Introduction to Genetic Epidemiology

offered as PH 797(B) (Current Issues in Public Health, Fall, 2007)

Instructor: John Grove, Dept. of Public Health Sciences and Epidemiology, JABSOM
Time: 2:50-4:05 PM Tuesday, Thursday
Room: Biomed. C 104
Textbook: *Thompson and Thompson Genetics in Medicine* by R.L. Nussbaum, R.R. McInnis and H.F. Willard
Credits: 3

Prerequisites: One semester of statistics at the 400 level or higher, plus two courses in either Zoology or Biology, plus two semesters of introductory chemistry.

The course will be an introduction to the principal topics of genetic epidemiology, one of the fastest growing fields in health research. Genetic epidemiology is population-based research on how genetic variation affects health. The course will include material on pedigree analysis, population genetics, the common study designs used in genetic epidemiology and their methods of statistical analysis, biochemical genetics, and variation in chromosome structure. Case studies will include examples from cancer, infectious disease resistance, cardiovascular disease, and genetics of ageing.

There will be two exams which will be worth 50% of the total grade plus additional homework assignments.

Course Learning Objects

1. Know the terminology of human genetics
2. Interpret pedigrees to determine the mode of inheritance of diseases or traits
3. Compute the coefficient of inbreeding from a pedigree
4. Choose appropriate segregation analysis models to analyze inherited diseases
5. Calculate a chi-square test to check for Hardy Weinberg equilibrium
6. Know the assumptions and controversies of genetic load theory
7. Know the basic forms of inherited epigenetic changes and their role in cancer formation
8. Know the basic study designs for linkage analysis and be able to perform a linkage analysis from data for which the parental phase is known
9. Know the strengths and weaknesses of the usual study designs for association analysis and compare this to linkage analysis
10. Know the underlying genetic basis of inherited susceptibility to selected chronic diseases and protection from selected infectious diseases

Specialization Competencies Addressed

AS1 Define a public health problem.
AS2 Determine appropriate use of data and statistical methods.
AS3 Collect and summarize data relevant to an issue.
AS4 Evaluate the quality and comparability of data and identify gaps in data sources.
AS6 Identify research designs used in public health, including advantages and flaws of specific designs, and determine designs appropriate to specific needs.
E5 Apply appropriate statistical tests for parametric and non-parametric settings and identify advanced statistical methods for analyzing both nominal and continuous data, for both univariate and multivariate applications.

Reading assignments: chapters in the textbook *Genetics in Medicine* are symbolized as “Ch”.

I. Formal genetics of diseases with simple Mendelian inheritance
    A. Chromosomes, meiosis and mitosis (Ch2-3)
    A. Pedigree analysis (Ch5)
    B. Computing the inbreeding coefficient and the coefficient of relationship from pedigrees
    C. Introduction to classical segregation analysis, adjustment for ascertainment bias
II. Introduction to Population genetics
    A. Conditions for Hardy Weinberg equilibrium
    B. Population structure and stratification – Wahlund's variance and random drift (Ch7)
    C. Equilibrium between selection against deleterious alleles and recurrent mutation
    D. Genetic load theory – controversy and evidence
    E. Variability within populations
III. Chromosome structure and disease
    A. Chromosome structure in bacteria and humans
    B. inactivation of an X-chromosome in female mammals
    C. Chromosomal abnormalities (Ch9-10)
    D. Parent-of-origin effect and methylation
    E. "Anticipation" from DNA miscopying (Ch9)
IV. Linkage analysis
    A. Method of maximum likelihood and likelihood ratio tests for linkage analysis, lod scores for Mendelian traits (Ch8)
    B. Adjustment of the critical value of lod scores for traits which are not known to be inherited.
    C. Study designs (full pedigree analysis, affected sib pairs)

(Exam 1)

V. Case-control designs for detection of genetic associations with diseases (class handouts)
    A. case only
    B. case-control design; problem of population stratification
    C. two parents + affected offspring design and the transmission-disequilibrium test
VI. Biochemical basis for mutation (Ch6)
VII. Genetic epidemiology of cardiovascular disease – class handouts
VIII. Genetic epidemiology of cancer (Ch16, class handouts)
IX. Genetic epidemiology of developmental disorders (Ch17)
X. Genetics of the immune system and variation in resistance to infectious diseases (Ch14, class handouts)
    A. Genetics of innate immunity
    B. Genes involved in antigen processing and presentation
    C. Genes affecting lymphocyte function and inflammatory response
    D. Examples of variable susceptibility (malaria, cholera, HIV, TB, bacterial meningitis, influenza)
XI. Genetics of ageing-related disorders (class handouts)

(Exam 2)