LUNG CANCER

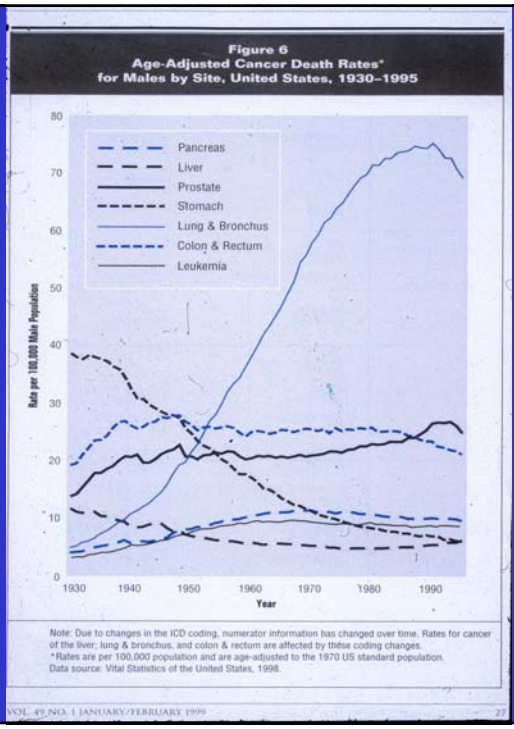
1. Etiology
2. Pathology
3. Manifestations
4. Therapy
5. Epidemiology

LUNG CANCER

Number of cases/year in U.S. approaches 200,000

Five year survival low – 10-15%

Commonest cause of cancer death in men and women



LUNG CANCER

ETIOLOGY

Cigarette smoking causes 90% of cases

Evidence is of two types:

1. Epidemiological
2. Experimental

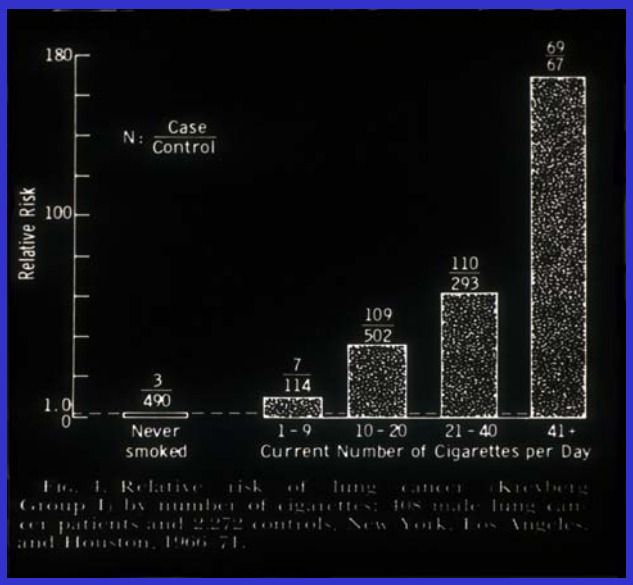


FIG. 1. Relative risk of lung cancer (Kreyberg Group I) by number of cigarettes: 105 male lung cancer patients and 2,272 controls, New York, Los Angeles, and Houston, 1966-71.

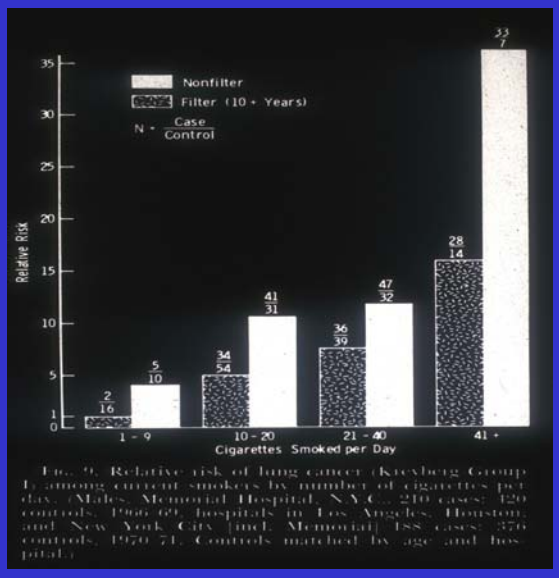


FIG. 9. Relative risk of lung cancer (Kreyberg Group I) among current smokers by number of cigarettes per day. (Males: Memorial Hospital, N.Y.C., 210 cases; 120 controls, 1966-69; hospitals in Los Angeles, Houston, and New York City [incl. Memorial], 188 cases; 376 controls, 1970-71. Controls matched by age and hospital.)

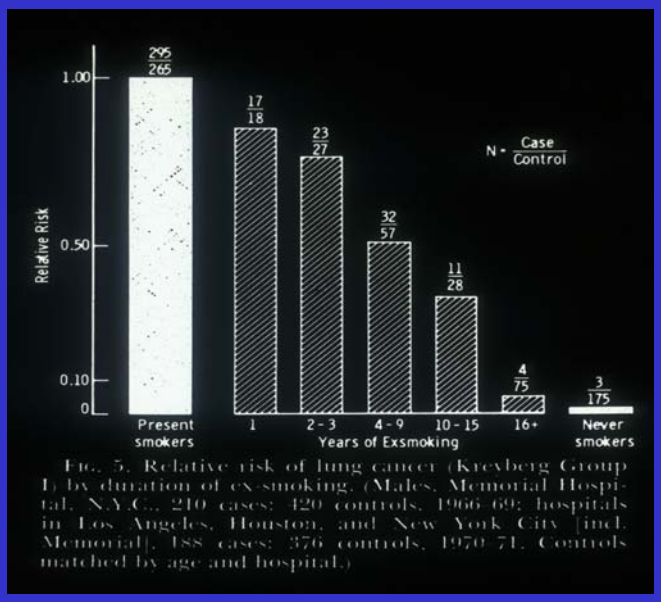


FIG. 5. Relative risk of lung cancer (Kreyberg Group I) by duration of ex-smoking. (Males, Memorial Hospital, N.Y.C., 210 cases; 420 controls, 1966–69; hospitals in Los Angeles, Houston, and New York City [incl. Memorial], 188 cases; 376 controls, 1970–71. Controls matched by age and hospital.)

Table 2. Major Toxic Agents in the Gas Phase of Cigarette Smoke (Unaged).*

Agent	Biologic Activity†	Concentration/Cigarette	
		Range Reported	US Cigarettes‡
Dimethylnitrosamine	C	1–200 ng	13 ng
Ethylmethylnitrosamine	C	0.1–10 ng	1.8 ng
Diethylnitrosamine	C	0–10 ng	1.5 ng
Nitrosopyrrolidine	C	2–42 ng	11 ng
Other nitrosamines (4 compounds)	C	0–20 ng	?
Hydrazine	C	24–43 ng	32 ng
Vinyl chloride	C	1–16 ng	12 ng
Urethane	TI	10–35 ng	30 ng
Formaldehyde	CT, CoC	20–90 μg	30 μg
Hydrogen cyanide	CT, T	30–200 μg	110 μg
Acrolein	CT	25–140 μg	70 μg
Acetaldehyde	CT	18–1,400 μg	800 μg
Nitrogen oxides (NO_x)§	T	10–600 μg	350 μg
Ammonia	T?¶	10–150 μg	60 μg
Pyridine	T?¶	9–93 μg	10 μg
Carbon monoxide	T	2–20 mg	17 mg

*Cigarettes may also contain such carcinogens as arsine, nickel carbonyl & possibly volatile chlorinated olefins and nitro-olefins.

†C denotes carcinogen, BC bladder carcinogen, TI tumor initiator, CoC cocarcinogen, CT cilia toxic agent, & T toxic agent.

‡85-mm cigarettes without filter tips bought on the open market 1973–1976.

§NO_x >95% NO; rest NO_2.

¶Not toxic in smoke of blended US cigarettes because pH <6.5, & therefore ammonia & pyridines are present only in protonated form.

LUNG CANCER

ETIOLOGY

Passive cigarette smoke

Associated with a small increased risk

Table 1. Odds ratios of lung cancer for various categories of tobacco use among ever smokers, adjusted for age and study center

Category of tobacco use*	No. of case patients	No. of control subjects	Odds ratio	95% confidence interval
Nonsmokers	117	1750	1.0	Referent
Cigars, pure smokers	16	42	5.6	2.9–10.6
Cigarillos, pure smokers	21	31	12.7	6.9–23.7
Cigars and cigarillos, pure smokers†	43	77	9.0	5.8–14.1
Pipe, pure smokers	61	129	7.9	5.3–11.8
Cigarettes, pure smokers	4204	3930	14.9	12.3–18.1
Mixed smokers‡	1182	1309	12.7	10.3–15.6

*Pure smokers are those considered to smoke only one type or category of tobacco product; mixed smokers are those who used cigarettes and cigars, cigarillos, or pipe tobacco.

†Combines pure smokers of cigars, pure smokers of cigarillos, and smokers of both cigars and cigarillos but not cigarettes or pipe tobacco.

‡Excludes 14 case patients and 60 control subjects who smoked cigars, cigarillos, and pipe tobacco but not cigarettes.

Journal of the National Cancer Institute, Vol. 91, No. 8, April 21, 1999

LUNG CANCER

ETIOLOGY

1. Asbestos
2. Radiation
3. Chemicals
   - chromium
   - benzpyrene
   - chloro-methyl-methyl ether

LUNG CANCER

ETIOLOGY

Asbestos

1. Long latent period
2. Brief exposures
3. Indirect (low level) exposures
4. Multiplied risk in cigarette smokers (synergistic effect)

LUNG CANCER

ETIOLOGY

Radiation

1. Uranium miners
   – synergistic interaction with cigarette smoking

2. Radon in homes
   – controversial, degree of risk (if any) debated

LUNG CANCER

PATHOGENESIS

Genetic Abnormalities

1. Deletion 3p
2. Mutations p53
3. Mutations *k-ras*

LUNG CANCER

PATHOLOGY

I. Non-small Cell Lung Carcinoma - 70-75%

1. Squamous (epidermoid)
2. Adenocarcinoma
3. Large cell

II. Small Cell Lung Carcinoma - 20-25%

III. Combined Patterns - 5 - 10%

LUNG CANCER

CLINICAL FEATURES

1. Growth at primary site
2. Metastatic spread
3. Paraneoplastic (remote) effects

LUNG CANCER

MANIFESTATIONS OF LOCAL TUMOR GROWTH

1. Hemoptysis – ulceration of tumor
2. Cough – stimulation of nerve endings
3. Wheezing – partial airway obstruction
4. Pneumonia – airway obstruction
5. Atelectasis – airway obstruction

LUNG CANCER

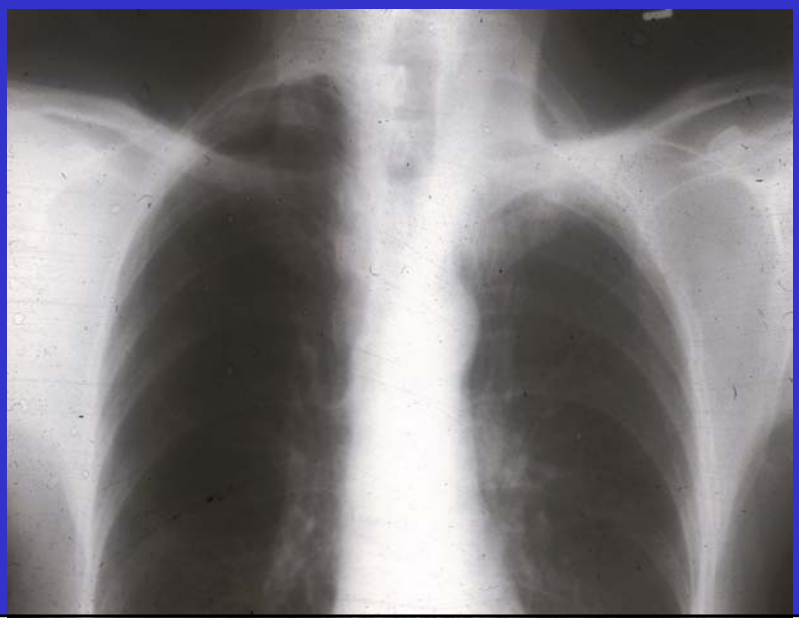
METASTATIC SPREAD

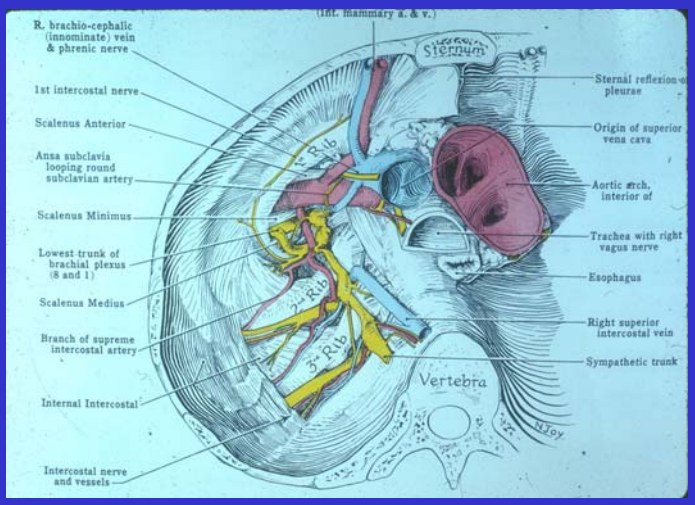
1. Direct extension
2. Lymphatic channels
3. Hematogenously

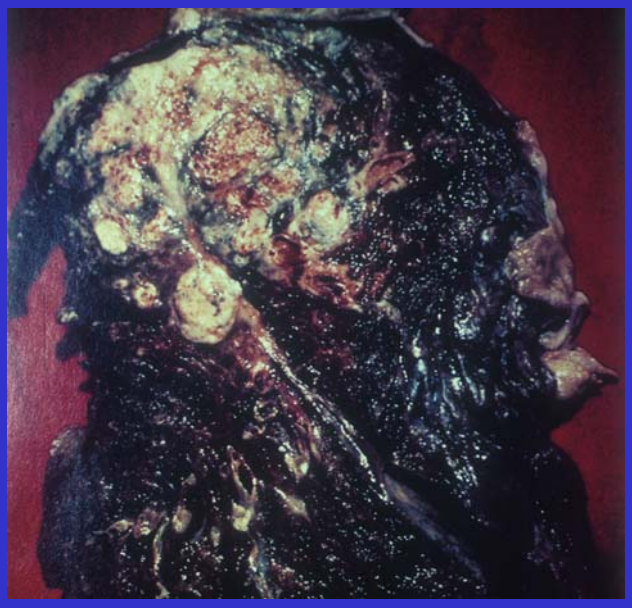
LUNG CANCER

DIRECT EXTENSION

1. Neurological structures
2. Pericardium
3. Pleura
4. Esophagus
5. Chest wall
6. Vertebral column



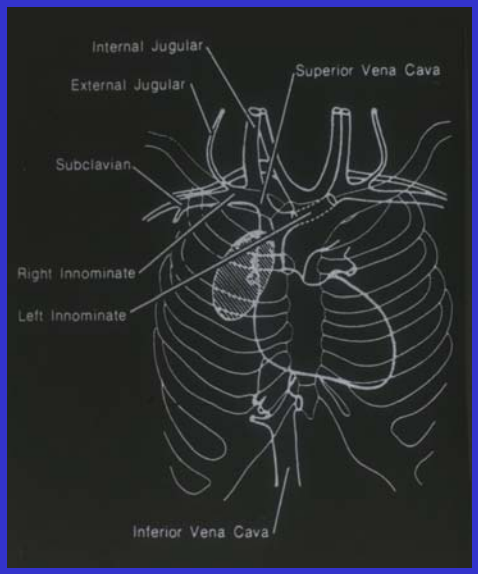

(Int. mammary a. & v.)
R. brachio-cephalic (innominate) vein & phrenic nerve
1st intercostal nerve
Scalenus Anterior
Ansa subclavia looping round subclavian artery
Scalenus Minimus
Lowest trunk of brachial plexus (8 and 1)
Scalenus Medius
Branch of supreme intercostal artery
Internal Intercostal
Intercostal nerve and vessels
Sternum
1st Rib
2nd Rib
3rd Rib
Vertebra
Sternal reflexion of pleurae
Origin of superior vena cava
Aortic arch, interior of
Trachea with right vagus nerve
Esophagus
Right superior intercostal vein
Sympathetic trunk



LUNG CANCER

LYMPH NODE METASTASES

1. Hilar
2. Ipsilateral mediastinal
3. Contralateral mediastinal



SUPERIOR VENA CAVA COMPRESSION

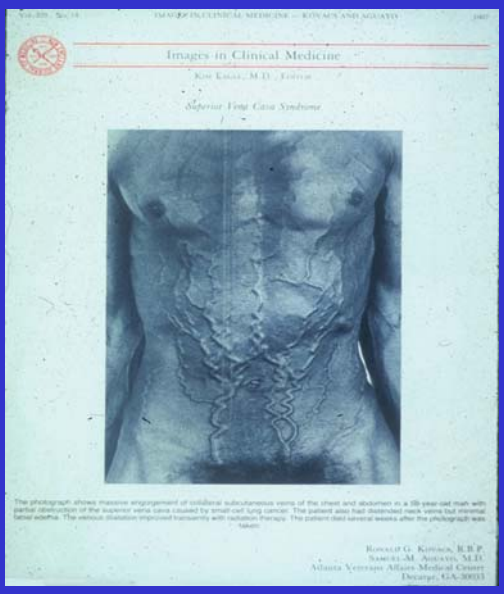
SYMPTOMS

1. Swelling of the face
2. Swelling of the arms
3. Shortness of breath
4. Cough

SUPERIOR VENA CAVA COMPRESSION

SIGNS

1. Distention of jugular veins
2. Distention of veins over shoulders, chest wall, upper abdomen
3. Edema of the face
4. Plethora of the face
5. Congestion of retina
6. Edema of arms, hands

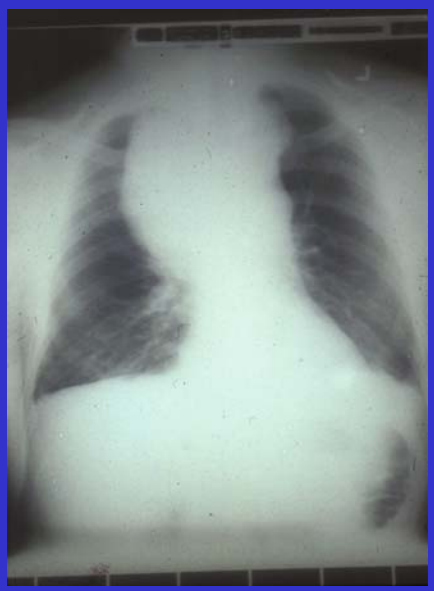


Images in Clinical Medicine

Superior Vena Cava Syndrome

The photograph shows massive engorgement of collateral subcutaneous veins of the chest and abdomen in a 59-year-old man with partial obstruction of the superior vena cava caused by small-cell lung cancer. The patient also had distended neck veins but minimal facial edema. The venous dilation improved transiently with radiation therapy. The patient died several weeks after the photograph was taken.

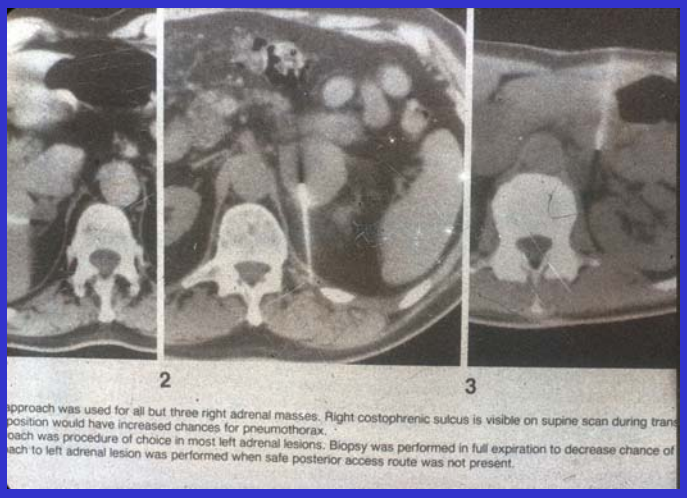
Ronald G. Kitnick, R.R.T.
Samuel M. Adams, M.D.
Atlanta Veterans Affairs Medical Center
Decatur, GA 30033



LUNG CANCER

SYSTEMIC METASTASES

1. Lungs
2. Liver
3. Bones
4. Adrenal glands



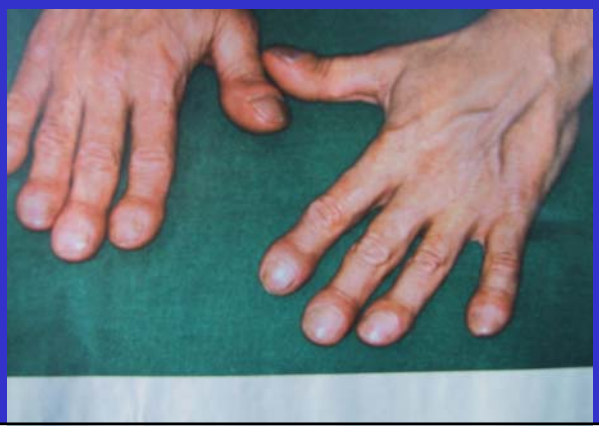
LUNG CANCER

PARANEOPLASTIC (REMOTE) EFFECTS

1. Cushing's syndrome (Ectopic ACTH)
   - small cell lung cancer
2. Syndrome of inappropriate ADH secretion
   - small cell lung cancer
3. Eaton-Lambert syndrome
   - small cell lung cancer
4. Hypercalcemia – PTHrP
   - non-small cell lung cancer
5. Pulmonary osteoarthropathy
   - non-small cell lung cancer

LUNG CANCER

Finger Clubbing



LUNG CANCER

THERAPY

Non-Small Cell Lung Cancer

1. Surgery
2. Radiation therapy
3. Chemotherapy

LUNG CANCER

THERAPY

Small Cell Lung Cancer

1. Chemotherapy
2. Radiation therapy
3. Surgery

LUNG CANCER

THERAPY

Non-Small Cell Lung Cancer

1. Surgery
2. Radiation Therapy
3. Chemotherapy

LUNG CANCER

THERAPY

Small Cell Lung Cancer

1. Rapidly proliferating cells

2. Systemic metastases have developed by time the primary lesion presents