"Breathing is truly a strange phenomenon of life, caught midway between the conscious and unconscious and peculiarly sensitive to both."

Dickenson Richards, M.D.
Columbia University College of Physicians and Surgeons
Nobel Laureate in Medicine, 1956

Roses are red,
Violets are blue;
Without your lungs,
Your blood would be, too

Goals and objectives for the pulmonary section: I

- Understand important categories and causes of lung disease in the United States and around the world
- Understand lung mechanics in health and disease
  - Lung mechanics (determination of efficiency of ventilation)
    - Work of breathing
    - Compliance
      - $\Delta V/\Delta P$
    - Resistance
      - P_{alv}-P_{mouth}/ flow
    - PEEP and Auto-PEEP

Goals and objectives for the pulmonary section: II

- Understand gas exchange in health and disease
  - Alveolar air equation and calculation of alveolar-arterial (A-a) gradient
    - $P_AO_2 = P_IO_2 - (PCO_2/R)$
  - Oxygen delivery to tissues
    - Oxyhemoglobin dissociation curve
    - $DO2 = CO \times CaO_2$
    - $CaO2 = ([Hgb] \times 1.39 \times \%sat) + (pO_2 \times .0036)$
  - Mechanisms of hypoxemia
    - Shunt
      - Does not correct with oxygen breathing
    - V/Q mismatch
      - Corrects with oxygen breathing
      - Exacerbated by exercise
    - Alveolar hypoventilation
      - Normal A-a gradient
      - Corrects with oxygen breathing
    - Diffusion limitation
      - Corrects with oxygen breathing
      - Exacerbated by exercise

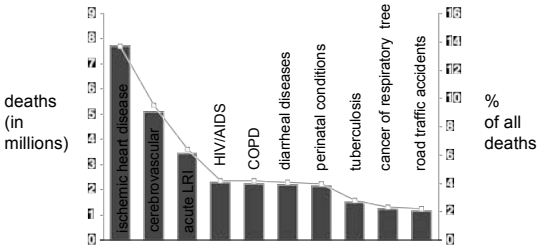
Goals and objectives for the pulmonary section: III

- Understand symptoms and signs of pulmonary disease
  - Symptoms
    - Dyspnea
      - Onset
      - Severity
      - Triggers
      - Progression
  - Signs
    - Wheezing
    - Crackles (rales and rhonchi)
    - Diminshed breath sound
    - Hyperresonant breath sounds
- Understand use of diagnostic testing in pulmonary disease
  - Pulmonary function testing
    - Restrictive and obstructive physiology
  - Arterial blood gas analysis
  - Chest radiograph
  - Lung pathology
    - Major types and patterns of injury and abnormality

Goals and objectives for the pulmonary section: IV

- Understand treatment approaches to patients with lung diseases
  - Symptomatic treatments
    - Oxygen therapy
    - Bronchodilators
    - Mechanical ventilation and PEEP
  - Disease specific treatments
    - Understand cellular and molecular basis of treatments for specific diseases
      - Steroids
      - Other immunosuppressives
      - Antibiotics
      - Anti-neoplastics
      - Pulmonary vasodilators

Leading causes of global mortality



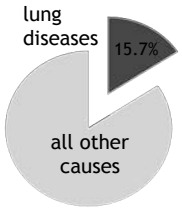
WHO, World Health Report, 2004

Leading causes of death in the world

- 2004
  - Ischemic heart disease
  - Cerebrovascular disease
  - Acute lower respiratory tract infections
  - HIV/AIDS
  - COPD
  - Diarrheal diseases
  - Perinatal mortality
  - Tuberculosis
  - Cancer of the respiratory tree
  - Road traffic accidents
- 2030
  - Ischemic heart disease
  - Cerebrovascular disease
  - HIV/AIDS
  - COPD
  - Acute lower respiratory tract infections
  - Cancer of the respiratory tree
  - Diabetes mellitus
  - Perinatal mortality
  - Stomach cancer

Mathers, PLOS Medicine 2006; 3: e442

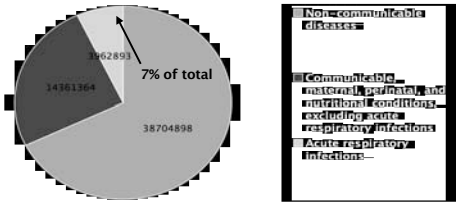
Impact of respiratory illness on global mortality



respiratory illnesses account for 8.43 million deaths per year, or 15.7% of total deaths in WHO member nations

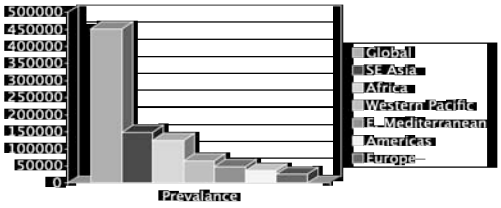
WHO, World Health Report, 2004

Global deaths due to acute respiratory infections



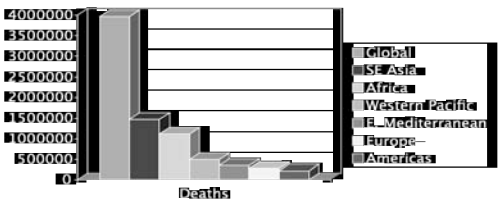
Source: WHO Global Disease Burden Report

Yearly prevalence (in 000s) of acute respiratory infections (ARI), by WHO region



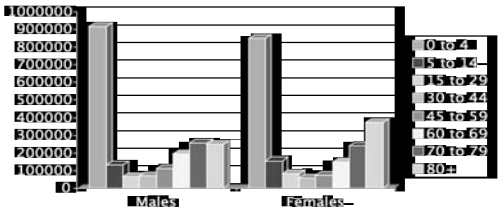
Source: WHO Global Disease Burden Report

Deaths due to ARI, by WHO region



Source: WHO Global Disease Burden Report

Deaths due to ARI, by age and sex, worldwide



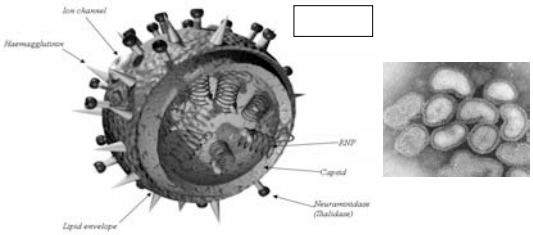
Source: WHO Global Disease Burden Report

Cause of death among children less than 5 years of age

Cause of Death	Africa	Global
	percent	
Acute respiratory infection	16	18
Diarrheal disease	14	15
Malaria	22	10
Measles	8	5
HIV or AIDS	8	4
Neonatal deaths	13	23
Other causes	19	25
	number	
All causes	4.5 million	10.9 million

Source: NEJM, WHO

Influenza

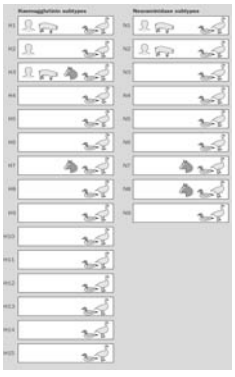


Influenza

- Roughly 20% of children and 5% of adults develop symptomatic influenza infections each year
- Infection is continuous in tropics, seasonal elsewhere
- Three types of influenza virus: A, B, C
- Only types A and B cause outbreaks
- Two major surface proteins:
  - Hemagglutinin: facilitates entry into host cells through sialic acid receptors
  - Neuraminidase: catalyzes cleavage of glycosidic linkages to sialic acid and assists in release of progeny virions from infected cells; drug target
- Influenza A:
  - 15 hemagglutinin subtypes
  - 9 neuraminidase subtypes

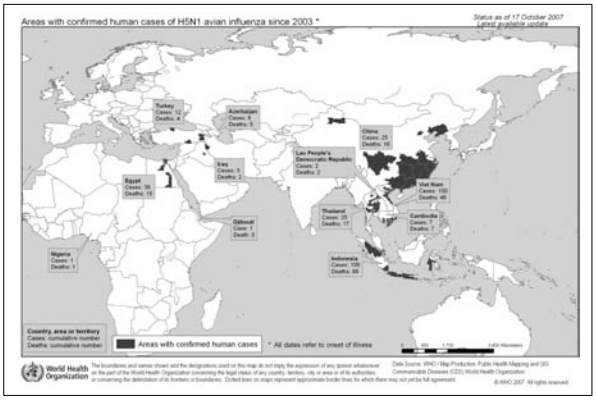
Natural hosts of influenza viruses

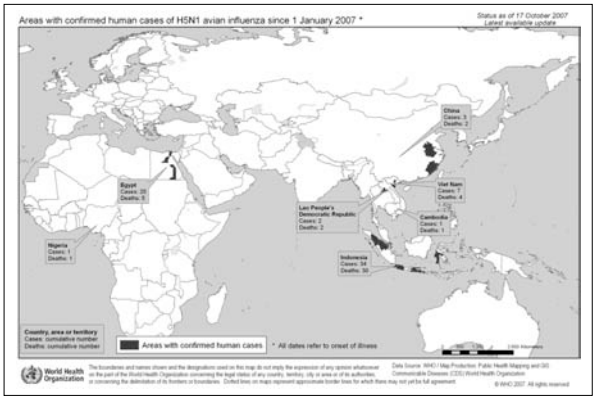
At present, only H1N1 and H3N2 are in circulation among humans



Pandemic influenza

- Caused by sudden appearance of a new subtype: antigenic shift
- 1918-1919
  - H1N1 "Spanish flu"
  - Arose in swine (?)
  - 20 million deaths in first year; 50 million deaths total
- 1957-1958
  - H2N2 "Asian flu"
  - Arose in fowl
  - Severe pandemic: 70,000 deaths in U.S.
- 1968-1969
  - H3N2 "Hong Kong flu"
  - Arose in fowl
  - Moderately severe: 34,000 deaths in the U.S.
- Future pandemics-
  - ?H5N1 ("Avian flu")
  - ? H7N7
  - Both are highly lethal, though little if any person-to-person transmission yet documented





Strategies for controlling influenza

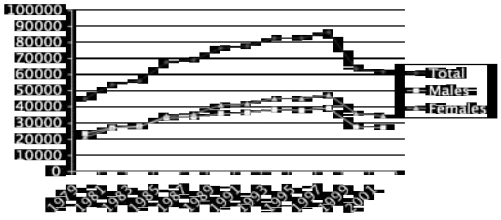
- Surveillance
- Vaccination
- Treatment

Leading causes of death in the U.S., 1980 and 2004

1980	2004
1. Heart disease	1. Heart disease
2. Cancer	2. Cancer
3. Cerebrovascular disease	3. Cerebrovascular disease
4. Unintentional injuries	4. COPD
5. COPD	5. Unintentional injuries
6. Pneumonia and influenza	6. Diabetes
7. Diabetes	7. Alzheimer's Disease
8. Chronic liver disease	8. Pneumonia and influenza
9. Atherosclerosis	9. Renal disease
10. Suicide	10. Sepsis

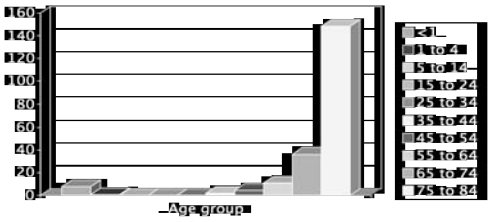
National Center for Health Statistics

Deaths due to pneumonia and influenza, U.S., by year and sex



Source: National Center for Health Statistics

Age-specific mortality for ARI, US, 2001

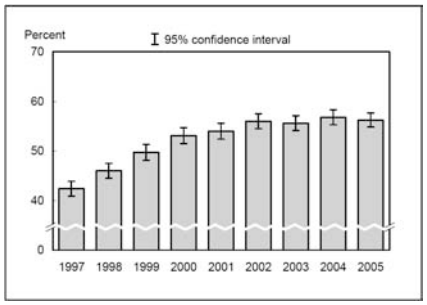


Source: National Center for Health Statistics

Risk factors for community acquired pneumonia

- Advancing age
- Tobacco use
- Air pollution
- Underlying chronic disease
- Malnutrition
- Alcohol use
- Chronic obstructive pulmonary disease
- Others including immunodeficiency, treatment with immunosuppressive drugs, malignancy, etc.

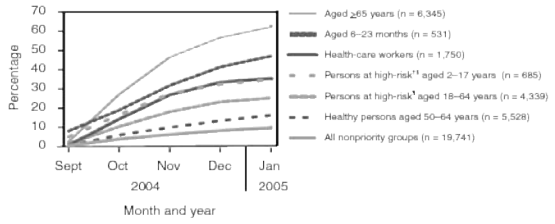
Pneumococcal vaccine coverage in persons > 65 years, U.S., 1997-2005



CDC, 2006

Influenza vaccine coverage, United States, 2004-2005

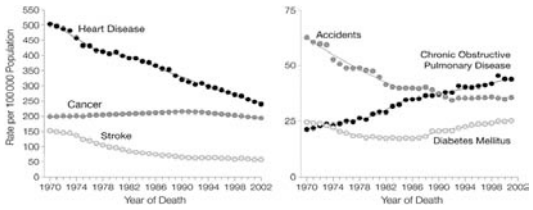
FIGURE. Monthly influenza vaccination coverage among selected priority populations, by month — Behavioral Risk Factor Surveillance System, United States, 2004–05 influenza season*



* Interviews were conducted during February 1–27, 2005.
† Does not include persons in households with infants aged <6 months, out-of-home caregivers of infants aged <6 months, or others with rare, high-risk conditions.
§ Asthma; other lung, heart, or kidney problems; diabetes; weakened immune system; anemia; or aspirin therapy for chronic conditions.
¶ Asthma; other lung, heart, or kidney problems; diabetes; weakened immune system; anemia; or pregnancy.

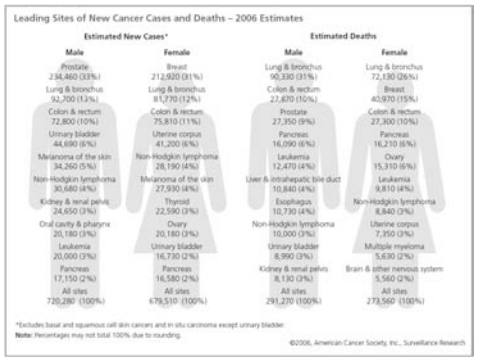
MMWR 2005; 54: 304-307

Trends in Age-Standardized Death Rates for the 6 Leading Causes of Death in the United States, 1970-2002



Jemal, A. et al. JAMA 2005;294:1255-1259.

Leading Sites of New Cancer Cases and Deaths – 2006 Estimates



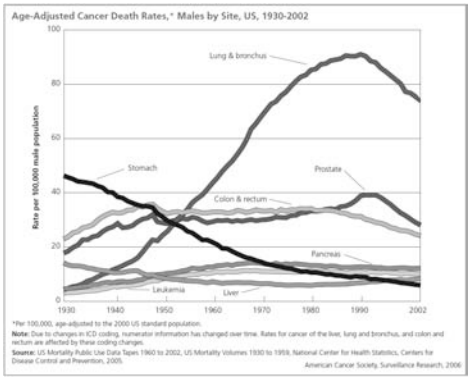
Source: American Cancer Society

2007 Estimated US Cancer Deaths*

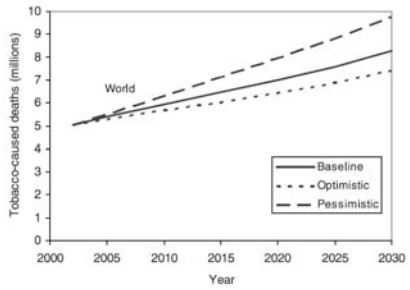
Lung & bronchus	31%
Prostate	9%
Colon & rectum	9%
Pancreas	6%
Leukemia	4%
Liver & intrahepatic bile duct	4%
Esophagus	4%
Urinary bladder	3%
Non-Hodgkin lymphoma	3%
Kidney	3%
All other sites	24%

•26%	Lung & bronchus
•15%	Breast
•10%	Colon & rectum
• 6%	Pancreas
• 6%	Ovary
• 4%	Leukemia
• 3%	Non-Hodgkin lymphoma
• 3%	Uterine corpus
• 2%	Brain/ONS
• 2%	Liver & intrahepatic bile duct
•23%	All other sites

ONS=Other nervous system.
Source: American Cancer Society, 2007

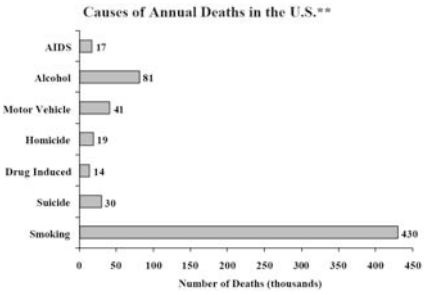


Global tobacco-related mortality, 2002-2030



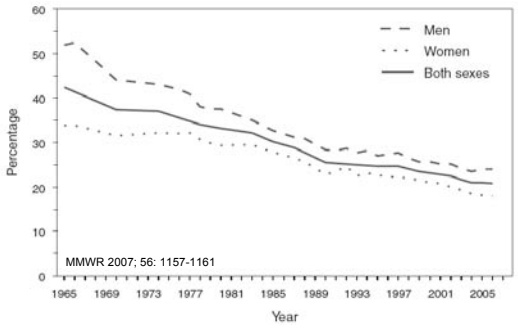
Mathers and Loncar, PLOS 2006; 3: e442

Tobacco-related deaths annually, U.S.

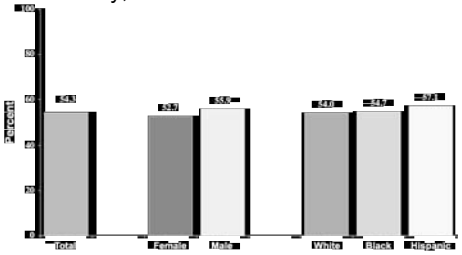


Source: CDC, ALA

Smoking trends, United States, 1965-2006



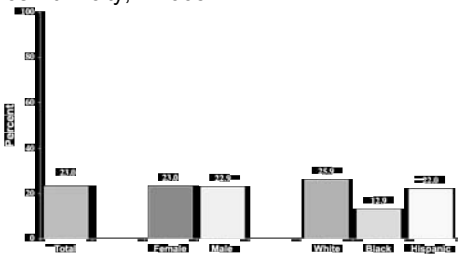
Percentage of High School Students Who Reported Lifetime Cigarette Use,* by Sex** and Race/Ethnicity, 2005



* Ever tried cigarette smoking, even one or two puffs
** M> F

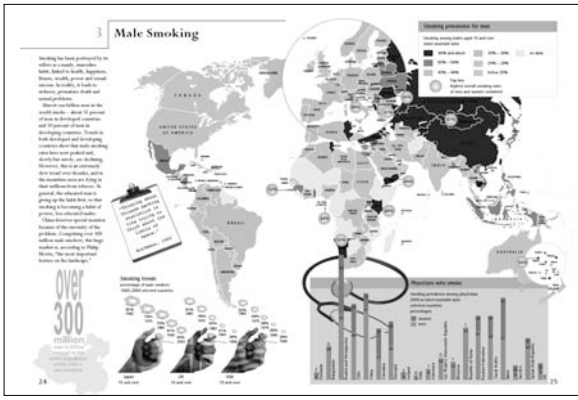
National Youth Risk Behavior Survey, 2005

Percentage of High School Students Who Reported Current Cigarette Use,* by Sex and Race/Ethnicity,** 2005



* Smoked cigarettes on ≥ 1 of the 30 days preceding the survey
** W, H > B

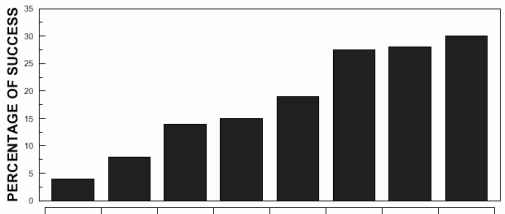
National Youth Risk Behavior Survey, 2005



Limiting morbidity and mortality from tobacco use

- Medical model
  - Smoking cessation
  - Early detection and treatment of smoking related illness:
    - Lung cancer screening
    - Prevention and treatment of COPD
- Public health model
  - Limiting access to tobacco
    - Raising cigarette tax
    - Enforcing age limits for purchase
    - Smoking restrictions in workplaces and public facilities
  - Discouraging use of tobacco
    - School-based initiatives
    - Counter advertising

FIGURE 10: SUCCESS RATES FOR VARIOUS CESSATION METHODS, 1998



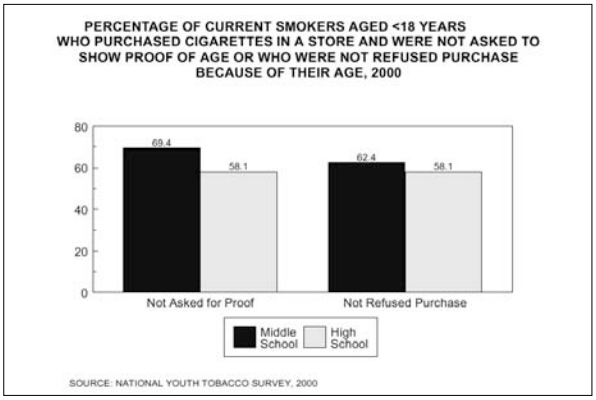
Self Help Only	Patch	Gum	Behavioral	Inhalers	Rplcmt + Bhvr	Prescriptions	Nasal Spray
4.0	8.0	14.0	15.0	19.0	27.5	28.0	30.0

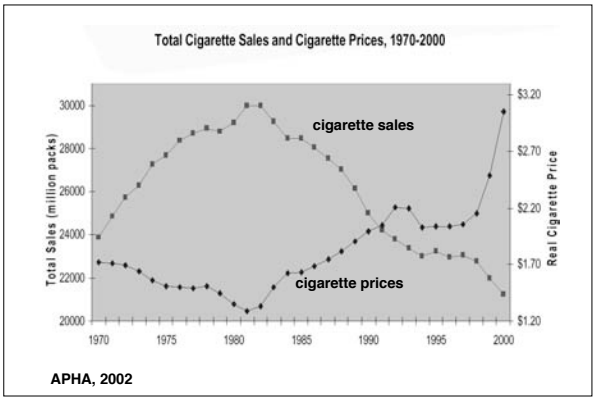
Source: CDC Office on Smoking & Health - Cessation Division

Hutchinson Smoking Prevention Project: Long-Term Randomized Trial of School-Based Tobacco Use Prevention

- 40 school districts in Washington State randomized to provide comprehensive anti-tobacco curriculum (based on CDC and NCI recommendations) in grades 3-12 or standard health curriculum
- Main study endpoints were smoking in grade 12 and 2 years after high school
- 8388 students entering third grade were subjects in the study; follow-up data available on 93%
- Prevalence of daily smoking at study conclusion: 24.66% in control districts, 24.41% in experimental districts

Peterson et. al., J Natl Can Inst 2000; 92: 1979-1991





APHA, 2002

Smoke-Free Workplace Act of 2002 (NYC Local Law 47)

- Law took effect March 30, 2003
- Bans smoking in all indoor workplaces in New York City, including bars and restaurants of any size.
- Exemptions for 7 currently existing cigar bars.
- Exemptions for owner operated bars.
- Restaurants will be allowed to build completely enclosed, negative pressure ventilated smoking rooms into which no employee will be allowed until the last customer of the day has left. Clause sunsets after three years.
- New York State has adopted a similar law that covers the entire state

Workplace smoking ban, Ireland

from McElvaney NG. NEJM 2004; 2231-2234