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NMDF211 SUBJECT STUDY GUIDE

As students in the ‘knowledge-age’, you are increasingly confronted with a vast array of information that is sometimes conflicting and contested. As students and practitioners, you must be able to seek, evaluate and synthesize information, and be active participants in the development of your own knowledge and understanding. Subsequently, you will become more responsive and dynamic practitioners who are able to ensure your ongoing capacity to effectively work within the changing nature and demands of society and enhance the field of Natural Health Practice.

A solid understanding of nutritional biochemistry is essential to facilitate critical enquiry, interpret mechanistic nutrition research and guides evidence-based practice. This subject integrates knowledge from biomedical science and Foundations of Human Nutrition to further advance students understanding of nutritional biochemistry. Lecturers can access the weekly readings for this subject in the students’ folder. Lecturers are encouraged to bring their own clinical experience to reinforce clinical application as appropriate. Students will have access to the following documents that are created, modified and managed by the Subject Coordinator:

1. Subject Outline
2. Subject Study Guide
3. Handout version of the lecture notes
4. Reading list
5. Weekly readings

Students can download these from Endeavour LMS.

How to best utilize directed self-learning

This Subject Study Guide (SSG) has been produced to assist you to explore, investigate, critically analyze and evaluate the principles and practice in this subject of study and to encourage you to achieve deeper levels of learning. As an approach to study, it is suggested that you read the questions for each session first. These questions will guide you through your reading, note-taking and research.

The following suggestions will assist you to pre-read effectively:

- Highlight the key points during your pre-readings.
- In the case of lengthy readings or documents, summarize and write your own synopsis.
- Answer questions or complete activities as directed.
- Jot down any queries, questions or concerns for discussion in class.

TO START

- Read the Subject Outline and pay particular attention to the Learning Outcomes, Set Texts and Assessment Tasks for this Subject of Study. Make certain that you understand what is expected of you to complete this subject successfully.

Textbook


Recommended readings:


**Recommended Readings:**

The reading materials listed in the weekly students folders on LMS provide additional research information and additional perspective for each weekly session in addition to the text recommended for the subject. Additional readings will enhance the students understanding of the topics covered in NMDF 211 Nutritional Biochemistry.

**Learning Outcomes**

1. Investigate the biochemical absorption, storage and metabolic function of macro- and micro- nutrients.
2. Illustrate an understanding of the major metabolic pathways including the role of nutrient cofactors, substrates, enzymes and coenzymes in dysfunction when compared with normal metabolic function within the body.
3. Demonstrate an understanding of the inter-relationship between the nutrients and their metabolites involved in metabolic and detoxification pathways.
4. Examine and explain the links between inflammation, oxidation and antioxidants and the impact these can have developing physiological dysfunctions.
5. Understand the microbiome and its modulation through diet with the strategic aim to prevent dysfunction.
6. Describe the role of the nutrients in the synthesis of hormones and neurotransmitters and their action on metabolic dysfunction.
SESSION 1: Macronutrient Pharmacokinetics

Learning outcomes
Understanding of the metabolism of macronutrients: breakdown, absorption, transportation, distribution, delivery and storage of carbohydrates, lipids and proteins.

Session Overview
This session is designed to give you an overview of digestion, absorption, transport and storage of major macronutrients: carbohydrates, lipids and protein. This session is of vital importance in overall nutritional understanding.

Session Aims
- Understand the biochemical processes underpinning the digestion, absorption, transportation and metabolism of:
  - Carbohydrates
  - Lipids
  - Proteins

Carbohydrates:
They are important food source of energy. The major sources of dietary carbohydrate are the starches and the disaccharides. In the course of digestion, these are hydrolyzed by specific glycosidases to their component monosaccharides, which are absorbed into the circulation from the intestine. The monosaccharides then are transported to the cells of various tissues, passing through the cells’ outer membrane by facilitative transport by way of transporters. Glucose is transported into the cells of many different tissues by the GLUT family of transporters.

Lipids:
Lipids are hydrophobic and require special handling while digesting. Ingested fat must be finely dispersed in the intestinal lumen in order to present a sufficiently large surface area for enzymatic digestion to occur. In the bloodstream, reassembled lipid must be associated with proteins to ensure its solubility in that environment while undergoing transport. The major sites for the formation of lipoproteins are the intestine, which produces them from exogenously derived lipids, and the liver, which forms lipoproteins from endogenous lipids.

Central to the processes of fat transport and storage is adipose tissue, which accumulates fat as triacylglycerol when the intake of energy-producing nutrients is greater than the body’s caloric needs. When there is energy demand, fatty acids are released from storage and transported to other tissues for oxidation.

Proteins:
Proteins in foods become available for use by the body after they have been broken down into their component amino acids. In the body, proteins play many vital roles including functions in structural capacities, and as enzymes, hormones, transporters, and immunological protectors, among other roles.

The amino acids are used in a variety of ways: (1) for synthesis of new proteins for growth and/or replacement of existing body proteins; (2) for production of important non-protein nitrogen-containing molecules; (3) for oxidation as a source of energy; and (4) for synthesis of glucose, ketones, or fatty acids. The liver is the primary site of amino acid metabolism.
Prescribed Reading from Text:
- Chapter 3 Carbohydrates
- Chapter 5 Lipids
- Chapter 6 Proteins

Additional Readings:
- Unit II Structure and Properties of the Macronutrients
- Unit III Digestion and Absorption of the Macronutrients

Revision Questions:
- Where does absorption of lipids occur in the body?
- Describe the essential components of protein digestion
- What is our main dietary source of energy? How does the body digest, transport and use these?

SESSION 2: Water Soluble Vitamins Pharmacokinetics

Learning outcomes
Understanding of the biochemical processes underpinning the digestion, absorption, transportation and metabolism of water soluble vitamins: Vitamin C, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B5, Vitamin B6, Vitamin B12, Folate, Biotin.

Session Aims
- Understand the biochemical processes underpinning the digestion, absorption, transportation and metabolism of the water soluble vitamins.

Session Overview
Vitamins are organic compounds with regulatory functions that are required in the diet if the species (humans) is unable to synthesise them. Thus, vitamins are considered essential (in fact *vita* means “life” in Latin). Moreover, because these substances must be supplied by the diet, their discovery often came about because of their absence in the diet. Vitamins, for the most part, are not related chemically and differ in their physiological roles. The broad classification of vitamins based on certain properties common to each group is:
- Water-soluble vitamins
- Fat soluble vitamins

This session will introduce you to all water soluble vitamins. The body handles the water-soluble vitamins differently from the way it handles the fat-soluble vitamins. Characteristics of water soluble vitamins:
- They are absorbed into portal blood, in contrast to fat-soluble vitamins,
- They cannot be retained for long periods by the body (exception: cobalamin (vitamin B12)).
- Storage occurs only as a result of their binding to enzymes and transport proteins.
Water-soluble vitamins are excreted in the urine whenever plasma levels exceed renal thresholds. With the exception of vitamin C (ascorbic acid), water soluble vitamins are members of the B complex. Most of the B-complex group can be further divided according to general function: energy releasing or hematopoietic.

Prescribed Reading from Text:

- Chapter 9 Water-Soluble Vitamins: Table 9.1 provides a brief description of Functions, Deficiency Syndromes, Food Sources, Recommended Intake, and Individuals at Risk for Deficiency.

Recommended Readings:


  [http://pubs.acs.org/doi/abs/10.1021/jf401545z](http://pubs.acs.org/doi/abs/10.1021/jf401545z)

Additional Readings:

- UNIT VI The Vitamins
  - 24. Niacin, Riboflavin and Thiamin
  - 25. Folate, Choline, Folic Acid, Vitamin B12, and Vitamin B6
  - 26. Biotin and Pantothenic Acid
  - 27. Vitamin C

Revision Questions:
- Compare the digestion and absorption of Vitamin C and Vitamin B6
- What is the active form of Folate?
- What inhibits absorption of Vitamin B1?
SESSION 3: Fat Soluble Vitamin and Macromineral Pharmacokinetics

Learning outcomes

Understanding of the biochemical processes underpinning the digestion, absorption, transportation and metabolism of: Vitamin A, Vitamin D, Vitamin E, Vitamin K, Calcium, Magnesium, Phosphorous, Sodium, Potassium.

Session Aims

- Understand the biochemical processes underpinning the digestion, absorption, transportation and metabolism of the fat soluble vitamins and macrominerals.

Session Overview

This Session addresses each of the four fat-soluble vitamins—A, D, E, and K and macrominerals.

Fat soluble vitamins:
The absorption and transport of the fat-soluble vitamins, in contrast to those of the water-soluble vitamins, are closely associated with the absorption and transport of lipids. As with dietary lipids, optimal fat-soluble vitamin absorption requires the presence of bile salts. Similarly, fat-soluble vitamins in the body initially are transported by chylomicrons. Moreover, the fat-soluble vitamins are stored in body lipids, although the amount stored varies widely among the four fat-soluble vitamins.

Refer Chapter 10 The fat-soluble Vitamins, Table 10.1 and 10.2 in Gropper S, Smith J (2016) Advanced Nutrition and Human Metabolism 7th ed, Wadsworth Cengage Learning, Canada, provides an overview of the discovery, function, deficiency syndrome, food sources, and recommended dietary allowance (RDA) or adequate intake (AI) of each of the fat-soluble vitamins.

Macro minerals:
The minerals constitute only about 4% of total body weight though they are of great importance in normal nutrition and metabolism.

Their functions are:
- Provide the medium essential for normal cellular activity,
- Determine the osmotic properties of body fluids,
- Impart hardness to bones and teeth, and
- Function as obligatory cofactors in metallo-enzymes.

Macro minerals, also called major minerals or macronutrient elements, are distinguished from the micro minerals by their occurrence in the body. The major minerals of the human body traditionally include calcium, phosphorus, magnesium, sodium, potassium, and chloride.

Refer Chapter 11 Macro minerals, Table 11.1 in Gropper S, Smith J (2016) Advanced Nutrition and Human Metabolism 7th Ed, Wadsworth Cengage Learning, Canada, for an overview of the macro minerals, including information on general functions, approximate body content, some enzyme cofactors, deficiency signs, food sources, and recommended intakes.

Prescribed Reading from Text:
- Chapter 10 Fat-Soluble Vitamins
- Chapter 11 Major Minerals
Discussion: Clinical issues of micronutrient metabolism:
Perspectives: Osteoporosis and Diet pp 450-453. Also in PDF version in Session 3 readings as necessary for class discussion.

Recommended Readings

Additional Readings:

- UNIT VI The Vitamins
  - 28. Vitamin K
  - 29. Vitamin E
  - 30. Vitamin A
  - 31. Vitamin D
- UNIT VII The Minerals
  - 32. Calcium and Phosphorus
  - 33. Magnesium
  - 34. Sodium, Chloride, and Potassium
  - 35. Body Fluids and Water Balance

Revision Questions:
- Compare the manufacture and production of Vitamins D and K
- Why are calcium and magnesium inter-dependent minerals?
- Explain the process of absorption, transportation and storage of Vitamin A.

SESSION 4: Micromineral Pharmacokinetics

Learning outcomes
Understanding of the biochemical processes underpinning the digestion, absorption, transportation and metabolism of: Iron, Molybdenum, Copper, Zinc, Selenium, Chromium, Iodine, Boron, Vanadium.

Session Aims
- Understand the biochemical processes underpinning the digestion, absorption, transportation and metabolism of the microminerals and ultra-trace elements.

Session Overview
This session covers most micronutrients and few ultra-trace elements. Micronutrients are also known as essential minerals or trace elements. Criteria to establish essentiality of a mineral:
- It is present in all healthy tissue of living things.
• Its concentration from one animal to the next is fairly constant.
• Withdrawing it from the body induces reproducibly the same physiological and structural abnormalities, regardless of species studied.
• Adding it either reduces or prevents these abnormalities.
• The abnormalities induced by deficiencies are always accompanied by specific biochemical changes.
• These biochemical changes can be prevented or cured when the deficiency is prevented or cured.

The difference in body content between the macro and microminerals is quite large. The body’s content of the macro minerals ranges from ~35 to 1,400 g, and that of the trace elements ranges from <1 mg to ~4 g. This session also covers two of the five ultra-trace elements (Boron and Vanadium). However, while copper, chromium, fluoride, iodine, molybdenum, and selenium are considered ultra-trace elements by definition, the Food and Nutrition Board includes them under “Micro Minerals,” based on the establishment of either an AI or an RDI.


Recommended Readings:


http://nutritionreviews.oxfordjournals.org/content/72/5/334

http://journals.cambridge.org/download.php?file=%2FBJN%2FBJN81_04%2FS0007114599000537a.pdf&code=43046599ea25ec3c3d961c531b3262e2

http://journals.cambridge.org/download.php?file=%2FBJN%2FBJN104_05%2FS0007114510001091a.pdf&code=09cf5654fe0aef06d4063bbf512011e1

Additional Readings:

• UNIT VII The Minerals
  o 36. Iron
  o 37. Zinc, Copper, and Manganese
38. Iodine
39. Selenium
40. Fluoride
41. Molybdenum and Beneficial Bioactive Trace Elements

Revision Questions:
- Which minerals act as antagonists to zinc?
- What is the process of absorption, transport, metabolism and storage of copper?
- Which minerals act as catalysts in the process of hormone production?

SESSION 5: Microbiome Prebiotics and probiotics

Learning outcomes
Understanding of the concept of microbiome and role of microorganism in maintaining gut integrity and thereby relevance for human health; probiotics and prebiotics: definitions, examples and mechanism of actions in strengthening microbiome and thereby moderating chronic diseases.

Session Aims
- Understand the biochemical processes of the nutrients that resist digestion, gut microbiota and their influence on gut health

Key Concepts
- SIBO / Gut dysiosis
- Effects of gut microbiota in prevention of dysbiosis
- Introduction to microbiome testing and use in prevention of dysfunctions
- Role of pro and prebiotics in moderating food intolerance, immunity and malabsorption syndromes

Prescribed Reading from Text:
- Chapter 4 Fiber

Recommended Readings:
SESSION 6: Liver detoxification

Learning outcomes
Understanding of the biochemical processes involved in liver detoxification phases 1 and 2 and alcohol detoxification and detrimental effects associated with excessive consumption.

Session Aims
- Review hepatic function (role of Kupfer cells, bile and filtration)
- Describe the liver detoxification pathways and the role of nutrient substrates, cofactors and enzymes involved in optimising liver function.
- Review of hepatic dysfunction including NAFLD.
- Discuss the harmful health impacts of alcohol consumption.
- Determine nutritional support for hepatic dysfunction and disease.
- Role of Glutathione in Liver detoxification.

Session Overview
We have seen that liver plays an important role in metabolism. It also filters and detoxifies the blood. The detoxification process occurs in liver and about 99% of blood gets purified in liver and only 1% of impurities/toxic materials are left for kidney to filter. This session describes the two phase process of liver detoxification. The phase I detoxification breaks down toxins and chemicals into intermediate metabolites. Phase II detoxification system conjugates intermediate metabolites with a variety of different enzymes and neutralizes the intermediate metabolite or makes the metabolite easier to eliminate via either bile or urinary excretion. Role of various nutrients and food is also established which control and regulate the whole biochemical process of liver detoxification.

Alcohol (ethanol) is consumed in the form of alcoholic beverages such as beer, wines, and distilled spirits. Though it is not a natural nutrient it yields 7 kcal/29 kJ per gram and may account for up to 10% of the total energy intake of moderate consumers and up to 50% for alcoholics. It is readily absorbed through the entire gastrointestinal tract and transported unaltered in the bloodstream and then oxidatively degraded in tissues, primarily the liver, first to acetaldehyde and then to acetate. Acetate subsequently is converted to acetyl CoA and oxidised via the Krebs cycle. Thus, the liver plays an important role in alcohol detoxification as well. At least three enzyme systems are capable of alcohol oxidation (detoxification):
- Alcohol dehydrogenase (ADH)
- The cytochrome P-450 system
- Catalase-H2O2 system

Importance of nutrients in alcohol detoxification, liver functioning and reducing alcohol cravings is also discussed under this session.
Prescribed Reading from Text:
- Chapter 5 Lipids; Ethyl alcohol: metabolism and biochemical impact

Recommended Readings:

Review Questions
- What are the principle differences in Phase 1 and Phase 2 liver detoxification?
- Which people may have difficulty metabolizing alcohol?
- List the nutrients important for reducing alcohol craving.

SESSION 7: Integration of Mind and Body

Learning outcomes
Revision of Endocrine system and an overview of HPA axis and its role in human health. Understanding of the biochemical pathways underlying hormonal regulation of biological processes.
Session Aims

- Understand the biochemical processes and the associated nutritional cofactors underpinning stress, HPA and endocrine systems and its significance for metabolic conditions in a human body.

Session Overview

- The session gives an overview of our endocrine system, classification of hormones, examples and functions of key hormones (cortisol, insulin) and their connection with HPA axis, list of nutrients required for their optimal synthesis, relationship of liver with managing these hormones and metabolic status (gut brain axis, gut-liver axis) and how stress affects HPA axis.

Recommended Readings:


Revision Questions:

- Explain role of HPA axis and effect of stress in dysfunction of HPA axis (100 words).
- List nutrients required for optimal functioning of cortisol and steroid hormones.
- Describe one evidence base lifestyle change that can modulate effects of stress on HPA.

SESSION 8: Nutrient Control of Gene Expression

Learning outcomes

Understanding of genetics and epigenetics and gene expression

Session Aims

Understanding of genetics and epigenetics and gene expression and ethical consideration in genetic testing

Session Overview

- DNA structure
- One carbon metabolism
- Epigenetics
- Methylation
- Ethics relating to genetic testing
The session explains DNA structure (purine, pyrimidine, synthesis, functions and nutrient necessary), epigenetic mechanisms (histone modifications, methylation) and role of telomeres in human ageing and diseases. The session also introduces one carbon metabolism that plays pivotal role in methylation, formation of methionine and glutathione and discusses its relevance in prevention of human health. Role of nutrients in modulating gene expression is discussed in detail in relation to disease prevention, ethical concerns in genetic testing are discussed.

Prescribed Readings from Text:

Activity Reading:


Recommended Readings:


Revision Questions:

- Discuss relevance of OCM in prevention of diseases
- Explain role of homocysteine in inflammatory conditions and nutrients to prevent it
- Functions of purines and pyrimidines
- List five ethical concerns in genetic testing

SESSION 9: Managing Oxidation

Learning outcomes
Understanding of the biochemical processes underpinning oxidative processes in the body, including both endogenous and exogenous free radicals and antioxidants; regeneration (Redox) pathways.
Session Aims
- Describe the nutritional biochemistry through which key nutrients have an anti-oxidant function.
- Describe the nutritional biochemistry through which key nutrients have a ‘redox’ effect on oxidised compounds
- State the importance of balance within the utilisation of key nutrients when utilising anti-oxidants.

Session Overview
- There are various nutrients in our body that function as antioxidants (Vitamins, peptides, coenzymes, minerals etc). This session comprehensively reviews how all of these individual nutrients function together to protect the body from destructive radicals and destructive non radical species. First half of the session reviews free radical chemistry. It then addresses how free radicals and selected non radicals are generated in the body, the damage caused by reactive oxygen and nitrogen species, and how the antioxidant nutrients function together to eliminate destructive radical and non-radical species.

Prescribed Reading from Text:
- Chapter 10, The Fat-soluble Vitamins; Perspective: The Antioxidant Nutrients, Reactive Species, and Disease.

Recommended Readings:

Review Questions:
- What are the main endogenous antioxidants?
- Name 3 exogenous antioxidants.
- Which nutrients effectively ‘recycle’ each other?

SESSION 10 Inflammation: Underlying Mechanisms of Origins of Diseases
Learning outcomes
Understanding of the biochemical processes underpinning inflammatory processes.
Session Aims

- Describe the biochemical pathways associated with inflammation and their associated nutritional cofactors.
- Describe the relationship between nutrition and immune function.
- Define the role of specific nutrients on immune function.
- Describe the impact of adiposity, metabolic syndrome on inflammatory processes.

Session Overview

This session explains the biochemical pathways associated with inflammation and their associated nutritional cofactors and describes relationship between nutrition and immune function. Metabolism of Eicosanoids - the most potent regulators of cellular function is also studied here. Functions of Eicosanoids include:

- Anti-inflammatory function
- Regulate smooth muscle contraction
- Increase water and sodium excretion
- Modulators e.g. some eicosanoids stimulate while others inhibit the same process.

This session describes role of various chemicals and nutrients that act as cofactors in each phase of inflammation and also covers the important anti-inflammatory nutrients.

Recommended Readings:


Review Questions:

- Describe eicosanoids and the functions they are involved in
Discuss role of specific nutrients in supporting immune system and downregulation of inflammation in context of prevention of metabolic diseases.

SESSION 11: Neurotransmitters

Learning outcomes

Understanding of classification and functions of neurotransmitters and their role in prevention of mental health.

Session Aims

- Synthesis of neurotransmitters
- Types of neurotransmitters
- Functions of neurotransmitters
- Nutrient and cofactors required for optimal function
- Relevance for mental health.

Session Overview

Definitions and functions with classification of key neurotransmitters is discussed. Food sources and nutrients required to maintain their balance is explained. Discussion on their role in key mental health issues are addressed.

Review Questions:

- Name three neurotransmitters that are synthesized from amino acid.
- Discuss functions of Dopamine
- List nutrients and foods required for optimal functioning of serotonin and acetylcholine

Activity reading


Recommended Readings:

SESSION 12: Mitochondrial Dysfunction

Learning outcomes

Understanding of the biochemical processes underpinning mitochondrial dysfunction.

Session Aims

Overview of mitochondria and CAC pathways

Nutrients and cofactors required

Role in chronic diseases

Session Overview

- This session explains the biochemical pathways in the mitochondria and their function/significance in energy production.
- In the cells, monosaccharides first are phosphorylated at the expense of ATP and then can follow any of several integrated pathways of metabolism. Cellular glucose can be converted to glycogen, primarily in liver and skeletal muscle, or it can be routed through the energy-releasing pathways of glycolysis, the tricarboxylic acid cycle (TCA cycle) or Krebs cycle and Electron Transport Chain (etc).
- Non-carbohydrate substances derived from the other major nutrients, the glycerol from triacylglycerols (fats) and certain amino acids, can be converted to glucose or glycogen by the pathways of gluconeogenesis. In gluconeogenesis, the reactions are basically the reversible reactions of glycolysis, shifted toward glucose synthesis in accordance with reduced energy demand by the body. The Cori cycle describes the liver’s uptake and gluconeogenic conversion of muscle-produced lactate to glucose.
- The fat mobilisation follows the adipocyte’s response to specific hormonal signals that stimulate the activity of the intracellular lipase. Fatty acids are a rich source of energy. Their mitochondrial oxidation furnishes large amounts of acetyl CoA for Krebs cycle catabolism, and in situations of low carbohydrate intake or use, as occurs in starvation or diabetes, the rate of fatty acid oxidation increases significantly with concomitant acetyl CoA accumulation. This causes an increase in the level of the ketone bodies—organic acids that can be harmful through their disturbance of acid-base balance but that also are beneficial as sources of fuel to tissues such as muscle and brain in periods of starvation.
- Current evidence in role of mitochondrial dysfunction with diseases and nutrients required to prevent this are explained.

Recommended Readings:


**Review Questions:**

• List five nutrients required to maintain mitochondrial function
• Give a brief overview of carbohydrates metabolic pathway in generating energy
• How to maintain optimum mitochondrial function to prevent diseases.

**SESSION 13: Homeostatic maintenance**

**Learning outcomes**

Understanding of the biochemical processes underpinning inflammatory processes.

**Session Aims**

• Body fluid, electrolytes and the role of the kidneys
• Acid-base balance and associated disorders
• Regulation of pH

**Key Concepts**

• Water distribution in the body and fluid compartments
• Osmotic pressure, characterisation of solutions and filtration forces
• Role of the kidneys
• Electrolytes and concentration in body fluids
• Acid-base balance and regulation of pH
• Acid-alkaline hypothesis
  • Estimating the potential renal acid load (PRAL) of foods
  • Primary benefits that may result from adherence to an alkaline diet

**Prescribed Reading from Text:**


• Chapter 12 Water and electrolytes

**Recommended Readings:**


  
  http://www.hindawi.com/journals/jeph/2012/727630/