**PRINCIPLES OF TOXICOLOGY**

PATB 4140/5140

Sample schedule

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| | | LECTURES |
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| I. | General background<br>In addition to serving as a general introduction to the subject, this block of material will serve a "remedial" function for students who haven't previously had pharmacology, physiology or pathology. | |
| A. | Introduction (history & evolution)<br>Historical highlights, eg. the Lex Cornelia and the Bergsucht, which are still relevant.<br>The "art & science" of toxicology: where it came from, what it can and can't do. | 1 |
| B. | Basic concepts<br>Receptor theory, dose response, "mechanisms". | 2 |
| C. | Toxicokinetics<br>Simple models, physiologic models. | 3 |
| D. | Elimination mechanisms<br>Routes of uptake & elimination, factors influencing uptake & elimination, methods for measuring. | 4 |
| E. | Xenobiotic metabolism<br>Phase I vs Phase II<br>Major important reactions<br>Detoxication vs metabolism<br>Examples: EtOH, $CHCl_3$, DBCP, EDB | 5 |
| F. | Mutagenesis<br>Biochemical and physiologic basis of mutagenesis<br>Models and metrics<br>Applications: regulatory and otherwise | 6 and 7 |
| G. | Carcinogenesis<br>Epigenetic vs genetic carcinogenesis<br>Metals<br>"Self" identification and regulation | 8 |
| II. | Systemic Toxicology<br>Basic overview, principles, clinical/field examples, methods of evaluating toxicity. | |
| A. | Liver 9,10<br>Hepatic xenobiotic biotransformation<br>Structure and function<br>Hepatocellular vs. biliary injury<br>Metrics: Functional, morphological, clinical chemical<br>Examples: $CCl_4$, Aflatoxin, TCDD, Pyrrolizidine alkaloids | |
| B. | Kidney<br>Structure and function in homeostasis<br>Relationship of S&F to xenobiotic induced injury<br>Research methodologies<br>Examples: Balkan endemic nephropathy, analgesic nephropathy, Itai-Itai | 11 and 12 |
| C. | Respiratory system<br>Pathophysiology of chemical injury<br>Synergism with infectious agents<br>Aerosols, vapors and systemic exposure<br>Paraquat, asbestos, "black lung" | 13 |
| D. | Gill (**Bergman/Meyer**)<br>Structure/function in homeostasis<br>Xenobiotic influences on mucus and gas exchange<br>Acid rain, AI, Ca | 14 |
| E. | Immune system (**Belden**) | 15 |

Nonspecific defense mechanisms
Recognition of "Self"
Major features of immune system (targets)

Midterm distributed 16

F. Integumentary system 17
Skin as a route of exposure
Isolated cell preps, whole animal, and mathematical models
Skin as a xenobiotic target

G. Male reproductive system 18
Hormonal feedback as a target (male and female)
Spermatogenesis and experimental protocols
Testicular xenobiotic metabolism and bioactivation
In vitro evaluation
DBCP, gossypol, EGME

H. Female reproductive system 19
Oogenesis as a target
Fertilization/implantation/gestational effects
Methods of evaluating reproductive effects
Zearalenone, plant estrogens, DDT

I. Teratogenesis 20
Stage of gestation
Placental "barrier"
Fetal vs maternal metabolism

J. Cardiovascular system 21
Basic cell biology of excitable membranes
Homeostatic mechanisms as xenobiotic targets
Beer drinker's cardiomyopathy, ionophores, cardiac glycosides

K. Hematopoietic system 22
Bone marrow, stem cells and maturation of formed elements of blood
Structure/function of mammalian Hb and CO
Oxidant stress as a cause of methemoglobinemia
Bracken fern, Pb, chloromycetin, fava bean, benzene

L. Nervous system 23
Including sensory organs, motor functions and autonomic nervous system.
Behavioral toxicology

III. Misc Topics

A. Pesticides and "environmental" chemicals 24
Major classes of insecticides & mechanisms of action
Contaminants as toxic agents (eg. dioxin)

B. “Natural” & Food borne toxicants 25 and 26
Mycotoxins
Bacterial toxins
Nutrient toxicology (Se, Vitamin A)

IV. Topics & Review

A. Presentations 27, 28, 29
Each student will be required to select a topic from current events and do a thorough, critical analysis of the topic on the basis of the principles we’ve covered in this class. This topic will be evaluated on the basis of a term paper and an oral presentation.

B. Review session (time permitting)