SOME ASPECTS OF NUTRITION

University of Papua New Guinea
School of Medicine and Health Sciences
Division of Basic Medical Sciences
M. Med Part I

VJ Temple

What is Hidden Hunger?

- Micronutrient deficiency {Vitamin and Mineral Deficiency (**VMD**)}, is widespread among women and children in resource limited countries,
- "VMD deprives about a billion people world-wide of their Intellect, Strength and Vitality",
- VMD prevents effective utilization of Macronutrients and leads to malnutrition,
- An adequate diet, rich in macronutrients but deficient in micronutrients, often results in "**Hidden Hunger**" – a condition whose sub-clinical signs are not easily detected,

- Individuals with VMD are in a state of Micronutrient Starvation,
- Suffering from "**Hidden Hunger**" that secretly suppresses their immune response, increasing the risk of developing infectious diseases,
- Adequate Micronutrients are needed at all ages,
- Effects of inadequate intake are 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:** essential for biosynthesis of **Thyroid hormones**:
  - Thyroxine (T 4) & Tri-Iodothyronine (T 3),
- Inadequate dietary intake of Iodine or consumption of foods containing **Goitrogens** (anti-metabolites of Iodine) can impair biosynthesis of Thyroid hormones, leading to 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 population with insufficient intake of iodine,**
- Severe ID that leads to Endemic Cretinism is reduced World-wide because of implementation of Universal Salt Iodization (USI) strategy,

What are some consequences of Iodine deficiency?

Some clinical consequences of ID: Severity vary:

- 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, underperformance in school, poor performance on tests of Psychomotor functions,

- **Dietary ID in Pregnant and Lactating women may have serious consequences**:
  - Maternal ID can compromise Thyroid status of the Fetus and Neonate,
  - Maternal T4 is required for Neurodevelopment of Fetus during 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 Neonates,
- **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 (Zn)** is in over 300 Metallo-proteins with wide range of biochemical functions,

Some metallo-proteins requiring Zn:

- **Regulatory and transport proteins, e.g.,**:
  - **Gustin:** Polypeptide in Saliva that is essential for normal development of Taste buds, (this account for decreased taste acuity in Zn deficient individuals),
- **Metallothionein (MT):** Zn induces its biosynthesis in GIT,
- **Gene-Regulatory Proteins:** "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 several Enzymes (examples):

- Carbonic Anhydrase: Regulation of HCO_3^- ion,
- Alcohol Dehydrogenase: Alcohol metabolism,
- Nucleoside Phosphorylase: Decrease activity due to Zn deficiency result in accumulation of toxic levels of Nucleotides, causes impaired cell division or cell death,
- Alkaline Phosphatase (ALP),
- Lactate Dehydrogenase (LDH),
- Glutamine Synthetase;
- Glutamate Dehydrogenase (GDH),
- Prolyl Hydroxylase: required for post-translational modification of Collagen,
- Porphobilinogen (PBG) Synthase: for Heme synthesis,
- RNA and DNA Polymerases, etc…

Zn acts to modulate metabolism of Vitamin A:

- Biosynthesis of Retinol-binding protein,
- Conversion of Retinol to Retinal for formation of visual pigments:
  - Process necessary for vision; thus 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 Zn accumulation on Retinol-binding protein;

ZINC NUTRITURE IN INFANTS

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

- **From Six months to two years of age**, adequacy of Zn intake becomes highly dependent on the amount and bioavailability of Zn from Complementary foods,
- Breast-fed, Low birth weight infants are usually at risk for Zn deficiency because of:
  - Increased requirements,
  - Potentially lower intake and/or
  - Lower absorption efficiency,
- Zn content of breast milk falls with duration of lactation,
- Prolonged breast-feeding without adequately prepared Complementary foods may reduce Zn intake, thereby increasing the risk of Zn deficiency in infants,

- Zn deficiency may occur in children fed with Cow's milk, because of the high levels of Phytate, Calcium and Casein that impairs Zn absorption,
- Same holds true for **Soymilk**, which contains high levels of Phytate,
- **NB:**
  - Zn 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 (Se):**
- Co-factor in Glutathione Peroxidase, an Antioxidant in cells,
- Essential component of **De-Iodinase** (Type 1) that catalyzes conversion of Thyroxin (T_4) to Tri-Iodothyronine (T_3),
  - De-Iodinase contains an Amino Acid: **Seleno-Cysteine,**
  - Conversion of T4 to Reverse T3 (r T3) is catalyzed by **5'-De-Iodinase** that does not require Se;
  - Deficiency of **Se** results in **decreased conversion of T4 to T3,** but causes **increase conversion of T4 to rT3, by 5'-Deiodinase** that does not contain Seleno-Cysteine,
- Deficiency of both **Se** and **Iodine** causes the severe condition **Myxoedematous Cretinism,**

How is Vitamin A transported in blood?

- In blood: **Vit A** is transported bound to Retinol Binding Protein (RBP) and Transthyrethrin (TTR) in molar ratio of **1:1:1**,
- RBP is produced in liver as **Apo-RBP**,
- RBP in circulation with Vit A is called **Holo-RBP,**
- In individual with normal Vit A status, Apo-RBP is not released in significant amount from liver unless Vit 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,
- Vit A is involved in biosynthesis of Transferrin,
  - **Vitamin A deficiency can cause non-responsive Iron deficiency anemia,**
- Vit A is involved in growth regulation and differentiation,
- Vit A 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 & 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 (Vit 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 affects Nutritional status of PLWHA because it:
  - Increases energy requirements,
  - Reduces food intake,
  - 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,
  - 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 Resting Energy Expenditure (**REE**),
- Allow for normal Activity-related Energy Expenditure (**AEE**),
- Both together represent 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 to contribute 12% to 15% of total energy intake,
- Fat to contribute about 30% to 35% of total energy intake,
- Carbohydrates to contribute 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 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 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 MUST be an integral part of all HIV/AIDS treatment programs;**

REFERENCES

- Textbook of Biochemistry with Clinical Correlations, 4th Ed, Edited by T. M. Delvin, Wiley-Liss, Brisbane, 1993; 1127 – 1128.
- Harper's Illustrated Biochemistry 26th Edition; 2003; Ed. By R. K. Murray et. al.
- Biochemistry, By V. L. Davidson & D. B. Sittman. 3rd Edition.
- Shils ME, Olson JA, Shike M, Ross AC, eds. Modern Nutrition in Health and Disease 9th Edition. Lippincott Williams & Wilkins, Sydney 1998; 223 – 239, 741
- Briefing Paper No. 7: WHO document on-line Publications@odi.com: World Health Organization, Geneva August 2006: 1 – 3
- 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.
- WHO; Nutrient Requirements for People Living with HIV/AID: Report of a Technical Consultation, World Health Organization, Geneva, 13 – 15 May 2003
- WHO; Nutrition and HIV/AIDS: Report by the Secretariat. 59th World Health Assembly; Provisional Agenda Item 11.3; A59/7, May 2006.
- 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
- VJ Temple Biochemistry 1001: Review and Viva Voce Questions and Answers Approach; Sterling Publishers Private Limited, 2012, New Delhi-110 – 020.