University of Papua New Guinea
School of Medicine and Health Sciences
Division of Basic Medical Sciences
M. Med Part I
Lecture: Some Aspects of Nutrition

- Micronutrient deficiency, now referred to as Vitamin and Mineral Deficiency (VMD), is widespread among women and children in resource limited (developing) countries
- "VMD deprives about a billion people world-wide of their Intellect, Strength and Vitality"
- Individuals with multiple deficiencies are in a state of Micronutrient Starvation
    - They suffer from the "**Hidden Hunger**" that secretly suppresses their immune response, increasing the risk of developing infectious diseases
- Adequate amount of Micronutrients are needed at all ages,
- Effects of inadequate intake are particularly serious during periods of rapid growth, pregnancy, lactation and early childhood
- Iron, Zinc, Iodine and Selenium among others are very important for Physical and Cognitive development of children

How important is Iodine?

- Iodine is essential for biosynthesis of Thyroid hormones:
    - Thyroxine (T 4) and Tri-Iodothyronine (T 3)
- Inadequate intake of dietary iodine or regular consumption of diet containing anti-metabolites (Goitrogens) of Iodine metabolism can impair biosynthesis of Thyroid hormones, leading to a Spectrum of diseases: Iodine Deficiency Disorders (IDD)
- **Iodine Deficiency (ID) is regarded as the single most common cause of preventable mental retardation and brain damage in a population where the intake of iodine is insufficient**
- Severe ID that leads to Endemic Cretinism has been reduced World-wide because of implementation of dietary iodine supplementation programs {Universal Salt Iodization (USI) strategy}

What are some of the consequences of Iodine deficiency?

- Some clinical consequences of ID:
    - Severity can vary from Mild Intellectual Blunting to Frank Cretinism,
        - May include Gross Mental Retardation, Deaf Mutism, Short Stature, and various other defects
    - Mild to Moderate ID is prevalent in several countries including PNG
    - Of great prevalence are the more subtle degrees of mental impairment, which occur in apparently normal children with low dietary intake of iodine
        - Manifestations range from small neurological changes, to impaired learning ability and underperformance in school, including poor performance on formal tests of Psychomotor functions
- Dietary ID in Pregnant and Lactating women may have serious consequences:
    - Maternal ID can compromise the Thyroid status of the Fetus and Neonate
        - Maternal Thyroxine (T4) is required for Neurodevelopment of Fetus during the first half of gestation
        - Fetal Neurodevelopment is most vulnerable to damage during early gestation in women with Mild to Moderate ID
- Maternal milk is major source of Iodine for Thyroid hormone in Neonates
- Importance of adequate intake of Iodine by Lactating mothers cannot be overemphasized

- In women of childbearing age: ID can cause Infertility and set the stage for Miscarriage, Abortion, or Stillbirth during pregnancy

What are some of the metabolic functions of Zinc?

- Zinc is present in over 300 Metallo-proteins with wide range of biochemical functions
- Metallo-proteins that require Zinc for normal functioning include:
  - **Regulatory and transport proteins such as**:
    - **Gustin:**
      - Polypeptide in Saliva that is essential for normal development of Taste buds, (this account for the decreased taste acuity in Zn deficient individuals)
    - **Metallothionein:** (Zn induces biosynthesis of MT in GIT)
    - **Gene-Regulatory Proteins** (e.g., "Zinc fingers" – involved in sequence-specific DNA recognition and Gene expression)
      - Nucleoproteins that are involved in DNA Replication and Transcription

  - **Zn as Co-factors for many Enzymes**:
    - Carbonic Anhydrase (regulation of HCO_3^- ion),
    - Alcohol Dehydrogenase:
      - Alcohol causes increase loss of Zinc in urine
    - Nucleoside Phosphorylase:
      - Decrease activity cause by Zinc deficiency may result in accumulation of toxic levels of Nucleotides, leading to impaired cell division or cell death
    - Alkaline Phosphatase (ALP); Lactate Dehydrogenase (LDH),
    - Glutamine Synthetase; Glutamate Dehydrogenase (GDH),
    - Prolyl Hydroxylase:
      - Plays major role in post-translational modification of Collagen
    - Porphobilinogen (PBG) Synthase:
      - Plays major role in biosynthesis of Heme,
    - RNA and DNA Polymerases,

  - **Zn acts to modulate metabolism of Vitamin A**:
    - Biosynthesis of Retinol-binding protein
    - Conversion of Retinol to Retinal:
      - A process that is necessary for vision, thus the impaired dark adaptation in Zn deficient individuals
    - Transportation of Retinol from Liver, to other organs is possible only if hepatocellular secretion can take place via Zinc accumulation on Retinol-binding protein

ZINC NUTRITURE IN INFANTS:

- **First Six months of life**: Period of rapid growth, and Zn intake varies with the mode of feeding
- Relatively high Zinc requirements during this period can be met satisfactory from breast-milk alone for most "**healthy"** infants
  - Healthy breast-fed infants usually do not develop Zinc deficiency, because of the High Bioavailability (80%) of Zinc in breast milk,

- Cow's milk contains higher Zinc content than human breast milk, but the bioavailability (35%) is lower
    - Difference in Bioavailability is due to higher levels of Citrate and Lactoferin in Human breast milk, compared to high Phytates, Calcium and Casein in Cow's milk
- **From Six months to two years of age**, adequacy of Zinc intake becomes highly dependent on the amount and bioavailability of Zinc from Complementary foods
    - Breast-fed infants, and Low birth weight infants may be at risk for Zinc deficiency because of:
        - Increased requirements,
        - Potentially lower intake and/or
        - Lower absorption efficiency
- Zinc content of breast milk falls with duration of lactation
- Prolonged breast-feeding without adequately prepared Complementary foods may reduce Zinc intake, thereby increasing the risk of Zinc deficiency in infants
- Zinc deficiency may occur in children fed with Cow's milk, because of the high levels of Phytate, Calcium and Casein that impairs Zinc absorption
- Same holds true for Soymilk, which contains high levels of Phytate

NB:

- Zinc supplementation enhances Linear Growth and significantly reduces incidence of Anemia in children
    - Stunted children benefit more than non-stunted children;
    - Children up to 24 months of age benefit more than older children

SELENIUM (Se):

- Selenium is a co-factor in Glutathione Peroxidase, a major Antioxidant in cells
- Selenium is an essential component of De-Iodinase (Type 1) that catalyzes conversion of Thyroxine (T_4) to Tri-Iodothyronine (T_3)
    - De-Iodinase contains a specific Amino Acid called **Seleno-Cysteine**
- Conversion of T4 to Reverse T3 is catalyzed by enzyme called 5'-De-Iodinase that does not require Selenium
    - Deficiency of Selenium results in decreased conversion of T4 to T3,
        - which at the same time causes an increase in the conversion of T4 to reverse T3 (rT3), by 5'-Deiodinase that does not contain Seleno-Cysteine
- Deficiency of both Selenium and Iodine causes severe condition Myxoedematous Cretinism

How is Vitamin A transported in blood?

- Vitamin A in blood is transported bound to Retinol Binding Protein (RBP) and Transthyrethrin (TTR) in 1:1:1 molar ratio
- RBP is produced in liver as Apo-RBP
- RBP in circulation with vitamin A is called Holo-RBP
- In individual with normal status of Vitamin A, Apo-RBP is not released in significant amount from liver unless vitamin A is available to form Holo-RBP
- In well-nourished individuals 85 – 90% of Vitamin A is transported in blood as Holo-RBP

What are some of the functions of Vitamin A?

- Vitamin A is involved in Visual cycle
    - Rhodopsin = **11-cis-Retinal** + Opsin

- Vitamin A is involved in biosynthesis of Transferrin (Iron transporter)
  - **Vitamin A deficiency causes non-responsive Iron deficiency anemia**
- Vitamin A is involved in regulation of growth and differentiation
  - It is essential for biosynthesis of:
    - Glycoproteins required for normal growth regulation
    - Glycosaminoglycans (GAGs), which are components of Mucus (Mucin) secreted by epithelial cells
- In Vitamin A deficiency status:
  - Differentiation process slows down,
  - Keratin producing cells replace Mucin-producing cells in epithelial tissues in the Eyes, Lungs and Gut
  - Reduction in Mucus secretion leads to drying of epithelial tissues in the Eyes, Lungs and Gut,
  - Excess Keratin production causes Keratinization (e.g., in eye – causing Xerophthalmia (dry eye) which can result in blindness

Water soluble Vitamins: Biological active forms and Metabolic Functions

Common Names & Chemical Nature	**Biologically Active / Coenzyme forms**	**Metabolic functions of biologically active forms**
Thiamine or Vitamin B_1	Thiamine Pyrophosphate (**TPP**)	Coenzyme in Oxidative Decarboxylase reactions (Pyruvate, Alpha-Oxo-Glutarate, Alpha-Ketobutyrate
Riboflavin or Vitamin B_2	❑ Flavin Adenine-Dinucleotide (**FAD**), ❑ Flavin Adenine-Mononucleotide (**FMN**)	Coenzyme in some Dehydrogenase reactions, and in some Red-Ox reactions
Niacin: Nicotinic Acid; Nicotinamide	❑ Nicotinamide Adenine-Dinucleotide (**NAD**) ❑ Nicotinamide Adenine Dinucleotide Phosphate (**NADP**)	Coenzyme in several Dehydrogenase reactions, and in several Red-Ox reactions
Pyridoxine, Pyridoxal, Pyridoxamine (Vitamin B_6)	Pyridoxal-Phosphate **(B_6-Phosphate)**	Coenzyme in several enzymes: Amino Acid Decarboxylase, Transaminases, Delta-amino-Laevulinic Acid Synthetase (ALA-Synthase)
Pantothenic Acid	❑ Coenzyme A, ❑ Acyl-carrier Protein (ACP)	Carrier of Acyl groups in Acylation reactions
Cobalamin (Vitamin B_{12})	❑ Methyl-Cobalamin, ❑ 5'-Deoxyadenosyl Cobalamin	Coenzyme for One-carbon transfer reactions ($-CH_3$)
Folic Acid, Folate, Foliacin (Vitamin M)	Tetra-hydro-folic acid, Tetra-hydro-Folate (**FH_4, or THF**)	Coenzyme for One-carbon transfer reactions
Ascorbic Acid, (Vitamin C)	L-Ascorbic Acid, Dehydro-Ascorbate	Reducing Agent (electron donor), Antioxidant
Biotin	Prosthetic group of Carboxylases	Carrier of active CO_2 in carboxylation reactions

Fat Soluble Vitamins: Biological active forms and Metabolic Functions

Common Names & Chemical Nature	**Biological Active Forms**	**Metabolic functions of Active forms**
❑ Retinol (Vitamin A), ❑ All trans Retinol	11-cis Retinal,	❑ Prosthetic group in visual pigments, ❑ Cofactor role in biosynthesis of Cholesterol, ❑ Role in membrane biogenesis ❑ Role in cell differentiation
❑ Cholecalciferol (Vitamin D_3) ❑ Calciferol or Ergocalciferol (Vitamin D_2)	1,25-Dihydroxy-Cholecalciferol, 1,25-DihydroxyVitamin D_3	❑ Absorption of Calcium in GIT, ❑ Reabsorption & Mobilization of Calcium and Phosphate in Bone
Tocopherols (Vitamin E)	Alpha-Tocopherol, Beta-Tocopherol	Antioxidants protecting polyunsaturated fatty acids in membranes,
Phytomenadione (Vitamin K)	Vitamin K	Cofactor in Post-translational gamma-carboxylation of N-terminal Glutamic acid residue in blood clotting factors

What is the energy and macronutrient intake for People living with HIV/AIDS?

- HIV/AIDS specifically affects Nutritional status of PLWHA because it:
  - Increases energy requirements, Reduces food intake, and Adversely affecting nutrient absorption and metabolism
- Responsiveness of PLWHA to nutritional interventions depends on:
  - Viral load, Stage of the disease, Concurrent treatment, Body Mass Index and Presence or absence of Opportunistic Infections

- PLWHA have greater energy needs than uninfected individuals,
  - Extent of increased energy needs depends on progression and stage of HIV infection

- In **Asymptomatic PLWHA**:
  - Energy needs are **10% higher** than the accepted levels for healthy non-HIV infected persons of the same age, sex and physical activity level
  - Increase energy is needed to maintain body weight and physical activity, which are highly desirable for preserving quality of life

- In **PLWHA with symptoms or any opportunistic infection**:
  - Energy needs are **20% to 30% higher** than the acceptable level for health non-HIV infected persons of the same age, sex and physical activity level
    - Increase energy is needed to support weight recovery during and after HIV related illnesses

- *The 20 to 30% increase in energy intake may not be easily achievable because of poor appetite, inadequate dietary intake or other reasons caused by acute infection/illness*
- *However, food intake should be encouraged and increased to the extent possible, particularly during the period of recovery*

- Estimated increased energy requirements are to:
    - Compensate for increased level of Resting Energy Expenditure (REE)
    - Allow for normal Activity-related Energy Expenditure (AEE),

- Both of which together represent the Total Energy Expenditure (TEE)
    - TEE = REE + AEE

- Amount of Macronutrients consumed by PLWHA should be the same as for non-HIV infected adults

- Recommended ranges of values are that:
    - Proteins should contribute 12% to 15% of total energy intake;
    - Fat should contribute about 30% to 35% of total energy intake
    - Carbohydrates should contribute about 50 – 55% of total energy intake

UNGASS Declaration:

- Declaration of the commitment by **United Nations General Assembly Special Session** (UNGASS) dedicated to HIV/AIDS recognizes the need to integrate Food Support as part of a Comprehensive Response to HIV/AIDS

- UNGASS Declaration of June 2006, Article 28 States that:
    - **"… all people at all times, will have access to Sufficient, Safe, and Nutritious Food to meet their dietary needs and food preferences for an Active and Healthy Life, as part of a comprehensive response to HIV/AIDS"**

- According to the UNGASS Declaration:
    - **"All member states of the United Nations General Assembly MUST recognized that where Anti-Retroviral Therapy is necessary, Food is a Key Element in Strategies to Promote Adherence to it and its efficacy"**

- Efficacy of HAART treatment partly depends on the nutritional status of PLWHA
- Therefore, Nutritional Assessment and Counseling should be an integral part of all HIV/AIDS treatment programs

ANTHROPOMETRY: Nutritional Status of infants using WHO Anthro 2005 Software:

- Please See the attached CD containing the WHO Anthro 2005 Software
- Read the two papers attached to this lecture notes

Reference:

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3. Briefing Paper No. 7: WHO document on-line Publications@odi.com: World Health Organization, Geneva August 2006: 1 – 3
4. Castleman T, Seamon-Fosso E, Cogill B. Food and nutrition implications of antiretroviral therapy in resource limited setting. Food and Nutrition Technical Assistance; Technical Notes No. 7, Revised May 2004; 2 – 13.
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6. WHO; Nutrition and HIV/AIDS: Report by the Secretariat. 59th World Health Assembly; Provisional Agenda Item 11.3; A59/7, May 2006.
7. U. S. President's Emergency Plan for AIDS Relief (US PEPAR): Report on Food and Nutrition for People Living with HIV/AIDS. Submitted by the office of the U.S. Global AIDS Coordinator, U.S. Department of State: May 2006