Environmental and Occupational Epidemiology

- As Environmental Health (4) on 23 Oct. 2014
- Key Concepts
  - Epidemiology: study of distribution and determinants of health and disease in human populations (incl. causal inference)
  - Environmental/Occupational epidemiology studies the role of exposures in the general environment/workplace by common methods
  - Epidemiological data complement other data (incl. toxicological data)
  - Optimal study design depends mainly on population's feature, exposure, and disease
  - Strength of conclusion is based on large sample size, accurate and precise measurement of exposure and disease
  - Avoiding bias (selection bias, information bias, and confounding) is important for valid causal inference
  - Necessary for risk assessment, standard-setting, policy-making

A primer on epidemiology

- Epidemiology pursues causal inference on exposure and disease: philosophical framework was given by Karl Popper (Rothman and Greenland, 1998)
  - All hypotheses are tentative and may be disproved by further testing
  - A hypothesis has a greater scientific value when it has more possibility (test methods) of disproval
- Several checklists of causation (Hill's criteria, 1965)
  - Temporal relationship (absolutely required!): Exposure must precede disease
  - Consistency: The association is repeatedly observed in many studies
  - Large effect size: The exposed have much more disease than nonexposed
  - Positive dose-response: More exposure causes more disease
  - Biological plausibility: Some biological explanation makes it reasonable that A (exposure) causes B (disease)
  - etc.

Kinds of epidemiological studies

- Descriptive studies
- Ecological studies (Correlational studies in group level) -> contributing to making hypothesis
- Analytical studies
  - Clinical trials (typical intervention studies)
  - Observational studies
    - Natural experiments: eg. John Snow's comparison of cholera deaths between water-supply companies
    - Cohort studies: Comparison of disease occurrence between exposed cohort and nonexposed cohort, using Incidence Rate Ratios, Incidence Rate Differences, Risk Ratios, Risk Differences
    - Case-control studies: Comparison of past exposures between cases and controls, using Odds Ratios, special attention must be paid for recall bias
    - Cross-sectional studies: Studies of relationship between exposed status and disease status at same time data, using Odds Ratio

Types of bias

- Selection bias: the relationship between exposure and disease in the study population doesn't represent that in general population
  - self-selection bias of the volunteer: eg. ethylene oxide -> breast cancer ?: if response was obtained from only 20% of the study population, the effect is overestimated
  - healthy worker effect
- Information bias
  - mismeasurement / misclassification: whether differential or nondifferential is important
  - recall bias
- Confounding: relating with both exposure and disease, and not the result of exposure
  - controllable by stratified analysis, restriction, and multivariate analysis

Types of data analyses

- For category variables (esp. dichotomous variables)
  - Rate Ratios, Odds Ratios - with confidence intervals
  - Fisher's exact test - calculating p-values (probability of getting the actual data under the null-hypothesis of independence): strong effect of sample size should be noted
- For continuous variables
  - Typically regression analysis (for exposure and disease)
    - linear regression model
    - logistic regression model
    - poisson regression model
    - multilevel model

Environmental epidemiology

- Environmental agents, large number of people are exposed involuntarily (vs. individual voluntary exposure to tobacco, alcohol)
- Both possibility to cause epidemics and endemic diseases
  - Neuropathy outbreak in Madrid in 1981 <- oil contaminant
  - Gastrointestinal illness outbreak in Milwaukee in 1993 <- drinking water contamination by cryptosporidium
  - Endemic diseases are caused by constant, low level exposure
    - possible contribution of radon gas in homes to lung cancer
    - dioxin in the diet contributing to cancer rates
    - environmental lead exposure to children causes neurological deficits
  - Relationship between environmental agents and background levels of disease in developed countries is a kind of endemic diseases' study (becoming a large study focus, but difficult to detect such associations)

Occupational epidemiology

- Illness or injury associated with workplace exposures
  - Stressful repetitive motion ~ carpal tunnel syndrome（手根管症候群 in Japanese）
  - Welding ~ lung cancer
  - Silica ~ kidney disease
  - Poor office ventilation ~ respiratory illness
- Relatively high level exposure to relatively small number of people, comparing with the target of environmental epidemiology
- Scientifically easy to study, but economically and politically controversial (often faces conflict of interest)
- Historically, occupational cancer was studied in relation to high level exposure to many kinds of occupational contaminants (asbestos, aniline dyes, silica, nickel, cadmium, arsenic, dioxin, beryllium, acid mists, radon gas, diesel fumes): It's already clear. Studies completed.
  - Much lower level environmental exposure has the same carcinogenicity? is still the target of the study (radon gas in homes, arsenic in water, asbestos are already clear, but dioxin's low level carcinogenicity is still unclear)
- Nowadays, subjects of occupational epidemiology involves issues more difficult to study (job stress ~ heart disease?, lifting ~ back strain?)

Finding the occurrence of clusters

- In both environmental and occupational epidemiology, finding disease clusters is important
- Cluster: an apparently elevated number of disease cases in a limited area over a limited period, suggests common cause
  - Sometimes difficult to find: eg. 3 cases of childhood leukemia were found in the same street -> unusual, but not found due to the ward of disease statistics being composed of a dozen streets
  - For rare diseases, statistical power is too small to detect the effect by cohort study, so that only case-control study is applicable to such situation
  - In most cases, researchers cannot find common cause from the cluster. (exceptions) Cluster of asthma in Barcelona in the early 1980s had common cause of soybean dust in the air.

Measuring exposure

- Measuring exposure with sufficient accuracy is very important (see, next topic)
- Most difficult exposure assessment may occur in the retrospective case-control study (avoiding recall bias is difficult)
  - Constructing job-exposure matrix (JEM) -> cross classification of jobs and exposure levels across time -> Based on recent exposure data, researcher can extrapolate past exposure by jobs
  - Measuring the biomarker of exposure -> alternative method to estimate past exposure
    - pesticide exposure ~ Parkinson's disease: organophosphate pesticide is rapidly metabolized, so that difficult to detect as biomarker, but organochlorine pesticide has longer biological half life and easy to detect. DDE is the principal metabolite of DDT, being still detected in serum of US population, though DDT use is already prohibited

Occupational epidemiology example

- Based on National Death Index (in USA), death certificate to determine cause of death for 4626 workers in the cohort, exposed to different silica level
- Stratified analysis to control confounding by age, race, sex, calender time
- 109 workers were killed by lung cancer
- 23 workers were killed by end-stage kidney disease
- (Source: Table 3.1 of Frumkin's text, pp.95)

	Exposure levels (Figures are rate ratio to national general population, same age, actual numbers of death are shown with parenthesis)			
Cause	Q1 low	Q2	Q3	Q4 high
Lung cancer	1.00 (17)	0.78 (21)	1.51 (20)	1.57 (16)
End-stage kidney disease	1.00 (2)	3.09 (5)	5.22 (6)	7.79 (5)
Silicosis	1.00 (1)	1.22 (2)	2.91 (4)	7.39 (7)

Environmental epidemiology example

- Recreational water quality: the number of gastroenteritis outbreaks ~ exposure to recreational water -> increased 3-4 times from 1978 to 2004
- Haile and others (1999): gastrointestinal illness ~ swimming in marine waters incl. untreated runoff from storm drains in Santa Monica Bay?
  - Are there different risks of adverse health outcomes among subjects swimming at different distances from the storm drains?
  - Are risks of specific health outcomes associated with the concentration of specific bacterial indicators of water quality or with the presense of enteric viruses?
    - Adjusted RR for 400 yards away from drains: 1.2 for eye discharge, sore throat, HCGI (highly credible gastrointestinal illness), 2.3 for earache
    - Adjusted RR for within 50 yards from drains: 1.2 for cough, diarrhea, chills, 1.9~2.3 for eye discharge, vomiting, HCGI

Epidemiology and risk assessment

- Past: Qualitative literature review
- Today:
  - Quantitative meta-analysis: Weighted average of quantitative results (already published) across studies. (Originally used in clinical trials, but now used for observational studies, it can combine different kinds of studies and measures.)
  - Pooled analysis: If raw data are available, this gives a common exposure-response coefficients.
  - Risk assessment: Determination of permissible (acceptable) exposure level. Occupational exposure usually permit higher level than general public.