NEXT GENERATION LEARNING

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USCAP
Creating a Better Pathologist
TIME TRAVELLING TO THE ORIGINS OF LUNG CANCER

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Dr. Anthony A. Gal declares he has no conflicts of interest to disclose.

Please turn off your cell phone: thank you!
LUNG CANCER IN THE EARLY 21st C

• Global epidemic
• Most common cause of cancer-related death in M & F
• Survival stage and histology dependent
• Majority (~80%) related to cigarette smoking
TIME TRAVELING

• Charles Dickens: A Christmas Carol (1843)
• H.G. Wells: The Time Machine (1895)
• Star Trek (1966–1969)
  30 Episodes (1966–7)
  Irwin Allen, Producer

http://www.imdb.com/title/tt0060036/
Project Tic-Toc

“Two American scientists are lost in the swirling maze of past and future ages, during the first experiments on America's greatest and most secret project, the Time Tunnel. Tony Newman and Doug Phillips now tumble helplessly toward a new fantastic adventure, somewhere along the infinite corridors of time.”
MID 20th C

52% men and 35% women cigarette smokers
Targeted markets: Virginia Slims (1970's) & Menthols (1960's)

especially for women because they are biologically superior to men.

That's right, superior. Women are more resistant to starvation, fatigue, exposure, shock, and illness than men are.

Women have two "X" chromosomes in their sex cells, while men have only one "X" chromosome and a "Y" chromosome...which some experts consider to be the inferior chromosome.

They are also less inclined than men to congenital blemishes, Allergies of the eyes, improperly developed sweat glands, color blindness of...

Virginia Slims.

Slimmer than the fat cigarettes men smoke. With rich Virginia has women like...

You've come a long way, baby.
Oscar Auerbach’s “Smoking Beagles” (1967-1970)

Changes in the Bronchial Epithelium in Relation to Smoking and Cancer of the Lung

Oscar Auerbach, M.D., J. Brewster Gere, M.D., Jerome B. Forman, M.D., Thomas G. Petrick, M.D., Harold J. Smolin, Ph.D., Gerald E. Muehsam, M.D., Dicran Y. Kassouny, M.D., and Arthur Purdy Stout, M.D.
US Surgeon General Smoking and Health (1964)

Luther Terry, M.D.
Epidemiological studies linking smoking to lung cancer (1950’s)

TOBACCO SMOKING AS A POSSIBLE ETIOLOGIC FACTOR IN BRONCHIOGENIC CARCINOMA
A Study of Six Hundred and Eighty-Four Proved Cases

ERNEST L. WYNDER
and
EVARTS A. GRAHAM, M.D.
St. Louis

BRITISH MEDICAL JOURNAL
LONDON SATURDAY SEPTEMBER 30 1950

SMOKING AND CARCINOMA OF THE LUNG
PRELIMINARY REPORT

BY
RICHARD DOLL, M.D., M.R.C.P.
Member of the Statistical Research Unit of the Medical Research Council

AND
A. ERADFORD HILL, Ph.D., D.Sc.
Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council
• Highest consumption of cigarettes
• Mass marketing, advertising, sponsorship
• Cigarette smoking & lung cancer [Oshner/Debakey (1939)]
Nazi anti-smoking campaign
INTERWAR YEARS

• Increasing tobacco consumption
• Cigarette advertising and sponsorship
• German autopsies: more cases of lung cancer
• Small cell carcinoma [Barnard (1926)]
• 1st histological classification [Marchesani (1924)]
ETIOLOGIES OF LUNG CANCER IN EARLY 20th C.

Industrial and occupational exposure
- Air pollution
- Benzene
- Arsenic
- Nickel
- Chromium
- Asbestos

Automobile related:
- Motor vehicle exhaust
- Asphalt
- Tarred-roads

Latent exposure from toxic gas injury during WW I

Chronic irritation following 1918-9 influenza pandemic
WW I

• “Doughboys” tobacco rations
• Cigarettes given by philanthropic organizations
Seductive and Romantic Advertising

EGYPTIENNE LUXURY Cigarettes

CORK TIP

Convincingly Mild

MURAD

Turkish Cigarettes contain no artificial flavoring and are therefore purer and better than other kinds of cigarettes. Murads are made only of 100% Pure Turkish Tobacco of the finest varieties grown, and are appreciated and desired by smokers who demand the best the world has to offer in cigarettes.

CIGARETTES XANTHIA

20c "Judge for Yourself —"
ISAAC ADLER, M.D. (1849-1918)

- *Primary Malignant Growths of the Lungs: a Pathological and Clinical Study* (1912)
- First book dedicated to lung cancer
- “Among the rarest form of disease”
- Suggested a link between cigarette smoking & lung ca
PRIMARY MALIGNANT GROWTHS OF THE LUNGS AND BRONCHI

A PATHOLOGICAL AND CLINICAL STUDY

BY

I. ADLER, A.M., M.D.,

Professor Emeritus at the New York Polyclinic, Consulting Physician to the German, Beth Israel, Hnt Moriah, and Peoples Hospitals, and Montefiore Home and Hospital

‘Oportet omnia sigin contemplari’

LONGMANS, GREEN, AND CO.
FOURTH AVENUE & 30TH STREET, NEW YORK
LONDON, BOMBAY, AND CALCUTTA
1912
TURN OF THE CENTURY

- Extremely rare: 140 cases [M. Kaminsky (1898)]
- “Polite smoking”
- Decline in pipe smoking
Radiography (Roentgen 1895)
Rigid bronchoscopy (Killian 1895)
Bonsack Cigarette Rolling Machine (1880)
American Tobacco Company
(1890-1994)

• James B. Duke (1859-1924)
• 90% of cigarettes
• 1911: Dissolved into 4 companies
MID 19th C

- Johannes Müller / Carl von Rokitansky / Rudolf Virchov
- TB vs. lung cancer: very difficult to separate
- “Growths” arose in lymph nodes
  - Invaded into bronchi
  - Cicatric, sclerosing, ulcerating
  - Encephaloid, lymphosarcoma, sarcoma primitif
Encephaloid carcinoma of the lung.
Cornil V, Ranvier L
A Manual of Pathological Histology,
Philadelphia, Henry C Lea. 1880, p. 429
EARLY 19th C

• Papelate via Spain

• Cigarette: Honoré de Balzac (Œuvres diverses, 1831)

• René-Théophile-Hyacinthe Laënnec (1781-1826)
  • Encéphaloïdes du poumon (1815)

• Gaspard Laurent Bayle (1774-1816)
  • Phthisie cancéreuse (1810)
Percival Pott (1714 -1788): scrotal cancer in chimney sweeps (1775)

Giovanni Morgagni (1682 -1771): *Ulcus cancrosum* (1761)

Bernadino Ramazini (1633 - 1714): *De Morbis Artificum Diatriba* [Diseases of Workers] (1700, 1713)
16th C

• “Everything comes from the mine" (Alles kommt vom Bergwerk her)

• Ore Mountains (Erzgebirge / Krušné hory)

• https://www.youtube.com/watch?v=sF_qovuATZw

• Rich in ores
  • Silver
  • Iron
  • Pitcheblende
Fatal pulmonary disease in miners

Mountain Disease

Bergsucht

Schneeberger Bergkrankheit

“Marry early & leave when they die in their early 40’s a large number of children”
GEORGIUS AGRICOLA (1494—1555)
GEORGIUS AGRICOLA (1494—1555)

• “Father of mineralogy”
• Town physician in St. Joachimsthal /Jáchymov (1527-1533)
• Joachimsthaler coins ➔ taler ➔ dollar
• Observed numerous diseases in miners
DE RE RE METALLICA (1556)
DE RE RE METALLICA (1556)

• 12 volumes: mining and metallurgy
• 270 woodcut images
• Described many diseases of the miners (Vol VI)
  • “Death pits”
  • “An angel choking old miners to death”
  • “If the dust has corrosive qualities, it eats away the lungs”
  • “Women have married 7 husbands….carried off to a premature death”
WHAT IS THIS MINERS’ DISEASE?

- Lung Cancer
- Tuberculosis
- Silicosis
- Mesothelioma
- Toxic fume-related injury
- Others / Combinations
Der Lungenkrebs, die Bergkrankheit in den Schneeberger Gruben.

Von

Bergarzt Dr. F. H. Härtling in Schneeberg

und

Bezirksarzt Dr. W. Hesse in Schwarzenberg.

Vierteljahresschrift für gerichtliche Medicin und öffentliches Sanitätswesen
New Folge 30 (1879) 296-309, 31 (1879) 102-132, 31 (1879) 312-337
ORE MINERS & LUNG CANCER

• Autopsies of miners & pathology reviewed at Pathological-Anatomical Institute @ Leipzig University
• “Lymphosarcoma” & “endothelial” carcinoma
• The endemic lung disease is lung cancer
• Responsible for 75% of deaths in miners
RADIATION CONNECTION

• Radioactivity: Henri Becquerel (1896)

• Erzgebirge pitcheblende ore rich in uranium, polonium, and radium
  • Pierre and Marie Curie (1898)

• Radon gas: Friedrich Ernst Dorn (1900)

• $^{238}U \rightarrow ^{226}Ra \rightarrow ^{222}Rn$

• Connection between radon and lung ca [Rajewsky (1939)]
RADIATION–RELATED LUNG CANCER

• USPHS: radiation studies in Colorado Miners (1949)
• Hiroshima Tumor Registry [Harada & Ishida (1960)]
• Geno Saccomanno (1915-1999) lung cancer in uranium miners (1960’s)
• Waggoner: NEJM Article (1965)

…..”excessive occurrence of respiratory cancer among uranium miners as well as a dose-response relation between airborne radiation and the incidence of respiratory neoplasia.”

• Radon-222 carcinogenic (International Agency for Research)
• Cancer WHO International Radon Project (2005)
CONCLUSIONS

• Lung cancer has been part of humanity
• Masked by other diseases
• Clues to pathogenesis in 16th C, but not until past 100 years
• 19th-21st C tobacco consumption
• Lung cancers in non-smokers
IN THE FUTURE
“Mission Possible”

• Next generation of pathologists and other time travelers
REFERENCES


Morgagni GB. De Sedibus, et Causis Morborum per Anatomen Indagatis. Venice: Typographia Remondini; 1761.


MOC Questions

1. The seminal paper by FH Härting and W Hesse (1879) showed:
   a. A link between atomic bomb blasts and lung cancer
   b. A link between mining and lung cancer
   c. A link between chimney sweeps and scrotal cancer
   d. A link between snuff and nasal cancer
   e. A link between asbestos and malignant mesothelioma

   Answer:
   b. A link between mining and lung cancer

   Their study showed that the endemic disease of miners was lung cancer, accounting for 75% of deaths.


2. In the 1920's which of the following was not considered to be a risk factor for lung cancer?
   a. Second hand smoking
   b. Air pollution
   c. Toxic gas injury during WW I
   d. Motor vehicle exhaust
   e. Post-influenza irritation

   Answer:
   a. Second hand smoking

   Although direct smoking of cigarettes was proposed as a potential etiology by Isaac Adler in 1912, the concept of second hand smoking as carcinogenic was proposed in the last quarter of the 20th C.

   REF:

3. The association between radon gas and lung cancer was first suggested in which century?
   a. 16th C.
   b. 17th C.
   c. 18th C.
   d. 19th C.
   e. 20st C.
e: 20th C.
Radon gas was discovered by Friedrich Ernst Dorn in 1900. The first to propose the link between lung cancer and radon gas was by Boris Rajewsky in 1939.

REF:

4. Which famous French author introduced the term cigarette?
   a. Marcel Proust

   ![Marcel Proust](image1)

   b. Alexandre Dumas

   ![Alexandre Dumas](image2)

   c. Victor Hugo

   ![Victor Hugo](image3)

   d. Honoré de Balzac

   ![Honoré de Balzac](image4)
Answer:

d: Honoré de Balzac introduced the term "cigarette" in 1831.

REF: Balzac H, Œuvres diverses., t. 2, p. 441, 1831 (Le Trésor de la Langue Française Informatisé)