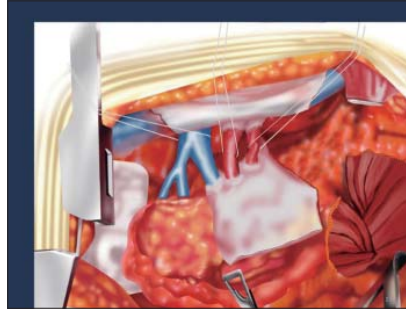
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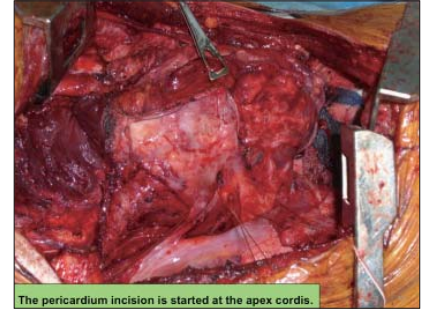
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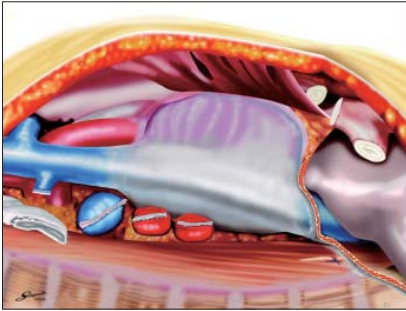
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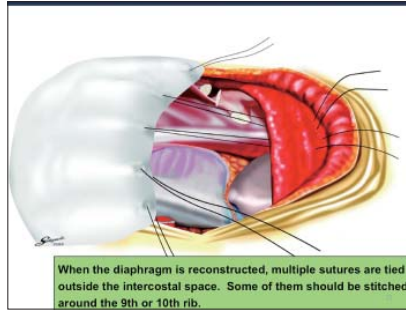
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10-31



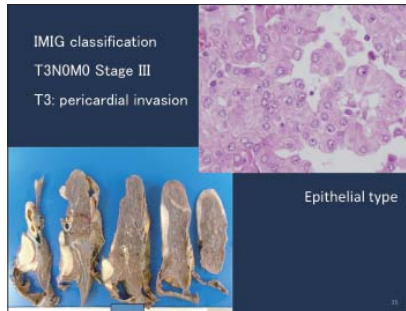
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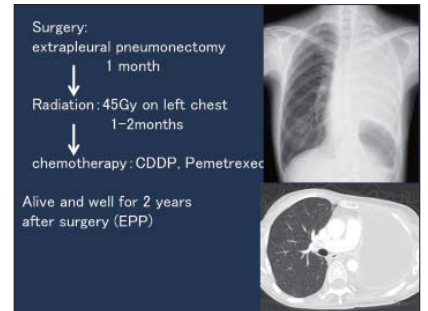
10-33



10-34



10-35



10-36

**Radiotherapy(2)**

- Hemithorax : 54 Gy (20 - 64 Gy)
- Median survival (EPP : 61patients) : 17months
- Stage I (2), II (17): 33.8 months
- Stage III (41), IV (1): 10months
- Recurrent site (EPP + rad: 54patient)
- local : 7 distant : 35

Rusch V, et al. J Thorac Cardiovasc Surg 2001; 122: 788-795.

10-37

**Prof. Sugarbaker (1999)**

RESECTION MARGINS, EXTRAPLEURAL NODAL STATUS, AND CELL TYPE DETERMINE POSTOPERATIVE LONG-TERM SURVIVAL IN TRIMODALITY THERAPY OF MALIGNANT PLEURAL MESOTHELIOMA: RESULTS IN 183 PATIENTS

David J. Sugarbaker, Raja M. Flores, Michael T. Jaklitsch, William G. Richards, Gary M. Strauss, Joseph M. Corson, Malcolm M. DeCamp, Jr, Scott J. Swanson, Raphael Bueno, Jeanne M. Lukianich, Elizabeth Healey Baldini and Steven J. Mentzer  
J Thorac Cardiovasc Surg 1999;117:54-65

EPP + chemotherapy + postop.radiotherapy

183 patients(m 140, f 43), average age 57y.o.

chemotherapy:  
doxorubicin + cyclophosphamide  
doxorubicin + cyclophosphamide + cisplatin  
carboplatin + paclitaxel

Radiation: 30 Gy, 40 Gy, 54 Gy

10-38

**Prof. Sugarbaker (1999)**

perioperative mortality: 7/183 (3.8%), morbidity: 50%

n = 176 (epith: 103, mixed/sarcomatous : 73)

2years survival 38%, 5years survival 15%

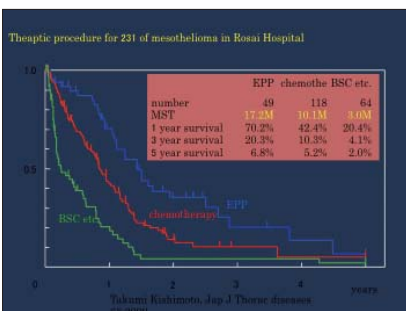
Median survival : 19months

Epithelial type with no lymph nodes metastasis 31

2 years survival :68%, 5 years survival :46%

Median survival :51months

10-39



10-40

**Conclusion**

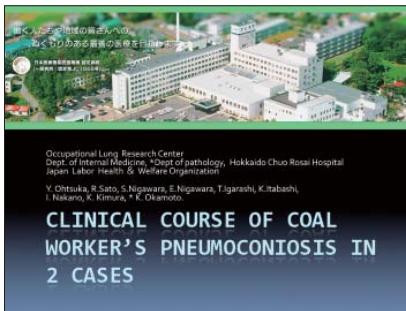
- No definite single modality treatment for MPM
- Surgery(EPP or P/D), induction chemotherapy or post-operative chemotherapy, and radiation will improve the prognosis.
- New modalities are strongly expected.

10-41

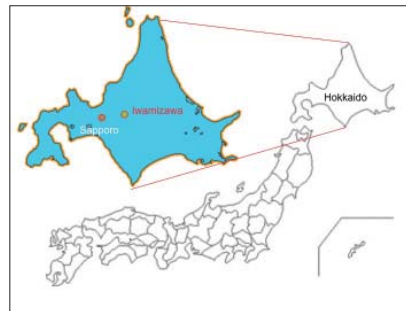
## II. 読影・症例研究編

## 02

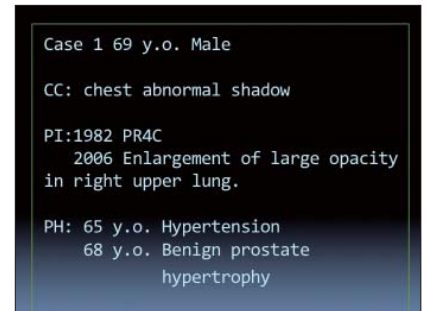
〈スライド〉  
炭鉱夫じん肺の症例研究(2症例)



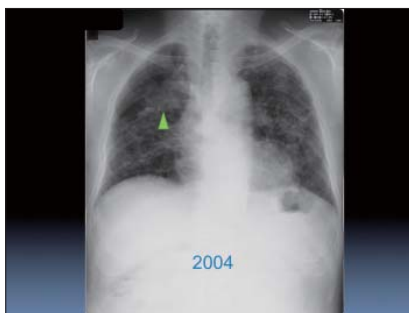
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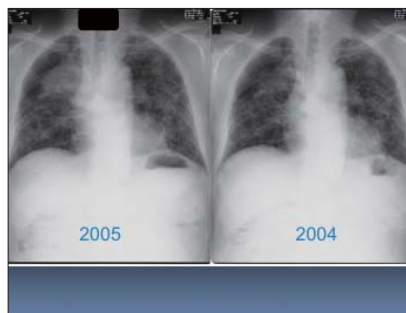
2-02



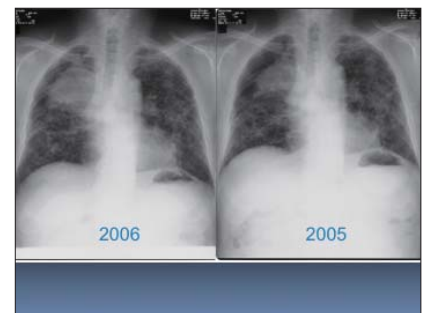
2-03



2-04



2-05



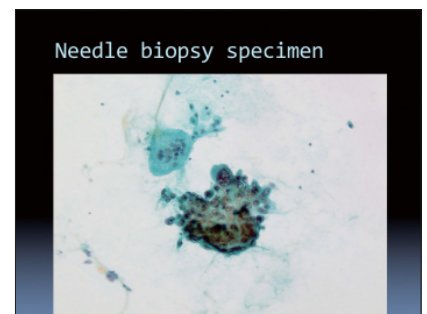
2-06



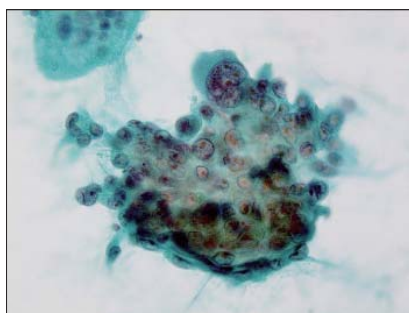
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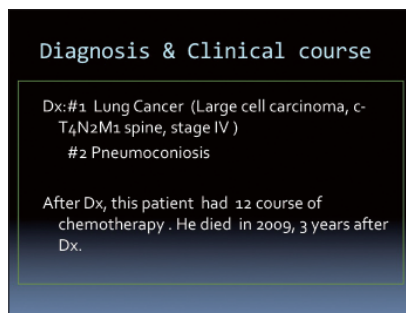
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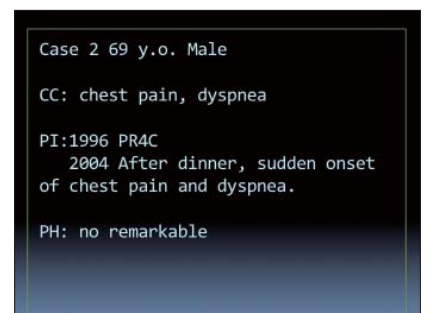
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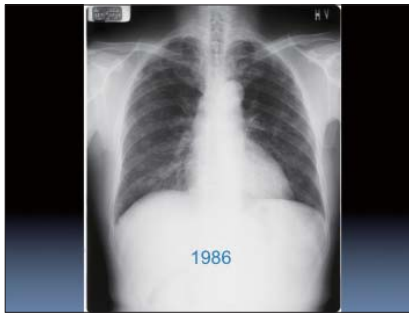
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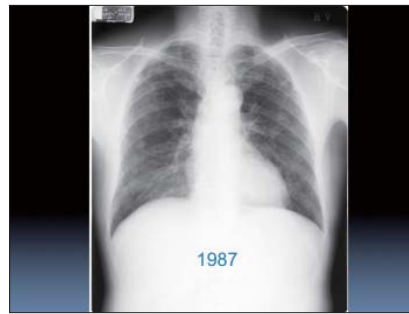
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2-12



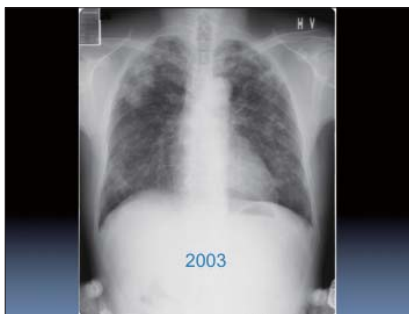
2-13



2-14



2-15



2-16



2-17

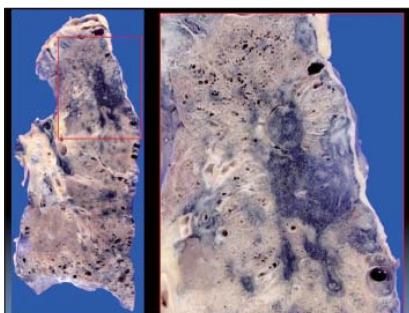
**Clinical Dx and course**

2004 Oct 29. Sudden chest pain with elevated ST segment in II, III, aVf, V1-V6 on ECG. Dx of acute myocardial infarction was made. PTCA and coronary stent installed.

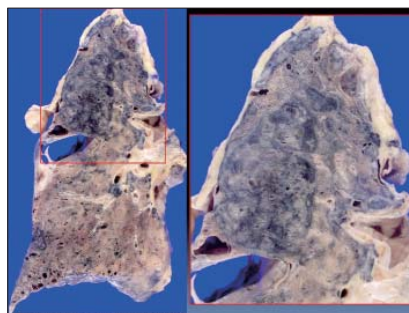
2004 Nov 9. Renal dysfunction was observed.

2004 Dec 3. With bacterial pneumonia and pulmonary edema, pulmonary dysfunction went further and died on Dec 14. Autopsy was proceeded.

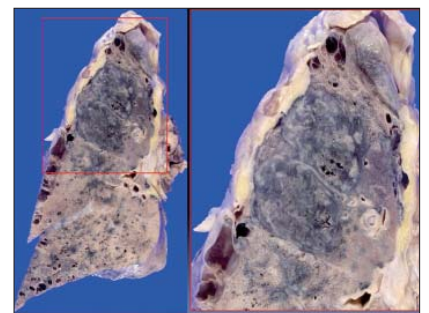
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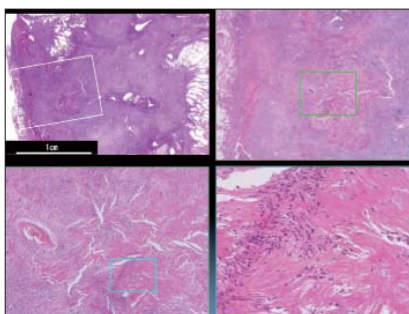
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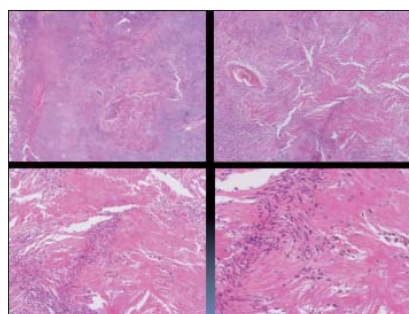
2-20



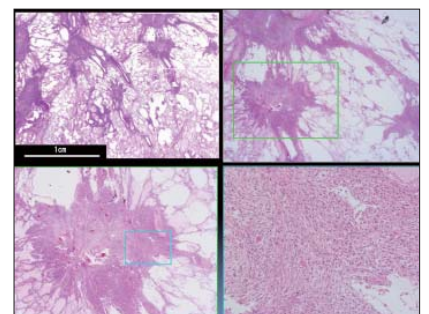
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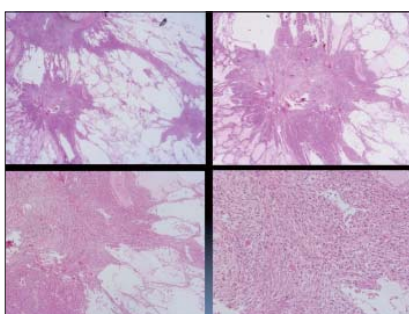
2-22



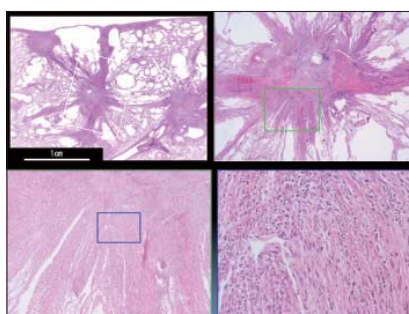
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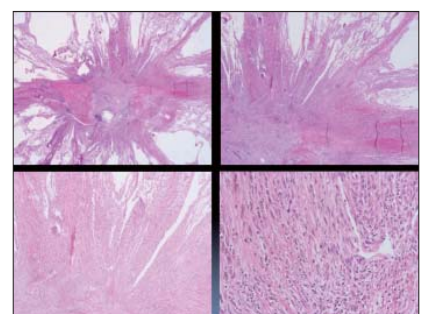
2-24



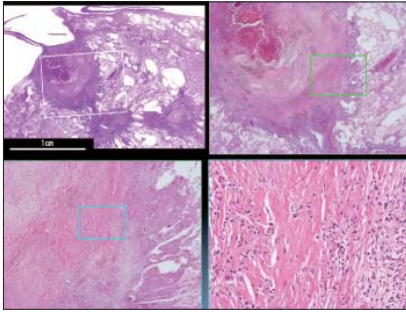
2-25



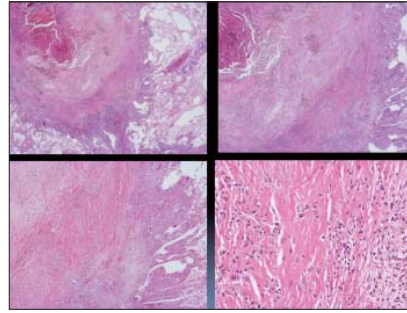
2-26



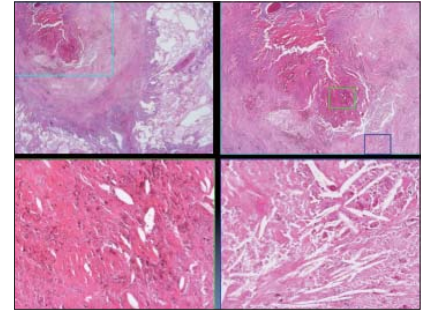
2-27



2-28



2-29



2-30

INTERNAL MEDICINE

ORIGINAL ARTICLE

**Progression of Pneumoconiosis in Coal Miners after Cessation of Dust Exposure: A Longitudinal Study Based on Periodic Chest X-ray Examinations in Hokkaido, Japan**

Kiyomichi Kimura, Yoshitoki Ohnaka, Hiroshi Kaji, Ryo Nakano, Kohiro Sakai, Kazuki Ishihara, Takashi Igarashi and Kenzo Okamoto

**Abstract**

**Background** The progression rate of pneumoconiosis in retired coal miners over ten years has not been studied in Japan.

**Methods** A retrospective longitudinal study was undertaken using chest X-rays of 1091 pneumoconiosis subjects in Hokkaido, Japan between 1985 and 2015.

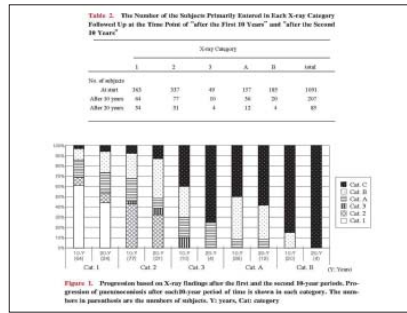
**Results** The final numbers of subjects were 207 (19% of the entry) after 1 decade and 85 (8% after 2 decades. Sixty-one percent of 207 subjects after 1 decade and 29% of 85 showed progression in 2 decades. Thirty-one percent of B0 category A and 59% of category 2 subjects showed progression to complicated pneumoconiosis after 1 decade, and 16% of category 1 and 50% of category 2 subjects progressed to complicated pneumoconiosis during 2 decades.

**Conclusions** The progression of pneumoconiosis was observed after the cessation of dust exposure, especially during the first 10 years.

Int Med. 49:1949, 2010.

**Key words** pneumoconiosis, coal mine, cessation, natural history, periodic medical examination

2-31



2-32

Take home messages from 2 cases

1. Pay attention to large opacity, even after diagnosis of pneumoconiosis is established.
2. Pneumoconiosis develops even after cessation of dust exposure.

Follow ups are necessary even after cessation of dust exposure.

2-33

Thank you very much for your attention.

2-34

II. 読影・症例研究編 04

〈スライド〉  
石綿肺を含むじん肺の胸部X線フィルム読影

Practice for reading films for asbestosis

Age	gender	occupational history	exposed term (years)
1) 86 years	male	insulator	31
2) 71 years	male	asbestos sprayer	12
3) 75 years	male	construction worker	29
4) 79 years	male	dismantling	20

4-01

Test trial: reading chest X-ray of pneumoconiosis including asbestosis September 17 th, 2011

Age	Gender	Occupational history	working periods (years)
5) 73 years	male	insulator	40
6) 66 years	male	asbestos sprayer	12

4-02

Practice for reading films for mesothelioma

Age	gender	occupational history	exposed term (years)
1) 54 years	male	Asbestos products	3
2) 84 years	male	Jap. naval shipyards	4
3) 74 years	male	carpenter in shipyards	10
4) 61 years	male	interior decoration	38
5) 57 years	male	wiring	27
6) 61 years	male	shipbuilding	37
7) 70 years	male	insulator	37
8) 69 years	male	pipng worker	43

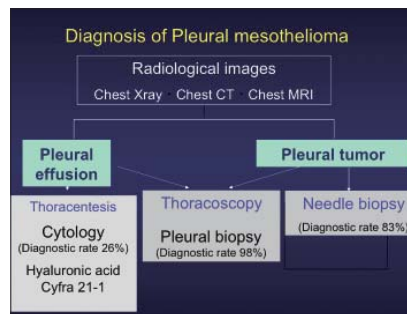
4-03

〈スライド(抄)〉  
石綿関連疾患の症例研究

### Clinical Diagnosis of Pleural Mesothelioma

Nobukazu Fujimoto  
Dept of Respiratory Medicine  
Okayama Rosai Hospital  
Okayama, Japan

5-01



5-02

### Diseases to be differentiated

- Pleural mesothelioma
- Pleural metastasis of cancer
- Tuberculous pleuritis
- Benign asbestos pleuritis

5-03

### Pleural mesothelioma

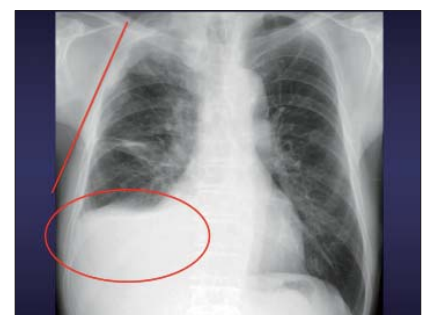
- Asbestos Exposure
- Pleural Effusion
- Hyaluronic acid
- Diagnostic Thoracoscopy
- Pemetrexed (Alimta®)

5-04

### Case 1

- 70 year-old Male
- Chief complaint:  
Dyspnea on Exertion
- Occupation: Plumbing
- Asbestos exposure (+)

5-05



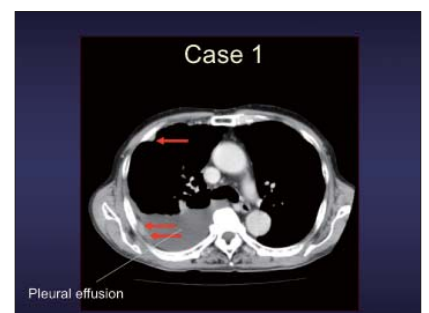
5-06



5-07



5-08



5-09

### Laboratory data

[CBC]		Chemistry	
WBC	6500 /μl	T-bil	0.6 mg/dl
Seg	47.5 %	AST	18 IU/l
Lym	41.8 %	ALT	16 IU/l
Mono	8.2 %	LDH	156 IU/l
Eos	2.0 %	γ-GT	27 IU/l
Baso	0.5 %	ALP	255 IU/ml
RBC	480 ×10 <sup>4</sup> /μl	BUN	13.3 mg/dl
Hgb	14.3 g/dl	CRE	0.63 mg/dl
Hct	43.0 %	TP	6.7 g/dl
PLT	27.3 ×10 <sup>4</sup> /μl	Alb	3.4 g/dl
		Na	142 mEq/l
		Cl	104 mEq/l
		K	4.2 mEq/l
		Ca	9.6 mg/dl
		CRP	0.6 mg/dl

5-10

### For the diagnosis

- Thoracentesis
  - Pleural effusion cytology
  - Hyaluronic acid
  - CYFRA
  - Carcinoembryonic antigen (CEA)
  - Adenosine deaminase (ADA)
- Thoracoscopy
  - Pleural biopsy

5-11

### Laboratory findings (Pleural effusion)

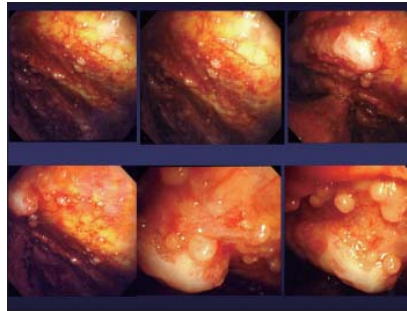
- Cytology class V malignant mesothelioma
- HA 94900 ng/ml
- ADA 28.3 U/ml
- CEA 1.0 ng/ml
- CYFRA 89.1 ng/ml

5-12





5-13



5-14

### Diagnosis

Pleural mesothelioma  
epithelioid type  
cT3N0M0 stage III

5-15

### Clinical course

- 2010.4 Thoracoscopy → Diagnosis
- 2010.5 Systemic chemotherapy  
Carboplatin + Pemetrexed  
Pemetrexed
- 2011.4 Vinorelbine
- 2011.7 Irinotecan

5-16

### Clinical course

Carboplatin [Progression bar]

Pemetrexed [Progression bar]

Vinorelbine [Progression bar]

Irinotecan [Progression bar]

2010.5      2011.4      2011.7

5-17

### Key Point

diagnostic thoracoscopy  
under local anesthesia

Enables to obtain a sufficient  
amount of tissue sample

Diagnostic rate: >90%

5-18

### Case 2

- 83 year-old Male
- Chief complaint:  
Dyspnea on Exertion
- Occupation: Pharmacist

Asbestos exposure (-)

5-19



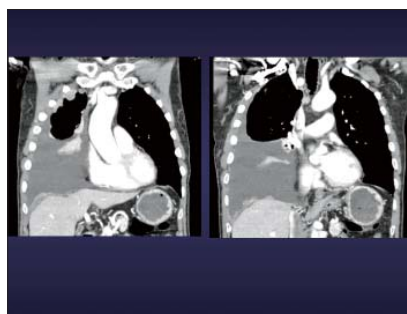
5-20



5-21



5-22



5-23

### Laboratory data

[CBC]		[Chemistry]	
WBC	5900 / $\mu$ l	T-bil	0.3 mg/dl
Seg	77.0 %	AST	22 IU/l
Lym	9.0 %	ALT	21 IU/l
Mono	8.0 %	LDH	227 IU/l
Eos	3.0 %	$\gamma$ -GT	30 IU/l
Baso	3.0 %	ALP	204 IU/ml
RBC	422 $\times 10^4/\mu$ l	BUN	13.2 mg/dl
Hgb	14.1 g/dl	CRE	1.03 mg/dl
Hct	40.6 %	TP	6.6 g/dl
PLT	19.0 $\times 10^4/\mu$ l	Alb	3.0 g/dl
		Na	142 mEq/l
		Cl	102 mEq/l
		K	3.6 mEq/l
[T-marker]		Ca	8.8 mg/dl
CEA	1.9 ng/ml	CRP	1.3 mg/dl
CYFRA	2.0 ng/ml		

5-24

### Laboratory findings (Pleural effusion)

- Cytology Class II  
reactive mesothelial cells
- Hyaluronic acid 11300 ng/ml
- ADA 15.2 U/ml
- CYFRA 40.0 ng/ml
- CEA 0.8 ng/ml

5-25

### Diagnosis

Pleural mesothelioma  
epithelioid type  
cT4N0M0 stage IV

5-26

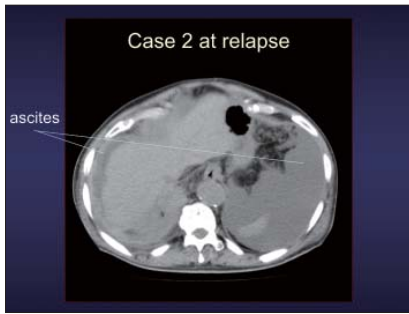
### Clinical course

Carboplatin [Progression bar]

Pemetrexed [Progression bar]

2010.1      2011.1

5-27



5-28

Key Point

**Asbestos exposure**

>80% of the patients have history of asbestos exposure

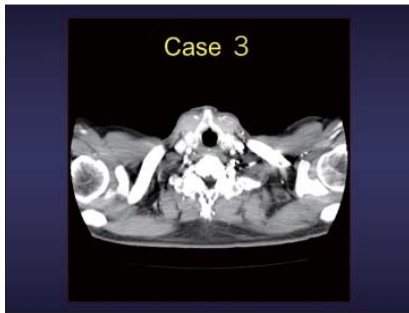
5-29

**Case 3**

- 73 year-old Male
- Chief complaint: abnormal shadow on CT
- Occupation: Chemical work

Asbestos exposure (+)

5-30



5-31



5-32



5-33

**Laboratory data**

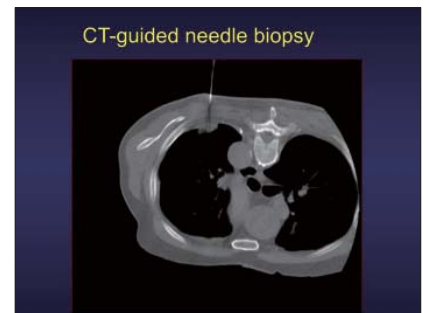
[CBC]		[Chemistry]	
WBC	64007 / $\mu$ l	T-bil	1.1 mg/dl
Seg	1.7 %	AST	25 IU/l
Lym	20.3 %	ALT	20 IU/l
Mono	5.7 %	LDH	203 IU/l
Eos	2.0 %	$\gamma$ -GT	46 IU/l
Baso	0.3 %	ALP	320 IU/ml
RBC	580 $\times 10^9/\mu$ l	BUN	12.2 mg/dl
Hgb	17.2 g/dl	CRE	0.60 mg/dl
Hct	51.1 %	TP	7.5 g/dl
PLT	21.6 $\times 10^4/\mu$ l	Alb	4.2 g/dl
		Na	140 mEq/l
		Cl	102 mEq/l
		K	4.0 mEq/l
		Ca	9.7 mg/dl
		CRP	0.8 mg/dl

5-34

**For the diagnosis**

- Thoracentesis
  - Pleural effusion cytology
  - Hyaluronic acid
  - CYFRA
  - Carcinoembryonic antigen (CEA)
  - Adenosine deaminase (ADA)
- Percutaneous needle biopsy

5-35



5-36

**Diagnosis**

Pleural mesothelioma  
biphasic type  
cT1N0M0 stage I

5-37

**Case 4**

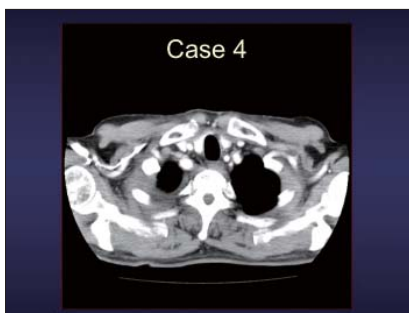
- 68 year-old Male
- Chief complaint: dyspnea on exertion
- Occupation: Shipbuilding

Asbestos exposure (+)

5-38



5-39



5-40

**Laboratory data**

[CBC]		[Chemistry]	
WBC	93007 / $\mu$ l	T-bil	1.7 mg/dl
Seg	8.1 %	AST	17 IU/l
Lym	14.2 %	ALT	14 IU/l
Mono	6.9 %	LDH	174 IU/l
Eos	0.5 %	$\gamma$ -GT	23 IU/l
Baso	0.3 %	ALP	253 IU/ml
RBC	503 $\times 10^9/\mu$ l	BUN	12.4 mg/dl
Hgb	15.4 g/dl	CRE	0.76 mg/dl
Hct	45.2 %	TP	7.8 g/dl
PLT	31.3 $\times 10^4/\mu$ l	Alb	4.2 g/dl
		Na	138 mEq/l
		Cl	99 mEq/l
		K	3.7 mEq/l
		Ca	9.4 mg/dl
		CRP	3.9 mg/dl

5-41

**Laboratory findings (Pleural effusion)**

- Cytology : class V strongly suspicious of malignant mesothelioma
- HA 23600 ng/ml
- ADA 13.6 U/ml
- CYFRA 70.0 ng/ml

5-42

### Diagnosis

Pleural mesothelioma  
biphasic type  
cT1bN0M0 stage IB

5-43

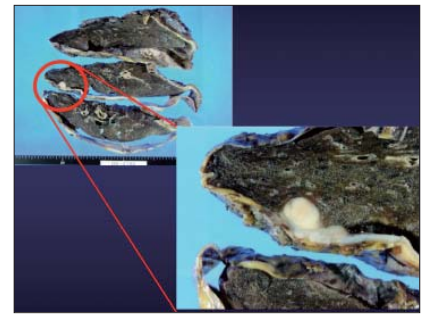
### Clinical course

Surgery (extrapleurectomy)

Cisplatin  
Pemetrexed

2009.9 → 2010.8

5-44



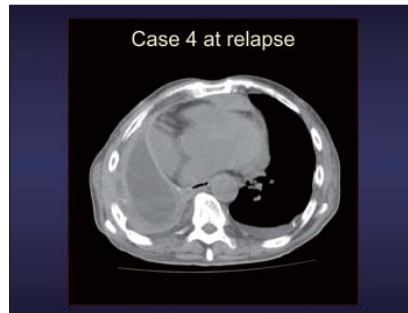
5-45

### Key Point

Cytology (pleural effusion)

Diagnosis is given in  
< 30% of the cases

5-46



5-47

### Case 5

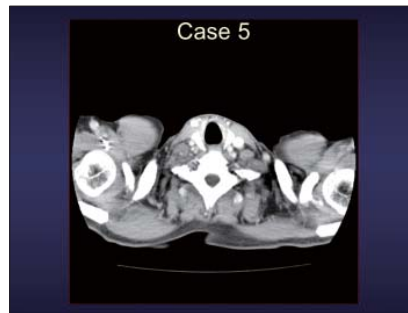
- 60 year-old male
- Chief complaint: chest pain
- Occupation: Asbestos products manufacturing

Asbestos exposure (+)

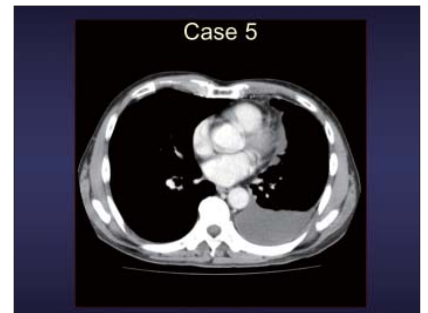
5-48



5-49



5-50



5-51



5-52



5-53

### Laboratory data

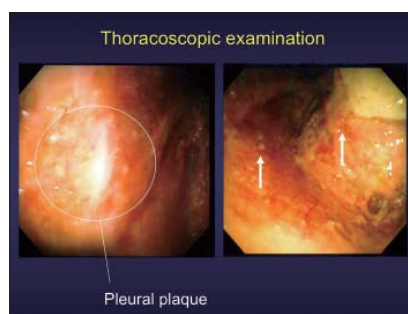
[CBC]		[Chemistry]	
WBC	7300 /μl	T-bil	0.9 mg/dl
Seg	81.9 %	AST	21 IU/l
Lym	11.3 %	ALT	20 IU/l
Mono	3.9 %	LDH	167 IU/l
Eos	2.6 %	γ-GT	14 IU/l
Baso	0.3 %	ALP	259 IU/l
RBC	481 ×10 <sup>4</sup> /μl	BUN	11.2 mg/dl
Hgb	14.7 g/dl	CRE	0.80 mg/dl
Hct	42.7 %	TP	7.5 g/dl
PLT	18.1 ×10 <sup>4</sup> /μl	Alb	3.8 g/dl
		Na	138 mEq/l
		Cl	98 mEq/l
[T-marker]		K	4.3 mEq/l
CEA	1.2 ng/ml	Ca	8.8 mg/dl
CYFRA	8.3 ng/ml	CRP	0.8 mg/dl

5-54

### Laboratory findings (Pleural effusion)

- Cytology : class V  
strongly suspicious of malignant mesothelioma
- Hyaluronic acid 895000 ng/ml
- ADA 45.1 U/ml
- CEA 1.5 ng/ml

5-55

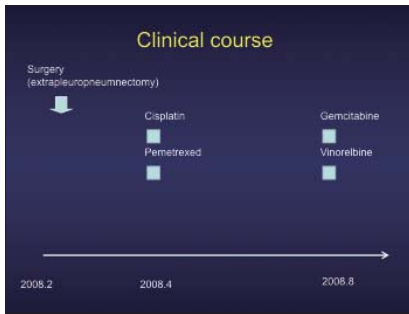


5-56

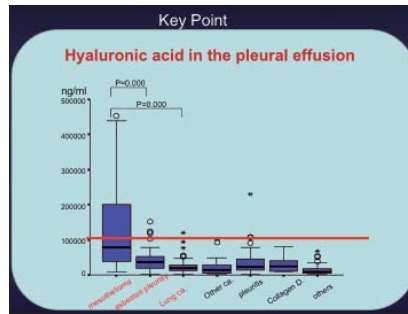
### Diagnosis

Pleural mesothelioma  
epithelioid type  
cT1aN0M0 stage IA

5-57



5-58



5-59

### Case 6

- 62 year-old male
- Chief complaint: Cough
- Occupation: heat insulation work

Asbestos exposure (+)

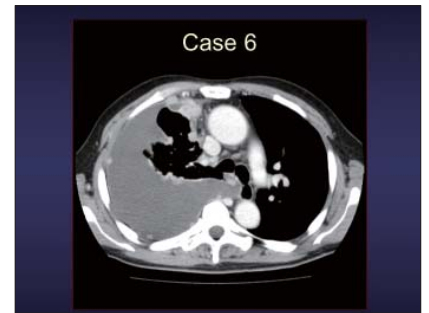
5-60



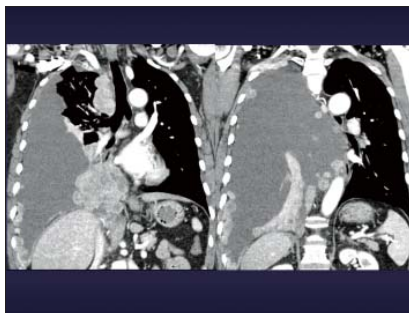
5-61



5-62



5-63



5-64

### Laboratory data

[CBC]		[Chemistry]	
WBC	9400 / $\mu$ l	T-bil	0.3 mg/dl
Seg	72.3 %	AST	23 IU/l
Lym	16.5 %	ALT	37 IU/l
Mono	9.7 %	LDH	177 IU/l
Eos	1.3 %	$\gamma$ -GT	72 IU/l
Baso	0.2 %	ALP	310 IU/ml
RBC	499 $\times 10^4/\mu$ l	BUN	8.9 mg/dl
Hgb	15.0 g/dl	CRE	0.87 mg/dl
Hct	44.9 %	TP	5.5 g/dl
PLT	36.6 $\times 10^4/\mu$ l	Aib	2.3 g/dl
		Na	141 mEq/l
		Cl	104 mEq/l
		K	5.0 mEq/l
		Ca	8.4 mg/dl
		CRP	5.7 mg/dl

5-65

### Laboratory findings (Pleural effusion)

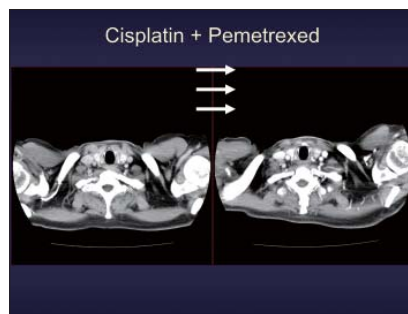
- Cytology: class IV: highly suspicious of malignant mesothelioma
- Hyaluronic acid      79300 ng/ml
- ADA 13.3 U/ml
- CYFRA 16.4 ng/ml
- CEA 0.8 ng/ml

5-66

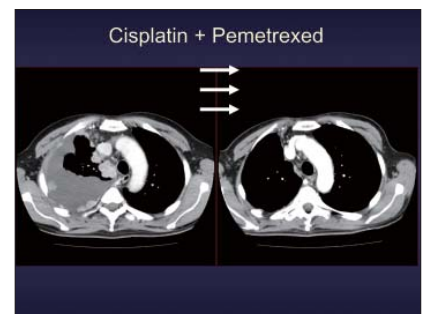
### Diagnosis

Pleural mesothelioma  
epithelioid type  
cT4N0M0 stage IV

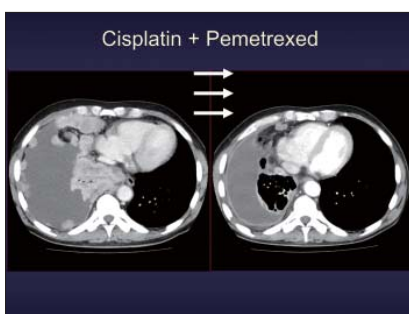
5-67



5-68



5-69



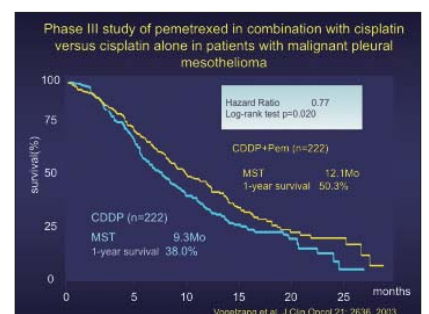
5-70

### Key Point

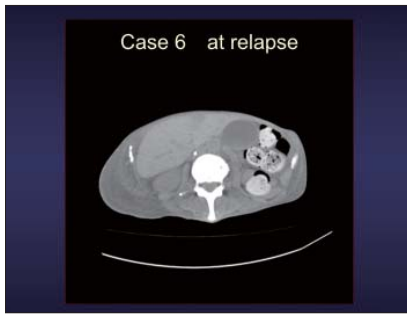
chemotherapy

Cisplatin (or Carboplatin)  
+  
Pemetrexed (Alimta®)

5-71



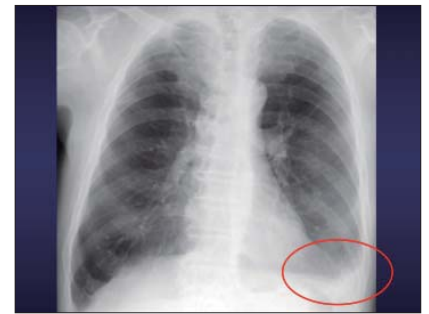
5-72



5-73

**Case 7**  
 73 year-old male  
 Chief complaint :  
 abnormal shadow of the chest  
 Occupation :  
 construction industry  
 Asbestos exposure (+)

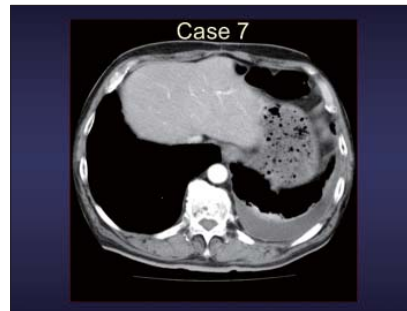
5-74



5-75



5-76



5-77

**Laboratory data**

[CBC]		[Chemistry]	
WBC	5500 / $\mu$ l	T-bil	0.3 mg/dl
Seg	76.3 %	AST	19 IU/l
Lym	16.3 %	ALT	17 IU/l
Mono	5.3 %	LDH	138 IU/l
Eos	1.6 %	$\gamma$ -GT	37 IU/l
Baso	0.5 %	ALP	366 IU/ml
RBC	454 $\times 10^4/\mu$ l	BUN	12.9 mg/dl
Hgb	14.5 g/dl	CRE	0.67 mg/dl
Hct	40.7 %	TP	7.4 g/dl
PLT	22.9 $\times 10^4/\mu$ l	Alb	3.6 g/dl
		Na	129 mEq/l
[T-marker]		Cl	92 mEq/l
CEA	N.D. ng/ml	K	4.4 mEq/l
CYFRA	N.D. ng/ml	Ca	9.3 mg/dl
		CRP	0.8 mg/dl

5-78

**Laboratory findings (Pleural effusion)**

- Cytology: class II
- Hyaluronic acid 55600 ng/ml
- ADA 17.7 U/ml
- CYFRA 28.7 ng/ml
- CEA 3.1 ng/ml

5-79

**Diagnosis**  
 Benign asbestos pleurisy  
 (Asbestos Pleuritis)

5-80

**Key Point**  
 Benign asbestos pleurisy  
 (asbestos pleuritis)  
 History of asbestos exposure  
 Pleural Effusion  
 No other cause of pleural effusion  
 No malignancy for 3 years (1 year)

5-81

**Case 8**

- 74 year-old male
- Chief complaint: Dyspnea
- Occupation: Construction

Asbestos exposure (+)

5-82



5-83



5-84

**Laboratory data**

[CBC]		[Chemistry]	
WBC	7800 / $\mu$ l	T-bil	0.6 mg/dl
Seg	65.3 %	AST	39 IU/l
Lym	25.0 %	ALT	25 IU/l
Mono	5.9 %	LDH	215 IU/l
Eos	3.5 %	$\gamma$ -GT	27 IU/l
Baso	0.3 %	ALP	255 IU/ml
RBC	431 $\times 10^4/\mu$ l	BUN	13.3 mg/dl
Hgb	15.5 g/dl	CRE	0.63 mg/dl
Hct	45.5 %	TP	6.7 g/dl
PLT	21.8 $\times 10^4/\mu$ l	Alb	3.4 g/dl
		Na	142 mEq/l
[T-marker]		Cl	105 mEq/l
CEA	3.7 ng/ml	K	4.2 mEq/l
CYFRA	1.2 ng/ml	Ca	9.3 mg/dl
		CRP	2.1 mg/dl

5-85

**Laboratory findings (Pleural effusion)**

- Cytology: class V: adenocarcinoma
- Hyaluronic acid 6330 ng/ml
- ADA 24.4 U/ml
- CYFRA 14.5 ng/ml
- CEA 2.6 ng/ml

5-86

**Immunohistochemistry**

- TTF-1 (+)
- CEA (-)
- Calretinin (-)
- CK AE1/3 (+)

5-87

## Diagnosis

Adenocarcinoma of the lung  
(asbestos related lung cancer)

5-88

## Immunohistochemical analysis for the differentiation of mesothelioma

	Mesothelioma (epithelioid)	Adenocarcinoma of the lung
Calretinin	100	8
Cytokeratin 5/6	100	2
WT1	93	0
D2-40	96	27
Mesothelin	100	38
N-cadherin	73	30
MOC-31	8	100
E-cadherin	40	88
TTF-1	0	74
CEA	0	88
Leu-M1(CD15)	0	72
Ber-EP4	18	100
EMA	93	100
Vimentin	55	38 (%)

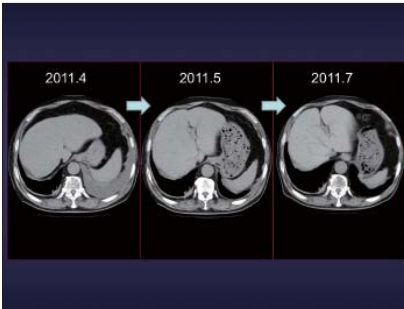
Ordones NG and Kushlani

5-89

## Systemic chemotherapy

- Carboplatin
- Pemetrexed
- Bevacitumab

5-90

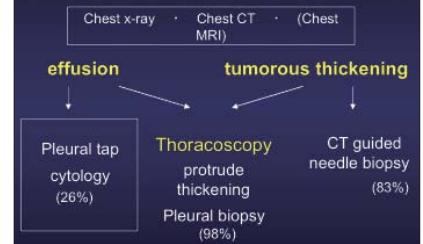


5-91

## Summary

5-92

## Diagnostic procedure for pleural mesothelioma



5-93

## Pleural mesothelioma

- Asbestos Exposure
- Pleural Effusion
- Hyaluronic acid
- Diagnostic Thoracoscopy
- Pemetrexed (Alimta®)

5-94

Thank you for your attention.



5-95