
Course Description:

This one-semester undergraduate course which provides a comprehensive review of toxic effects of a variety of drugs, chemicals and carcinogens with a core focus on the modern approaches in prevention, detection, diagnosis and treatment of acute and chronic toxicities. It is uniquely designed for biology, chemistry, biology-chemistry and sports science majors who wish to pursue higher education in health professions (pharmacy, medicine, nursing and physical therapy) as well as a career in academia, industry and other research settings. Core topics will train the students to understand how chemical entities interact with biological processes and the ultimate fate of foreign chemicals in human body, the significance of biotransformation reactions and its consequences in the human body. The impact of xenobiotics on the cellular, subcellular and molecular targets yielding to pathophysiological responses relevant to human health will be discussed in depth. Additional focus will be on: drug metabolism and to identify underlying susceptibility factors (pharmacogenomics and toxicogenomics) which contribute to the ability of chemicals to elicit toxigenic effects leading to human disease. Analysis of the role of toxicology in human health and disease will be a common theme of this course.

Class Meeting Times and Locations: TBD.....

Course Faculty

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Office hours: by appointment only

Type of Course: Chemistry/Biology

Course Time Commitments: 3 Credit- 45 hours/semester

Lecture Hours: 4 hours per week

Homework/Self-study Hours: Approximately 3 hours/week

Students are required to watch web-based animations when assigned by the Professor.

Prerequisite Courses: Biology (103, 229), Chemistry (111, 113), Physiology and/or Health Sciences related courses or a combination thereof.

Prerequisite Knowledge: Basic principles of biology, chemistry, biochemistry and physiology or combinations

Attendance Policy: Attendance is mandatory. Attendance will be routinely monitored.

Policy Concerning Students with Special Needs: If there is any student who believes that he or she may need an accommodation for any type of disability, the student should contact me as soon as possible.

Textbooks and Other Required and Recommended Learning Resources:

Assigned chapters from 'Encyclopedia of Toxicology', 3rd Edn, Copyright© 2014 by The Elsevier Publishing, Inc. Ed.

Phil Wexler (Available at MU Library).

Assigned chapters from Goldfrank's Toxicologic Emergencies, 9th Edn, Copyright© 2010 by The McGraw-Hill Companies, Inc. Editors: Neal E. Flomenbaum, Lewis R. Goldfrank, Robert S. Hoffman, Mary Ann Howland et. al.; ISBN#0-07-147914-7 (Available via Access Pharmacy to MU students).

Internet access: MU E-resources for downloading course materials from time to time.

Handouts: Lecture-specific materials will be provided in the class. Actual lecture materials will be made available through MU web resources.

► **This Course will assist the Student in Meeting the Following Curricular Endpoints:**

- Identify and understand toxic effects emanating from therapeutic and non-therapeutic, intentional and unintentional chemical exposures and recognize toxic effects on humans and other experimental models.
- Monitor adverse reactions originating from toxic exposures in research, accidental or public settings, and medication errors in healthcare setting.
- Predict possible toxicological consequences after exposure to drugs/chemicals in safe limits.
- Evaluate and interpret relevant information from toxicology literature, understand toxicological interactions and identify preventable causes.
- Identify the roles toxicologists can play in academia, regulatory and clinical research settings, pharmaceutical and healthcare industry, and during natural or man-made disasters.

► **This Course will assist the Student in Meeting the Following Course-specific Endpoints:**

- ❖ This course will empower students with knowledge and working insight into outcomes after intentional, accidental and/or therapeutic exposures to drug and chemical entities including environmental disasters.
- ❖ Students will develop a thorough critical understanding of the issues in modern toxicology with a view to developing practical problem-solving skills.
- ❖ Students will be able to apply basic principles and applications within the science of toxicology, and they will be able to recognize various stressors that have known effects on individuals or populations.
- ❖ Students should be able to classify the different routes of toxic exposure, metabolic pathways, mechanisms of distribution within the body, and elimination processes.
- ❖ Students should be able to understand/interpret the effects of different toxicants and stressors in terms of target effect on the cellular-, organ system- and whole body-levels.
- ❖ Students will be able to recognize different populations at risk based on past history, age, geography, and occupational and environmental exposures.
- ❖ Students should be able to predict therapeutic applications for individual drugs based on knowledge of chemical and/or pharmacologic classification, and address appropriately adverse drug reactions, drug-drug interactions, nutritional effects, and lack of efficacy.
- ❖ Students should be able to suggest appropriate use of antidotes in the prevention of disease or the modification of

normal bodily function, and recognize potential problems in disease prevention initiatives by utilizing knowledge of toxicological principles.

❖ Students will gain experience with library, on-line and other toxicology information resources and acquire skills to interpret/suggest appropriate toxicological tools for evaluation in diverse settings.

❖ After appropriate professional experience, students should be able to pursue professional examinations in toxicology such as those offered by the American Board of Toxicology.

► **Course-specific Learning/Behavioral Objectives: After taking this course student should be able to:**

❖ Describe the importance of the drug metabolism (bioactivation) process for those drugs/chemicals which become pharmacologically & toxicologically more active as compared to the parent compound following biotransformation.

❖ Explain the mechanisms for drug and chemical-induced toxicity in in vivo and in vitro models, and appropriately design and interpret drug screenings.

❖ Describe the importance of poisoning and overdose, their manifestations, prevention strategies utilized in the mgmt. of prototype drugs and chemicals.

❖ Describe the general treatment of drug overdose (gastric lavage, emesis, activated charcoal, charcoal-resin hemoperfusion, hemodialysis, peritoneal dialysis, cathartics, pressor agents, cardiac monitoring, and support of airway)

❖ To understand and interpret the general principles of clinical toxicology and pinpoint factors (genetic, nutritional, environmental etc.) that influence toxicity.

❖ To understand the initial approach to the poisoned patient in terms of setting immediate priorities, and to appreciate the necessity to conduct, as the first order of business, those procedures that evaluate and preserve vital signs.

❖ To understand role and function of Poison Control Centers and TESS (Toxic Exposure Surveillance system] in toxicity mgmt. and designing specific approaches for reducing/antagonizing various toxic substances/poisons and minimizing episodes in any given setting.

Grading Policy: Course grades will be based upon 3 exams, 3 quizzes, and 4 assignments to be administered during the semester (1st exam: 20%; Midterm: 20%, Final: 30%; Quizzes: 10%; Assignments: 20%). The final grading will be on a standard scale as follows:

100-93 A	92-90 A-	89-87 B+	86-83 B	82-80 B-	79-77 C+	76-73 C
72-70 C-	69-67 D+	66-63 D	62-60 D-	59-0 F		

Course Assessment: 3 Quizzes (15% each- Total 45%) and 1 Final Exam (55%)

Format: MCQ type; Short essay type; Problem solving (case studies).

Seating during Exams: Every other row, 1-2 seats apart; Professor will notify seating arrangement prior to each exam.

Policy for missing an exam: Only on medical grounds with doctor's note. MU policies will be enforced.

Professional Behavior Expectations: Manchester University rules & regulations will be strictly enforced. Visit: <http://www.manchester.edu/catalog/academic.htm>

LEARNING AND TEACHING METHODS:

Each lecture will follow an intense discussion session which will involve students individually and as a group (3-4 students). Discussion sessions will critically analyze sample case studies. A stress-free learning atmosphere will be created to facilitate the best learning environment, where everyone will be actively engaged in the thinking process. Content presentation style will be designed to understand concepts and minimize memorization. Every effort will be made to cultivate understanding and analytical skills to facilitate learning. Real life scenarios will be discussed to enhance problem solving ability.

ASSESSMENT METHODS:

The instructor will design questions to enhance problem-based learning via multiple skills, such as, (i) understanding, (ii) recall, (iii) analytical, and (iv) conceptual. This will promote critical thinking and problem solving ability. Assignments will be primarily learner-driven, instead of teacher-driven. Students will collaborate with other students (Think-pair-share' strategy), when appropriate, to discuss and complete collaborative assignments and activities. Collaborative team/group activities and independent activities will be monitored.

XVI: Lecture Schedule and Topics:

Introduction	1 hour
General Principles/Mechanisms	3 hrs (1 hr TBL)
Principles of Hepatotoxicity	3 hr (1 hr TBL)
Principles of Nephrotoxicity	2 hr (1 hr TBL)
Principles of Neurotoxicity	2 hr [Lec + Quiz]
Principles of Immunotoxicity	2 hr
Principles of pulmonary toxicity	2 hr
Principles of Reprod./Dev. Tox	3 hr (1 hr TBL)
Principles of Cardiotoxicity	2 hr
Principles of Hematotox.	1 hr [Lec + Quiz]
Principles of Dermatotoxicity	2 hr
Principles of GI toxicity	1 hr
Carcinogens, Teratogens and Mutagens	3 hr (1 hr TBL)
Role of Poison Control Centers	2 hr
Antidotes/Poisoning management	3 hr (1 hr TBL)
Clinical Toxicology and Drug screening	3 hr [Lec + Quiz]
Bioterrorism preparedness	1 hr
Chemical and nuclear terrorism preparedness	1 hr
Toxicology of Recombinant DNA products	2 hr
Food Toxicology (inclu. microbial tox.)	2 hr
Conclusions/ Exam Review	2 hr
Final Exam	2 hr [Final]

XXVII: Lecture Schedule: Fall 2016 session-

Introduction: 1 hour

Various subdisciplines of toxicology, organ toxicology and role of various Govt and non Govt agencies.

General principles: 3 hours

Intracellular targets (plasma membrane, mitochondria, nucleus, cytoplasm) of toxicants; Brief review of drug metabolism (major biotransformation reactions; concept of inhibitors, inducers, substrates); Role of free radicals and BRIs (biological reactive intermediates) in promoting adverse reactions; role of oxidative stress in drug-induced organ injury. Metabolizer phenotypes, other factors that influence toxicity (pharmacogenomics, age, gender, pre-existing condition, ethnic backgrounds, nutrition, diet etc.). Contribution of genetic polymorphisms in toxicology, significance of drug concentrations in Blood, significance of clinical toxicology, and its relevance to cell injury, cell death and target organ injury; accidental (necrosis) and programmed (apoptosis) cell death; Significance of serum chemistry markers. Acute vs. Chronic toxicity, introduction to various types of toxic interactions (antagonism, potentiation, synergism, additive effects); Toxicant exposure routes and their differential impact on target organs; Mechanisms of actions of antidotes; Drug interactions originating from therapeutic exposures and representative drug Interaction mechanisms.

Principles of hepatotoxicity: 3 hours

Concept of intrinsic and idiosyncratic hepatotoxins; Over the counter medications; Mechanism of action of prototype hepatotoxins (acetaminophen, CCl₄, ethanol, aflatoxin, and INH; clinically distinct forms of liver injury (hepatitis, cholestasis, fibrosis, fatty liver etc.); Liver injury diagnosis and prevention methods, anti-hepatotoxic antidotes.

Principles of nephrotoxicity: 2 hrs

Distinct forms of nephrotoxicity (nephritic syndrome, acute and chronic tubular necrosis, acute vs. chronic interstitial nephritis, forms of renal failure etc.); Mechanism of action of prototype nephrotoxins (NSAIDs, metals, CHCl₃, antineoplastics, radiocontrast agents etc.); Kidney injury prevention strategies, anti-nephrotoxic antidotes; Nephrotoxicity testing methods.

Principles of neurotoxicity: 2 hrs

Various forms of neurotoxicity (axonopathy, neuronopathy, myelinopathy etc.); Neurological disorders of originating from drug and environmental toxin exposure; Parkinsons, Alzheimers diseases; Mechanisms of action of prototype neurotoxins (Ex. Lead, Mercury, organophosphates, INH, Ethanol, MPTP etc.); Neurotoxicity testing methods; CO poisoning and neurotoxicity.

Principles of immunotoxicity: 2 hrs

Types of immunotoxicity (Ex. Type I to Type IV Hypersensitivity reactions); Manifestation of immunotoxicity (decreased T & B Cell count, antibody production etc.); Mechanisms of actions of prototype immunotoxins (drugs and chemicals: Ex. Cyclosporin, Nitrosamines, Lithium carbonate, TCDD, PCBs, Heavy metals, ochratoxins etc.); Clinical diagnosis and prevention strategies; Immunotoxicity testing methods.

Principles of Pulmonary toxicity: 2 hrs

Various forms of pulmonary toxicity (Ex. asthma, interstitial pneumonitis, pulmonary fibrosis, bronchiolitis obliterans organizing pneumonia, noncardiogenic pulmonary edema, hypersensitivity- induced pneumonitis etc.); Mechanisms of actions of prototype drugs and chemicals (Ex. bleomycin, Poly Aromatic Hydrocarbons, cigarette smoke, asbestos etc.); Lung injury manifestations and clinical diagnosis; Lung injury prevention strategies and lung injury testing methods.

Principles of Reproductive/Developmental toxicology: 3 hrs

Concept of reproductive toxicity (Ex. gonadal dysfunctions/hypertrophy, decreased sperm count, abnormal menstrual cycles, decreased libido, oligospermia, infertility) and developmental toxicity (Ex. abortifacients, reduced birth weight, Fetal Alcohol Syndrome, organ malformation etc.); Mechanisms of actions of prototype drugs and chemicals (Ex. steroids, cyclophosphamide, methotrexate, DES, ethanol, opioids, nitrofurantoin, tobacco smoke etc.); Discussion on

prototype reproductive and developmental toxin exposures originating in various settings; Prevention strategies of reproductive/developmental toxicity and teratogenesis; including testing methods.

Principles of Cardiotoxicity: 2 hrs

Distinct forms of cardiotoxicity (cardiomyopathy, myocarditis, pericarditis, Myocardial infarction, coronary heart disease, congestive heart failure, arrhythmia etc.); Mechanisms of actions of prototype cardiotoxic drugs (doxorubicin, cyclophosphamide, ethanol, calcium channel blockers etc.); manifestations and clinical diagnosis; Cardiotoxicity prevention strategies and testing methods.

Principles of Hematotoxicity: 1 hr

Various forms of hepatotoxicity (EX. agranulocytosis, sideroblastic anemia, megaloblastic anemia, aplastic anemia, methemoglobinemia, idiopathic neutropenia and interference with coagulation factors etc.); Mechanisms of action of prototype hematotoxic agents (EX. INH, chloramphenicol, metals, colchicine, omeprazole, penicillin, carbamazepine, nitroglycerine, nitrofurantoin,); Toxicity testing and prevention methods.

Principles of dermatotoxicity: 2 hrs

Various forms of dermatotoxicity (Ex. irritation, chemical burns, chloracne, acne, alopecia, eczema, hirsutism or hypertrichosis, exfoliative dermatitis or erythroderma, erythema multiforme/stevens- johnson syndrome, purpura, TEN etc.); Mechanisms of actions of prototype dermatotoxic agents (Ex. allopurinol, barbiturates, carbamazepine, phenytoin, sulfonamides etc.); Clinical diagnosis; Dermatotoxicity testing and prevention strategies; Special discussion on USFDA warnings: Skin reactions induced by Carbamazepine, Heparin, Antiepileptic drug Dilantin-Phenytoin, Fentanyl Patch, Promethazine etc. Effects of UV-A/UV-B etc.

Principles of GI toxicity: 1 hr

Distinct forms of GI toxicity (Ex. Gingivitis, edema, pain/ulceration, drooling, dry mouth, tongue discoloration, stomach pain, dysphagia, vomiting, hematemesis, diarrhea, constipation etc.) Mechanisms of action of prototype GI toxic agents (Ex. antineoplastics, pneytoin, nicotine, phencyclidine, salicylates, methylene blue, Reverse transcriptase inhibitors etc.); Toxicity testing and prevention strategies.

Carcinogens, Teratogens and Mutagens: 3 hrs

Definitions, mechanisms of induction, drugs and chemicals that induce these aberrations, molecular and pathological screening methods, control and prevention strategies.

Role of Poison Control Centers: 2 hrs

Role and functions of Poison Control Centers (AAPCC); Interpretation of AAPCC data and TESS (Toxic Exposure Surveillance System); Briefly discuss top 10 categories of toxic exposures.

Antidotes and Poisoning management: 3 hrs

Role of: cathartics, gastric emptying (IPECAC/Lavage), activated charcoal, whole bowel irrigation, antidotes (importance of time, dose, route, vehicle etc.); Significance of ABC assessment, developing a care plan for the nature of emergency; Detailed discussion on management of various poisonings.

Clinical Toxicology and Toxicology of Drug Screening: 3 hrs

Various types of controlled drugs and their use; Interpretation of drug screens, Rules-regulations, Federal/State standards; Testing methods; Testing methods and procedures and substances of importance. Interpretation of serum chemistry (normal and abnormal); interpretations of health screenings; Routine and molecular approaches to toxicology testing (healthcare setting and forensic setting); Importance of clinical toxicology in medicine.

Bioterrorism Preparedness: 1 hrs

Discussion on various forms of bioterrorism; Toxicologists role in emergency preparedness and response; Discuss role of various agencies and information retrieval system from CDC, Indiana State dept, FEMA, EPA-Counterterrorism program,

