New Course Outline

Course Number: PHM142H1

Course Title: Metabolic Biochemistry and Immunology

Outline Version Code:

Course Description:

This course examines aspects of mammalian biochemistry, metabolism, and molecular immunology pertinent to pharmacologically significant drug actions in vivo. Where appropriate the biochemical basis, mechanism, and effect of specific drugs on human physiology are also discussed. In addition, this course examines the biochemical basis of pharmacogenetics and metabonomics differences seen in different human populations.

Semester: ☒ Fall  ☐ Winter  ☐ Summer

Course Type:  ☐ Elective  ☐ Selective  ☒ Mandatory

1. Course Learning Objectives:
Upon completion of this course, students will have achieved the following level of learning objectives:
Introductory = knowledge and comprehension of concepts, definitions
Intermediate = application of concepts to simple situations
Advanced = application of concepts to more complex situations with ability to synthesize and evaluate
Knowledge
Introductory Level:

Intermediate Level:

Advanced Level:

Skills
Introductory Level:

Intermediate Level:

Advanced Level:
2. Rationale for Inclusion in the Curriculum:

Biochemistry is perhaps of the most basic and principle skill set required of a PharmD. Without an understanding of biochemistry PharmD's would have no concept of the mechanism by which the drugs they dispense act.

3. Pre-requisites:

4. Co-requisites:

5. Course Contact Hours and Teaching Methodologies:

<table>
<thead>
<tr>
<th>Methodology</th>
<th>Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Didactic (lecture)</td>
<td>27</td>
</tr>
<tr>
<td>Large group problem-based/ case-based learning (group size: )</td>
<td></td>
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<tr>
<td>Laboratory or Simulation</td>
<td></td>
</tr>
<tr>
<td>Tutorial/Seminar/Workshop/Small Group (group size: )</td>
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</tr>
<tr>
<td>Experiential</td>
<td>12</td>
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<tr>
<td>On-line</td>
<td>39</td>
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</table>
6. Estimate and description of student's weekly out-of-class preparation time excluding exam preparation:

3 hours

7. Topics Covered and Lecture Specific Learning Objectives

**Week 1**

**Lecture Topic:** OXYGEN AND THE BIOCHEMISTRY OF CELLULAR STRESS: ECTOPIC MODIFIERS OF OXYGEN TRANSPORT AND DELIVERY

**Lecture Learning Objectives:**

- Review properties of hemoglobin, myoglobin and oxygen delivery
- Erythrocyte development and the biochemistry of heme: genesis, distribution, destruction, re-utilization, clinically useful indicators
- Biochemistry of redox energy metabolism in vascular (and other) systems (sites, synthesis and properties of mammalian redox species, Pentose monophosphate shunt, consequence to erythrocyte function and oxygen delivery)
- Endogenous regulators of redox stress (synthesis, catabolism, and actions of Glutathione, Catalase, SOD1 and Nrf2; direct and indirect actions in drug detoxification - paracetamol)
- Exogenous toxicants / drugs which modify erythrocyte function (ROS-generating drugs; cyanide, carbon monoxide and methemoglobinemia; Favism; drug-induced hemolytic anemia, Malaria biochemistry)
- Genetic modifiers of redox stress / erythrocyte function (G6PD deficiency, Sickle cell anemia, biochemistry, thalassaemias)

**Week 2**

**Lecture Topic:** IRON HOMEOSTASIS, TRANSPORT AND TOXICITY: TREATMENTS OF ANEMIA

**Lecture Learning Objectives:**

- Biochemistry of iron (uptake, export and homeostatic regulation, intracellular transport and conversion, iron storage, ferroreductases, DcytB, Ferritin, hepcidin, ferroprotin, hephaestin)
- Iron distribution in the body (molecular biology of iron signaling - transferrin, clatherin mediated cycling of the transferrin receptor, reciprocal control of ferritin and transferrin receptor etc.)
- Causes of iron deficiency (dietary and drug induced) and anemias (major classes)
- Medical conditions and drugs which they alter iron uptake / distribution
- Clinical indicators of iron, diagnostic criteria used to identify class and type of iron deficiency
- Iron supplementation (dietary, pharmacuentic, drug interactions)
- Iron overload (environmental, clinical, drug induced, genetic) early indications and mechanisms of iron toxicity. Therapeutic approaches to iron overload.

**Week 3**

**Lecture Topic:** BIOCHEMISTRY OF ONE CARBON METABOLISM
Lecture Learning Objectives:

- Folic acid: sources, synthesis and mechanisms of deficiency and clinical pathology (environmental and drug-based)
- Biochemistry of tetrahydrafolate (THF): absorption, distribution, metabolic isoforms
- THF cycle I: purine biosynthesis and catabolism
- THF: Chemotherapeutic drugs and mechanisms in 1C metabolism
- THF II and III: The remethylation cycle, transport of 1C units from amino acids, critical role of B vitamins in 1C metabolism, S-adenosyl methionine (SAM) cycle
- Regulation of THF cycles (Methionine synthase and the folate trap)
- DNA methylation and cancer, genetic derangements of one carbon metabolism
- Vitamin B12: synthesis, mechanisms of absorption and distribution, clinical pathology of B12 deficiency and its treatment

Week 4
Lecture Topic: INTRODUCTION TO IMMUNOLOGY AND IMMUNE DRUGS

Lecture Learning Objectives:

- Overview of the immune system, organs and cells of immune function, development of immune response (classical studies), innate versus acquired immunity
- Mechanisms and classes of immune function: The T-cell receptor, T cell sub-classes and function; B cells – immunoglobulin function; proliferation, selection, deletion and anergy of immune cells
- Common immunodeficiency syndromes
- Introduction to transplantation, biochemistry of immunosuppressive drugs (calcineurin, cyclosporin, mTOR, steroid-mediated)
- Network derangements (cellular) in autoimmunity

Week 5
Lecture Topic: MOLECULAR MECHANISMS OF WHITE BLOOD CELLS

Lecture Learning Objectives:

- Neutrophils, eosinophils and chemical warfare NADPH oxidase (Nox) activation, myeloperoxidase, drug induced hepatic neutrophil infiltration, inflammatory liver injury. Inflammatory mediators and inhibitors. Inflamasomes, Autoimmunity diagnosis using anti-neutrophil cytoplasmic antibodies (ANCA c,p,x).
- Autoimmunity: Role of Macrophages, Kupffer cells, Lymphocytes
- Autoimmunity problems e.g. penicillamine
- Autoimmune disease treatment: corticosteroids, alkylating cytostatic drugs, antimetabolites, antimacrophage therapy, anticytokine antibody therapy.
- Idiosyncratic drug toxicity mechanisms Liver toxicity, skin rash, agranulocytosis, bone marrow toxicity. Immune molecular mechanisms contributing to idiosyncratic drug toxicity. Reactive metabolites, Hapten theory, Danger signals released by immune cells, Animal models for idiosyncratic drug toxicity.
- Leukocytes and leukotriene formation: eosinophils and asthma
Week 6
Lecture Topic: INTERMEDIARY METABOLISM OF WHITE BLOOD CELLS

Lecture Learning Objectives:

- Leukocytes classes, Macrophages, Eosinophils: Chemical Warfare. Leukocyte modifiers of migration and inflammation: cytokines and interferons, and pharmaceutical modification
- Molecular mechanisms of leukocyte function
- Genetic diseases e.g., CGD disease
- Cell adhesion molecules in inflammatory disease, drugs and inflammatory disease
- Macrophages: function, growth factors and cytokines: Multiple organ failure, ARDS, sepsis, Macrophage-induced tissue injury.
- Rheumatoid arthritis and therapeutics
- Endothelial and Smooth Muscle Cells
- Cell death and inflammation signaling Cytokines, NFkB and TNF signalling, organ failure

Week 7
Lecture Topic: FATTY ACID OXIDATION AND METABOLISM

Lecture Learning Objectives:

- Arachidonic acid metabolism (platelets, influence of nutrition on AA and PHS, Prostaglandins and heart disease; COX inhibitors and NSAIDs. Endothelial cells: Prostacyclin formation, Angiotensin
- Gluconeogenesis inhibitor drugs, hypoglycemic drugs and the treatment of Type 2 Diabetes
- Genetic diseases: Mitochondrial myopathies and treatment (mitochondrial medicine) Supplement: Carnitine therapy, Drug induced fatty liver, steatohepatitis (NASH),alcohol induced hepatitis (ASH).
- Metabolism of monoamines/alcohol/aldehydes
- Genetic diseases: Porphyria, porphyrin toxicity
- Biosynthesis of haem for cytochromes. Drug induced porphyria. Hepatic Detoxication of monoamines, alcohols, purines, heme, bilirubin, Rhabdomyolysis, Kernicterus

Week 8
Lecture Topic: SPECIAL TOPICS IN BIOCHEMISTRY

Lecture Learning Objectives:

- MODULATION OF METABOLISM BY HORMONES AND CALCIUM (1 hour)
- NITRIC OXIDE SYNTHESIS AND METABOLISM (1 hour). Role of endothelial cells in regulating blood pressure.
  - Biochemistry of smooth muscle contraction, cGMP, Ca2+, cAMP.
  - Nitric oxide formation, signaling and toxicity.
  - Use of drugs that generate NO.
• **UREA CYCLE AND NITROGEN CATABOLISM (1 hour)**
  - The Urea Cycle, nitrogen catabolism of amino acids, detoxification of ammonia

• **INTERMEDIARY/DRUG METABOLISM: HEPATOCYTES (1 hour)**

**Week 9**
**Lecture Topic:** INTERMEDIARY METABOLISM: PEROXISOMES VERSUS CYTOSOL

**Lecture Learning Objectives:**
- Role of peroxisomes in Intermediary metabolism. Inborn errors of metabolism. Synthesis and export of uric acid, proteins, cholesterol, steroids
- Nitrogen Catabolism of Nucleic Acids (uric acid excretion)
  - a) Role in Ischemic Reperfusion Injury (also heart)
  - b) Biochemistry of Gout, Lesch-Nyhan syndrome: Drug treatment
  - c) Purine Nucleotide Biosynthesis and N-catabolism to endogenous toxins.
- Drug / Steroid metabolism. Steroid Synthesis and Metabolism. Detoxification of Drugs, Steroids and other Physiological Substrates
- Cytochrome P450 Isozymes and polymorphism (Dr. D.H. Grant). Pharmacogenomics, Protein Synthesis and Targeting.
- Export of Albumin Transport Proteins and Proteins Involved in Blood Clotting (Fibrinogens, Prothrombin, Factors). Biochemistry of antithrombotic drugs

**Week 10**
**Lecture Topic:** CHOLESTEROL AND CHOLESTEROL LOWERING DRUGS

**Lecture Learning Objectives:**
- Synthesis and Export of Cholesterol
- Utilization of cholesterol and fatty acids by extra-hepatic tissues for membrane biosynthesis
- Molecular diseases of cholesterol and lipoproteins
- Mechanism of LDL oxidation in foam cell mediated plaque formation
- Biochemistry of Cholesterol lowering drugs (statins and non-statins)
- Synthesis and function of coenzyme Q

**Week 11**
**Lecture Topic:** ENOCRINE BIOCHEMISTRY, DISORDERS OF THE THYROID AND TREATMENTS

**Lecture Learning Objectives:**
- The thyroid, its interactions and control of metabolism, the biochemistry of iodide
Biochemistry of the hypothalamic-pituitary axis, actions and regulation
Thyroid hormones: synthesis, activation and inactivation
Pharmaceutics and dietary agents which alter thyroid function (adverse)
Clinical indicators of thyroid function, biochemistry of thyroid pharmaceutics
Thyroid syndromes: Hyperthyroidism (Graves disease, thyroid cancer, thyroid storm)
Thyroid syndromes: Hypothyroidism (Hashimoto’s thyroiditis, cretinism)

**Week 12**
**Lecture Topic:** BIOCHEMISTRY OF THE CNS: NEUROTRANSMITTERS, MODIFIERS AND MIMICS

**Lecture Learning Objectives:**

- CNS structure and function, principles of neural processing and neurotransmission, roles of excitation and inhibition (Glutamate, GABA and epilepsy)
- Biochemistry of mood altering substances: CNS stimulants
- Psychomotor: caffeine, nicotine, cocaine, amphetamine
- Psychomimetics: LSD, PCP, THC
- Structure function relationships between neurotransmitters and drugs of abuse
- Mechanisms of Anxiolytics (benzodiazepines and non-barbiturate sedatives)
- Mechanisms of Antidepressants (Tricyclics, SSRI’s, MAO inhibitors)

**Week 13**
**Lecture Topic:** See course website and Syllabus for CORRECT assignment of 13 weeks of lectures

**Lecture Learning Objectives:**

8. **Assessment Methodologies Used:**

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Course Learning Objectives Addressed</th>
<th>Assessment Method Used</th>
<th>Percent of Course Grade</th>
<th>For Group Work: Individualized or same mark for all group members</th>
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<tr>
<td>☒ Assignment</td>
<td>Differential diagnosis</td>
<td>Written formative assessment</td>
<td>15%</td>
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</tbody>
</table>
Expectation for pass grades for all Pharmacy courses is 60%

9. Policy and procedure regarding late assignments/examinations/laboratories:

Standard as per existing Pharmacy policy

10. Policy and procedure regarding missed assignments/examinations/laboratories:

Standard as per existing Pharmacy policy

11. AFPC Education Outcomes addressed (check all those that apply):
- Refer to AFPC Educational Outcomes for Professional Programs for further information about the role and key competencies.

As Care Providers, pharmacy graduates:

**CP1 – Practice within the pharmacist scope of practice and expertise**

☒ CP1.1 Apply knowledge from the foundational sciences to make decisions relevant to the contemporary and evolving scope of pharmacist practice;

☒ CP1.2 Integrate AFPC Communicator, Collaborator, Leader-Manager, Health Advocate, Scholar, and Professional roles in their practice of pharmacy;

☐ CP1.3 Recognize and respond to the complexity, uncertainty and ambiguity inherent in pharmacy practice;

☐ CP1.4 Explain the benefits, risks and rationale associated with pharmacist-provided care as an important step in obtaining and documenting consent to pharmacist care;

☐ CP1.5 Recognize and take appropriate action when signs, symptoms and risk factors that relate to medical or health problems that fall into the scope of practice of other health professionals are encountered.
CP2 – Provide patient-centred care

☐ CP2.1 Collect, interpret, and assess relevant, necessary information about a patient’s health-related care needs;

☐ CP2.2 Formulate assessments of actual and potential issues and in collaboration with the patient and other health team members as appropriate, prioritize issues to be addressed in a given patient encounter;

☐ CP2.3 Create and document plans in collaboration with the patient and other health team members as appropriate, and make recommendations to prevent, improve or resolve issues;

☐ CP2.4 Implement plans in collaboration with the patient and other health team members as appropriate, including:
  
  CP2.4.1 obtaining consent
  CP2.4.2 making a referral or consulting others
  CP2.4.3 adapting, initiating, renewing/continuing, discontinuing or administering medication as authorized
  CP2.4.4a dispensing and/or
  CP2.4.4b compounding and/or
  CP2.4.4c delegating/authorizing such tasks to others appropriately
  CP2.4.5 engaging the patient or care-giver through education, empowerment and self-management, and
  CP2.4.6 negotiating the role of pharmacy and non-pharmacy team members in continuity and transitions of care.

☐ CP2.5 Follow-up by monitoring, evaluating progress toward achievement of the patient’s goals of therapy, adjusting plans in collaboration with the patient and health team members across the care continuum.

CP3 – Actively contribute, as an individual and as a member of a team providing care, to the continuous improvement of health care quality and patient safety

☐ CP3.1 Recognize and respond to harm and potential harm from health care delivery, including patient safety incidents;

☐ CP3.2 Adopt strategies that promote patient safety and address human and system factors;

As Communicators, pharmacy graduates:

CM1 – Communicate in a responsible and responsive manner that encourages trust and confidence

☒ CM1.1 Select and use oral, non-verbal and written communication strategies (tools, techniques, technologies, etc.) effectively so that the patient’s best interests are foremost;

☑ CM1.2 Provide timely, clear responses that are tailored to the context and audience;
CM1.3 Express facts, evidence, opinions and positions accurately and effectively, with clarity and confidence;

CM1.4 Listen, actively solicit and respond appropriately to ideas, opinions and feedback from others;

CM1.5 Use language, pace, tone, and non-verbal communication that is suitable for:
   a) the intended outcomes of the communication, and
   b) the complexity, ambiguity, urgency and/or difficulty of a situation, conversation or conflict

CM1.6 Seek and synthesize relevant information from others in a manner that ensures common understanding and where applicable, clarifies and secures agreement and/or consent;

CM1.7 Compose and share oral, written, and electronic information in a manner that optimizes patient safety, dignity, confidentiality, and privacy.

CM2 – Communicate in a manner that supports a team approach to health promotion and health care

CM2.1 Engage in respectful, empathetic, compassionate, non-judgmental, culturally safe, tactful conversations with patients, communities, populations, and health team members;

CM2.2 Demonstrate awareness of the impact of one’s own experience level, professional culture, biases and power and hierarchy within the health team on effective working relationships, communication and conflict resolution with health team members and adapt the approach to the situation appropriately;

CM2.3 Demonstrate accuracy and appropriateness of communication as well as respect for the role of other health team members when disclosing information about harmful or potentially harmful situations;

CM2.4 In word and in action, convey the importance of teamwork in patient-centred care, patient safety, health care quality improvement and health program delivery.

As Collaborators, pharmacy graduates:

CL1 – Work effectively with members of the health team including patients, pharmacy colleagues and individuals from other professions

CL1.1 Establish and maintain positive relationships;

CL1.2 Recognize, respect and negotiate the roles and shared/overlapping responsibilities of team members;

CL1.3 Join with others in respectful, effective shared decision-making.

CL2 – Hand over the care of the patient to other pharmacy team members and non-pharmacy team members to facilitate continuity of safe patient care
☐ CL2.1 Determine when and how care should be handed over to another team member;

☐ CL2.2 Recognize, respect and honour the negotiate shared and overlapping responsibilities of patients, pharmacy team members and other health members when handovers occur;

☐ CL2.3 Demonstrate safe handover of care, using oral, written, and electronic communication, during a patient transition to a different care provider or setting.

As Leader-Managers, pharmacy graduates:

**LM1 – Contribute to optimizing health care delivery and pharmacy services**

☐ LM1.1 Work with others to apply quality improvement strategies and techniques to optimize pharmacy care;

☐ LM1.2 Contribute to a culture of patient safety;

☐ LM1.3 Confirm the quality, safety, and integrity of products;

☐ LM1.4 Use health informatics to improve the quality of care, manage resources and optimize patient safety.

**LM2 – Contribute to the stewardship of resources in health care systems**

☐ LM2.1 Apply evidence and management processes to achieve cost appropriate care;

☐ LM2.2 Allocate health care resources for optimal patient care;

☐ LM2.3 Contribute to the management of finances and health human resources in pharmacy practice settings;

**LM3 – Demonstrate leadership skills**

☐ LM3.1 Demonstrate leadership skills to enhance pharmacy practice and health care.

**LM4 – Demonstrate management skills**

☐ LM4.1 Work with others to apply the principles of effective management and supervision of health human resources and medication use systems;

☐ LM4.2 Use effective strategies to manage and improve their own practice of pharmacy.

As Health Advocates, pharmacy graduates:

**HA1 – Respond to an individual patient’s health needs by advocating with the patient within and beyond the patient care environment**
HA1.1 Work with patients to address determinants of health that affect them and their access to needed health services or resources;

HA1.2 Work with patients to increase opportunities to adopt healthy behaviours;

HA1.3 Incorporate disease prevention, health promotion and health surveillance into interactions with individual patients.

HA2 – Respond to needs of communities or populations they serve by advocating with them for system-level change in a socially accountable manner

HA2.1 Work with community or population to identify the determinants of health that affect them;

HA2.2 Participate in health promotion and disease prevention programs.

As Scholars, pharmacy graduates:

SC1 – Apply medication therapy expertise to optimize pharmacy care, pharmacy services and health care delivery

SC1.1 Use knowledge and problem-solving to arrive at recommendations and decisions that are appropriate, accurate, and practical;

SC1.2 Use professional experience to solve routine, previously encountered problems;

SC1.3 Use established decision-making frameworks and apply learning required to manage new situations and problems.

SC2 – Integrate best available evidence into pharmacy practice

SC2.1 Generate focused questions related to needs for information, recommendations and decisions in practice;

SC2.2 Use systematic approaches in the search for best available evidence;

SC2.3 Critically appraise health-related research and literature;

SC2.4 Incorporate best available evidence in the decision-making process.

SC3 – Contribute to the creation of knowledge or practices in the field of pharmacy

SC3.1 Apply scientific principles of research and scholarly inquiry;

SC3.2 Apply ethical principles that underlie research and scholarly inquiry.

SC4 – Teach other pharmacy team members, the public and other health care professionals including students
SC4.1 Provide effective education to others;
SC4.2 Employ appropriate teaching roles when teaching others;
SC4.3 Deliver effective feedback in teaching and learning situations;
SC4.4 Use appropriate learning assessment and evaluation strategies when working with patients, team members, students and teachers.

As Professionals, pharmacy graduates:

PR1 – Committed to apply best practices and adhere to high ethical standards in the delivery of pharmacy care

PR1.1 Exhibit professional behaviour whether face-to-face, in writing, or via technology-enabled communication. Professional behaviour includes, but is not limited to:
   a) demonstrating honesty, integrity, humility, commitment, altruism, compassion, respect for diversity and patient autonomy;
   b) being accessible, diligent, timely and reliable in service to others;
   c) abiding by the principle of non-abandonment;
   d) maintaining appropriate interpersonal boundaries;
   e) maintaining professional composure, demeanor, and language even in difficult situations, and;
   f) maintaining privacy and confidentiality;

PR1.2 Use ethical frameworks as one component of professional judgment;
PR1.3 Recognize and respond to situations presenting ethical dilemmas, including conflicts of interest;
PR1.4 Engage in activities that:
   a) protect the public, and;
   b) advance the practice of pharmacy.

PR2 – Able to recognize and respond to societal expectations of regulated health care professionals

PR2.1 Take responsibility and accountability for actions and inactions;
PR2.2 Demonstrate a commitment to patient safety and quality improvement;
PR2.3 Honour the laws, ethical codes, and regulatory requirements (by-laws, standards, policies) that govern the self-regulated profession of pharmacy;
PR2.4 Demonstrate an understanding of federal, provincial/territorial, and municipal laws, policies and standards that apply to pharmacy workplaces;
PR2.5 Demonstrate an ability to maintain competence to practice through evaluating areas for improvement and planning, undertaking learning activities to address limitations in competence and/or performance and incorporating learning into practice;

PR2.6 Identify and respond to unprofessional, unethical, and illegal behaviours in pharmacists, other pharmacy team members, and other health professionals.

PR3 – Committed to self-awareness in the management of personal and professional well being

PR3.1 Set professional and personal goals, priorities, and manage their time to balance patient care, workflow, and practice requirements;

PR3.2 Examine, reflect upon, and manage personal attributes (knowledge, skills, beliefs, biases, motivations, emotions, etc.) that could influence self-development and professional performance;

PR3.3 Adapt their practice of pharmacy to fulfill evolving professional roles;

PR3.4 Recognize and respond to self and colleagues in need.