



# ICOOG



## CAMPUS

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# UPDATES ON NUTRITION IN WOMEN



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## PRESIDENT'S MESSAGE

Dear Friends,

Warm Greetings!

Population across urban and rural areas in India suffers from many forms of malnutrition and non-communicable diseases (NCDs) due to unhealthy dietary habits.

Unhealthy dietary habits and low physical activity are major concerns that contribute not only to overweight and obesity, but also to a significant proportion of the disease burden (NCDs) in the country. Proper nutrition and diet are the major contributors to shape the health of the individuals. If diet diversity is promoted along with other dietary modifications among individuals in the community, the panoramic view of the current scenario of malnutrition can be flipped.

As per the World Health Organization (WHO), 3.9 million deaths and 16.0 million disability adjusted life years (DALYs) are attributable to low fruit and vegetable (F&V) consumption. Diet alone contributed to 56.4% of risk for CVD DALYs in India.

The World Economic Forum (2014) reported that 3.55 trillion \$ will be lost in India due to NCDs between 2012-2030 and CVD is the top most disease to cause the economic loss. Therefore, decreasing the DALYs of NCDs & CVDs is a national priority which might be achieved on consuming 500g / fruits and vegetables.

This year my FOGSI slogan is SwasthNari, SukhiNari. My CSR activity is defined as Badlaav (Change) including three arms- Ekikaran (integration of thought and action), Samanta (equality of treatment irrespective of economic status) and Takniki (technology to achieve these objectives). These academic conferences will be a step ahead towards making a difference in women care in our country. I would like to request you all to join forces and become a volunteer for our Badlaav initiative by conducting free gynecology checkups in your clinics on 18th of every month.

### BADLAAV - BEHAVIORAL CHANGE

Increasing the consumption of F&V remains to be a challenge to most of the developed and developing countries in the world. Behaviour change communication intervention to re-shift diets from ultra-processed foods to minimally processed foods is the need of the hour.

Improvement in dietary habits among population has the potential to Reduce the burden of stunting, wasting, anaemia Reduce the burden of overweight, abdominal obesity Reduce the burden of non-communicable diseases (NCDs) Increase productivity and reduce cost of hospital expenditure.

This ICOG CAMPUS ON NUTRITION is going to help to understand the importance of Nutrition in various phases of life of women.

I congratulate ICOG Chairperson Dr. Laxmi Shrikhande, and Dr. Vidya Thobbi, Editor and all contributors of this issue.

**Dr. Hrishikesh Pai**  
President, FOGSI



## CHAIRPERSON'S MESSAGE

Dear Fellows & Members,

It brings me great pleasure to present this year's ICOG Campus on the issue of 'Updates on Nutrition in Women'. My motto as Chairperson of this esteemed college is to 'Refresh, Research and Reform' the knowledge and skills of all ICOG members and fellows in a comprehensive manner. This 'RRR' approach is designed to help us effectively face the challenges posed by complex clinical scenarios in our daily practice.

In this endeavour, we conceived the idea of discussing an issue with broad implications for women's health. Nutrition is a basic human need and a prerequisite to a healthy life, from the womb-to-tomb. Knowledge on the role of nutrition at critical stages of a woman's life is of paramount importance for the well-being of women and especially so in today's era, considering the dual challenge of nutrient deficiencies and the rapidly increasing rates of overweight / obesity in the population. If a woman is healthy, her family is healthy and in turn, the nation is healthy.

We have carefully curated the topics, adopting a life-course approach to address nutrition issues so as to bridge the gap in understanding key nutritionally-sensitive life stages. Although it is not possible to cover each and every topic in a small campus, we are confident that we have provided a holistic view and a starting point for the integration of nutrition services in healthcare settings.

I extend my gratitude to the issue editor Dr. Vidya Thobbi for her untiring efforts in preparing this issue of the ICOG campus. I hope the readers find this exercise useful. I look forward to a very eventful year and solicit your participation in all our academic activities.

YOU ARE WHAT YOU EAT

HAVE A FRUITFUL READING

**Dr. Laxmi Shrikhande**  
Chairperson, ICOG



## VICE CHAIRPERSON'S MESSAGE

India is facing a burden of malnutrition, nearly a quarter of women of reproductive age are undernourished, with a body mass index (BMI) of less than 18.5 kg/m (and on the contrary, we have incidence of obesity rising. It is estimated nearly one-third of women of reproductive age and nearly half of the pregnant women are anaemic all across the world. The WHO has classified India as a country with severe anaemia among pregnant women. Men and women have different nutritional needs due to their biological differences in the body. Hormonal changes associated with menstruation, childbearing, and menopause make women at higher risk of anaemia, osteoporosis, and various nutritional deficiencies. Moreover, in developing nations women are more likely to experience nutritional inadequacies due to socioeconomic factors such as low social status, poverty, and illiteracy. Additionally, inequalities in household work can also put a woman at risk of malnutrition. According to UNICEF, Indian women's diets are frequently insufficient to meet their nutritional demands. Thus it is imperative that we as health care providers of women should understand these needs and issues.

The ICOG campus talks about various aspects of nutritional issues and will be a helpful ready reckoner for clinicians. I must appreciate all the authors who have contributed to the issue on nutrition. A special appreciation to our Governing council member Dr. Vidya Thobbi for compiling these articles and Dr. Laxmi Shrikhande, Chairperson of ICOG for her constant encouragement.

Happy reading.

**Dr. Parag Biniwale**  
Vice Chairperson, ICOG



## SECRETARY'S MESSAGE

Dear Friends,

Namaskar!

Greetings from Indian College of Obstetricians & Gynecologists,

Globalization has affected eating habits and has enforced people to consume fancy and high calorie foods "JUNK FOODS".

Lifestyle changes has compelled us so much that one has so little time to really think what we are eating is healthy. Nutrition is a critical part of health and development especially in different phases of life like adolescent and mid life. A well-balanced diet rich in fruits, vegetables, and whole grains provides the proper nutrition to support a healthy lifestyle. Good nutrition not only improves infant, child and maternal health but also strengthens immune systems, lower risk of non-communicable diseases (such as diabetes, cardiovascular disease, stroke, some cancers, osteoporosis), and improves longevity. The articles on Vitamin B12, D and Calcium are going to update and enrich the readers.

It gives me immense pleasure to introduce this edition of ICOG Campus on "Nutrition" which is covering all the related aspects.

I congratulate the editor and her team for bringing out Campus.

Happy reading

**Dr. Ashok Kumar**  
Secretary, ICOG



## FROM THE EDITORS DESK

### GREETINGS

It gives us immense pleasure to present to you the “ICOG CAMPUS Nutrition in Women”. I am grateful to Dr. Hrishikesh Pai, President FOGSI and Dr. Madhuri Patel Secretary General FOGSI, our dynamic Chairperson ICOG Dr. Laxmi Shrikhande for constant encouragement and entrusting us with this opportunity.

On behalf of the editorial team I thank all the authors for their valuable contributions in covering important aspects of nutrition in women in their articles. We have covered some of the rare topics like nutrition in immunocompromised women and Oncology and Nutrition

As you are aware According to national level surveys 40% of the population, majority is of women, in India consume are that, undernutrition continues to be a major public health issue in India associated with mortality and poor health outcomes among children and prevent them from reaching their full potential. This is coupled with undernutrition among women during their pregnancy, a significantly prevalent scourge which takes its toll not only on the mother herself, but also on the newborn baby.. Better nutrition means stronger immune systems, fewer incidences of illness and better health. The nutritional status of women is important both for the quality of their own lives and the survival and healthy development of their children.

The first 1,000 days are a time of tremendous potential and enormous vulnerability. How well or how poorly a mother and child are nourished and cared for during this time has a profound impact on the women’s health & well-being and child’s ability to grow, learn, and thrive. This is because the first 1,000 days are when a child’s brain begins to grow and develop and when the foundation for their lifelong health is built. As health care providers and leaders within the health care delivery system, we have a critical role to play for ensuring optimum health for women and young children. There is a felt need to enhance the capacities of health care practitioners in both public and private sector to provide quality nad evidence based maternal infant and young child nutrition services, creating a mother baby friendly health systems environment. The second phase of POSHAN Abhiyaan launched recently to accelerate the reduction of under-nutrition in the first 1,000 days of life, reiterates government’s commitment at highest level.

A critical component towards improving this situation is the capacity of healthcare providers for optimal Maternal, Infant and Young Child and Adolescent Nutrition (MIYCAN) service delivery by translating knowledge into practice.

HAPPY READING

EAT RIGHT BE BRIGHT

**Dr. Vidya Thobbi**  
Issue Editor

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## ADOLESCENT NUTRITION : DEVELOPING VULNERABILITY AND LOSING OPPORTUNITIES

**Dr. Parag Biniwale**

Vice Chairperson  
ICOG

Adolescence is the transitional phase of life between childhood and adulthood where growth and maturation of all organ and physiological systems are happening at a rapid pace. Typically ranging from 10 to 19 years of age, it is a unique stage of human development and an important time for laying the foundations of good health. Growth and development are also transformative phenomena and have been found to have profound consequences not only for an individual's health in later life but might impact subsequent generations. The phase of accelerated growth and development in adolescence can be seen in physical, cognitive, and psychosocial domains; affects how adolescents feel, think, make decisions, and interact with the world around them.

Currently, adolescents contributing to the world's largest population (approximately 253 million, 20% of the total population of India) is a huge opportunity for India to invest in its future health. The current generation of adolescents is growing all over the world and especially in India, at a time of unprecedented changes in food environments, whereby nutritional problems of micro nutrient deficiency and food insecurity persist, and overweight and obesity are increasing.

### **Adolescence and Nutrition : Understanding the Physiology**

Adolescence is a nutrition-sensitive period for growth, in which the benefits of good nutrition extend not only to many physiological systems but also have a formative role in milestones of the adolescence. Adolescence physiologically starts between the age of 8 and 13 years in girls and 9 and 14 years in boys. However, in the last two decades, several studies have shown that the onset of puberty has moved earlier by 12-18 months. Some of the hypotheses trying to explain this change include the role of nutritional status, obesity, and the influence of extrinsic factors such as exposure to endocrine-disrupting chemicals (EDCs), as well.

The hypothalamic-hypophysis-gonadal axis develops during embryo genesis, and except for a period of activation immediately after birth, remains suppressed until the onset of pubertal development. At the beginning of puberty, the pulse generator is reactivated, probably due to progressive stimulatory influences on GnRH neurons from glial signals and neurotransmitters.

Nutrition is also one of the determinants of the timing and pattern of puberty, adult height, and muscle and fat mass accrual. Nutrition in adolescence also plays a critical role as a risk factor for non-communicable diseases, cardiorespiratory fitness, neuro-development, and immunity in later years of life. High rates of early adolescent pregnancy in many countries is a major concern and continue to jeopardize the growth and nutrition of female adolescents.

**Pubertal maturation** : The onset and duration of puberty are significantly affected by the pattern of childhood nutrition. Among healthy girls in LMICs during 2009-17, the mean age at menarche was estimated to be 12.3 years. In some LMIC populations, where nutrition has improved to a lesser extent than in typical LMIC populations, the mean age of menarche has been significantly delayed. Adiposity is associated with the pubertal form. For girls, the mean age of the larche (ie, breast budding) an early indicator of gonadal maturation is 10.2 years for individuals with underweight, 10.4 years for

individuals with normal weight, and 8.4 years for individuals with overweight. In boys, the mean age of puberty onset indicated by the scrotum becoming pendulous is - 11.3 years for individuals with underweight, 11.0 years for individuals with normal weight, and 10.3 years for individuals with overweight.

Other factors that influence pubertal maturation are childhood obesity, maternal obesity before conception, lesser duration of breastfeeding, high intake of animal proteins, and high intake of carbohydrates and fats contribute to early gonadal maturation and early onset of puberty.

**Linear growth :** Adolescent linear growth has the highest velocity after infancy and occurs in a two-step cellular process at the growth plate. First, bone elongation cells that are chondrocytes Second, bone-secreting cells that are osteoblasts. Many nutrients are important for chondrocyte function and for ensuring mineral consolidation. Any nutritional intervention to ameliorate retardation in linear growth should consider both of these steps, with the added challenge that the underlying cause originates from past conditions in which the child lived and might be neither evident nor reparable due to missed opportunity, epigenetic effects, or both. And hence Nutrition-specific interventions alone are not likely to restore lost growth. Other environmental factors such as socioeconomic conditions, daily exercise, or physical hardship, affect the Linear growth. Higher linear growth was found to be associated with a high dietary intake of milk throughout childhood, and scarcity of food especially during famine or droughts was associated with lesser mean height attained at puberty.

**Body composition :** During adolescence, changes in the proportions and distribution of bone, muscle, and fat form the foundation of metabolic and musculoskeletal health. The onset and duration of puberty and nutrition can affect peak bone mass. Late onset of puberty has been associated with a 10% decrease in bone mineral density and an increased risk of hip fracture in later life. Lean muscle mass increases in girls and boys during adolescence; however, the lean muscle mass acquisition rate is higher in boys. Independent of chronological age, puberty is associated with an average 1.14 kg/year increase in absolute fat mass in girls. In boys, absolute fat mass is relatively stable over the pubertal period, which results in a decrease in body fat percentage during adolescence as a result of rapid increases in lean mass.

### **Nutritional Requirements During Adolescence**

The growth spurt in adolescence requires rapid tissue expansion with special nutrient requirements, including amino acids for the growth of striated muscle, as well as calcium and vitamin D to accommodate bone growth. Energy and nutrition requirements must match the needs of the adolescents as they typically engage in physical work or recreational exercise (boys on average more than girls), which benefits striated muscle mass enlargement.

Appetite increases during adolescence, and sedentary individuals are more likely to accumulate fat if they have access to high-energy food. Thus, low activity levels among adolescents are a key factor that underlies increases in adolescent obesity across the globe. Adolescent males' caloric requirements are higher than adolescent females, owing to greater increases in height, weight, and lean body mass.

Recently, there has been an increase in the trend toward excess consumption of total fat and saturated fat, cholesterol, sodium, and sugar. There appears to be an increasing prevalence of obesity among adolescents worldwide, explained by wide spread nutrition transitions to lipid-rich diets and a decrease in physical activity, especially among urban adolescents. Other unhealthy behaviors, such as smoking, drinking, and illicit drug use, often begin during adolescence and are closely related to physiological and nutritional aspects.

## Healthy Eating in Adolescence

Growth and development in puberty require additional energy. This energy is to be provided by healthy foods. Healthy eating involves a diet rich in fiber, with restricted salt intake, and adequate fruits, and vegetables. Chicken and fish are healthy options for a non-vegetarian diet over red meat.

Carbohydrates are the most important source of energy contributing to about 50-60% of total energy with no more than 10-25% of calories derived from sugars, such as sucrose and high fructose. It is recommended that only 30% of energy should be obtained from fat of which saturated fat should be <10%. Protein requirement is determined by lean body mass, which provides 10-15% of the total energy requirement. Dietary fiber intake should be 15.5-34.5 g/day for adolescent males and 16-28.5 g/day for adolescent females. Fluid is required to maintain hydration. Vitamins and other micronutrients are essential for normal body functioning.

Eating patterns and behaviors are influenced by many factors during adolescence, including peer influences, parental modeling, food availability, food preferences, costs, convenience, personal and cultural beliefs, mass media, and body image. These could be broadly classified as personal factors, including attitudes, beliefs, food preferences, self-efficacy, and biological changes; environmental factors, including family, friends, peer networks, school, fast food outlets, and social and cultural norms; and macro system factors, including food availability, food production, distribution systems, mass media, and advertising

Healthy eating in adolescents can be achieved by adopting one or multiple ways such as experimenting with recipes, ensuring breakfast intake, keeping healthy snacks available, proving or suggesting healthy choices for eating out, ensuring plenty of fluid intake daily, and restricting screen time to 2 hours a day. Additionally, at least 60 minutes of moderate-intensity physical activity is recommended for an adolescent. This should include daily aerobic exercises and exercises to strengthen bones for 3 days a week, and exercises to build muscles for the remaining 3 days.

### Addressing the knowledge gaps in adolescent nutrition

There are several knowledge gaps in adolescent nutrition that are considered to be the risk factors for poor nutrition in adolescence as follows

High fat, high sugar, low nutrient foods like French fries, chips, and carbonated drinks are of low cost and available easily

The false belief that healthy foods are not tasty

Poor knowledge and awareness

Poor parental modeling

Disordered eating due to fear of weight gain, building muscle mass (Anorexia Nervosa, Bulimia)

Social media influence

Addressing these risk factors, in one or multiple of the following ways, offers promising avenues for improving health and development in this age group.

First, both **micronutrient and macronutrient** supplements targeted at adolescents have significant potential to improve nutritional status. Iron and folic acid supplements have been given to address micronutrient deficiencies and anemia among adolescents and pregnant women. Macronutrient

supplements may also have positive effects on catch-up growth during adolescence, although evidence in this area is lacking. Macronutrient interventions can help to manage prevalent adolescent under nutrition, and although they could be provided to all adolescents to promote optimal nutrition during a critical window of growth, it is imperative to consider adverse consequences for adolescents who are overweight or obese.

Second, **food system interventions** offer a promising avenue to improve the availability and access to healthy foods for adolescents. One-third of adolescents globally are food insecure.

Globally, poor dietary quality is the leading risk factor for poor health. Average fruit and vegetable intake is below the WHO-recommended 400 g/d for adults in all regions of the world with the exception of East Asia; the average global intake of vegetables is ~200 g and has not shifted much over the past 2 decades. Low vegetable and fruit intake is an important risk factor for the global burden of disease. Increasing food security and improving dietary quality for 10-19-year-olds may have positive implications for dietary habits into adulthood. School settings offer one possibility for improving adolescent food security and dietary quality. Health-promoting schools, also known as healthy schools or schools for health, are vehicles to promote school attendance, better cognitive performance, physical activity, better hygiene practices, healthier diets, and better nutrition. Coupling school gardens with nutrition education and linking programs to community and household-level approaches may be more effective for increasing dietary diversity and nutritional status. In addition, offering nutritious meals at schools (including through the use of produce from school gardens) may also help to improve school retention and enrolment.

Third, **nutrition programs run by the government**, POSHAN Abhiyan 2018-2020 launched to improve adolescent nutrition and focus on improving nutritional outcomes of children, adolescents, and pregnant, and lactating mothers through various alliances and strategies.

Kishori Shakti Yojana, to improve nutrition, health, and development of adolescent girls aged 11-14 years. This scheme is followed by Adolescent Girls Scheme, 2010, under ICDS, which cover around 508 districts by 2018. This provides a home ration or hot cooked meal for 11-14-year-old girls, 600 calories, 18-20 g protein, and SABLA, 2011, provides them with nutrition, health, education, self-development, and empowerment.

However, these programs should be integrated with sexual and reproductive health interventions such as menstrual hygiene, adolescent-friendly contraception, prevention of STIs and RTIs etc. Globally, the adolescent fertility rate is 43.9 per 1000 women aged 15-19 y. Every year, ~23 million adolescent girls in developing countries become pregnant. Almost 20% of women in developing countries have a live birth by the age of 18. Delayed pregnancy offers a complementary strategy for improving adolescent nutrition and health. Delaying marriage and pregnancy improves maternal health and birth outcomes.

Fourth is **food literacy**, which is a set of skills and knowledge that are integral to diet. It is common among teenagers to not have the basic food literacy skills needed to consume a healthy diet. Higher parental education and higher median neighborhood family income, the use of mobile health applications, liking to cook, as well as confidence in reading and understanding food labels, were all consistently associated with increased food and nutrition knowledge. Findings may help guide future research toward optimal methods for delivering food literacy interventions to effectively educate teenagers.

## Future Research Focus

Research on adolescent health is challenged by the social changes that have transformed its object of scientific inquiry from a relatively contained life stage to an increasingly complex life period. This will require sustained effort from multiple sectors including health, agriculture, education, and engagement of adolescents, their parents, and communities.

- Delineation of nutrition requirements for adolescents (early (12-15) and late (15-19)) across various contexts, including LMICs and determining the likelihood of obesity and diabetes and wasting among adolescent girls with different nutritional backgrounds.
- Identification of modifiable predictors of adolescent nutritional practice, such as early imprinting of eating behavior and taste and food preferences.
- The physiology of pregnancy among adolescent girls who have different dietary histories and body composition, its impact on subsequent pregnancies, pregnancy outcomes, and offspring health.
- Relationship of nutrition Status and Interventions to growth spurt, final height, puberty onset and development, sleep and activity patterns in adolescence.
- Role of intervening in adolescents for healthy reversal of stunting, and on brain development in previously malnourished adolescents.

Importantly, adolescents should be included in the design of research programs in order to ensure youth-friendly interventions. Data collection platforms at national and sub-national levels, including demographic and health surveys as well as health and demographic surveillance systems, will need to be enhanced to track nutrition and health indicators across the full age range of adolescence. Evidence-based solutions for adolescent nutrient supplements, food system, and dietary quality interventions. and integration with delayed pregnancy strategies presents crucial opportunities for improving adolescent health and well-being. Greater investment in advancing adolescent nutrition is critical to promote their health and development now and has lifelong implications for them and their future families.

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**Table 1 : Recommended Dietary Allowances (RDA) in Adolescents for some major nutrients**

Nutrients	Age (years)	Adolescent girls	Adolescent boys
Total energy (kcal/day)	10-12	2060	2220
	13-15	2400	2860
	16-18	2500	3320
Proteins (g/day)	10-12	33	32
	13-15	43	45
	16-18	46	5
Fat (%)	10-18	25	25
Calcium (mg/day)	10-12	650	650
	13-18	800	800
Iron (mg/day)	10-12	28	16
	13-15	30	22
	16-18	32	26
Zinc (mg/day)	10-12	8.5	8.5
	13-15	12.8	14.3
	16-18	14.2	17.6
Iodine (ug/day)	10-12	100	100
	13-18	140	140
Thiamine (mg/day)	10-12	1.4	1.5
	13-15	1.6	1.9
	16-18	1.7	2.2
Riboflavin (mg/day)	10-12	1.9	2.1
	13-15	2.2	2.7
	16-18	2.3	3.1
Folate (ug/day)	10-12	225	220
	13-15	245	285
	16-18	270	340
B12 (ug/day)		2	2
Vitamin C (mg/day)	10-12	50	55
	13-15	65	70
	16-18	70	85
Vitamin A (ug/day)	10-12	790	770
	13-15	890	930
	16-18	860	1000
Vitamin D (IU)	10-18	600	600

**Table 2 : Major nutrients, their sources, and their physiological role in adolescence**

Nutrients	Dietary Sources	Functions
Proteins	Pulses, ground nuts, cashew, almond, meat, egg white, cheese	Muscle mass
Fats	Vegetable oil, ghee, vanaspati	Steroidal hormones
Iron	Bengalgram, beetroot, apple	Heme synthesis
Calcium	Ragi, cheese, milk, fish, cauliflower, curry leaves	Bone health
Vitamin A	Carrots, spinach, eggs, milk, cheese	Night vision, affect sexual maturation, prevent infectious diseases
Vitamin C	Broccoli, strawberries, citrus fruits, sweet potato, amla	Collagen synthesis, antioxidant, non-heme iron absorption
Vitamin D	Cheese, butter, fish, fortified milk	Calcium metabolism, bone health
Vitamin B6	Mint, spinach, pulses, liver	DNA, RNA synthesis
Vitamin 12	Milk, milk products, eggs	Methionine, Homocysteinesynthesis



## NUTRITION IN PCOS



**Shilpa Joshi RD**

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Lifestyle modification should be the first line of treatment for women with PCOS. American Society for Reproductive Medicine (ASRM) 2018 Guidelines state that it is the first line treatment of PCOS<sup>1</sup>. Lifestyle modification includes dietary management, exercise and also stress management. Often lifestyle intervention is prescribed to a lay without offering detailed solution to how this lifestyle intervention should be carried out. This may be because there is limited data about role of these agents in management of PCOS or there are no defined specific guidelines which give in detail what is expected to be done to achieve results. Also, most of the nutritional guidelines give details nutrient wise and do not give food suggestion. Foods and cooking methods change every couple of kilometres in India, hence converting the dietary recommendations into food suggestions becomes very important. Also, busy clinics of gynaecologist / physicians, makes it impossible for them to address these issues in details.

Insulin resistance is core problem in PCOS and diet and exercise impact it by improving the insulin sensitivity. Weight loss, curtails increased androgen production<sup>2</sup>. Weight loss in obese women, reduces sex hormone binding globulin (SHBG) levels, which results in increased bioavailable androgen delivered to target tissue.<sup>3,4</sup> Besides reproductive effects, obesity also increases the risk of metabolic syndrome, diabetes mellitus, dyslipidaemia, and insulin resistance.<sup>5,6</sup>

Dietary Recommendations for PCOS :

**Calories** : The International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome (2018) recommends a goal of lowering body weight by 5% as this has been shown to reduce serum insulin and testosterone levels and improve menstrual and reproductive function<sup>7,8,9</sup>. PCOS weight loss guidelines are similar to those which are recommended for the general population. It has been observed that in obese / overweight individuals a calorie deficit of 300-500 K cal / day helps in achieving weight loss. It has been observed that most of the insulin resistance symptoms associated with PCOS improve with 5 -10% loss of initial body weight<sup>7,8,9</sup>.

**Practical tips :**

1. It has been recommended that a well chalked out diet plan by dietitian help in faster reduction of weight as well as ensures maintenance in the long term.
2. Reducing portion size of each meal also ensures that there is a considerable caloric reduction.
3. Avoiding snacking in between the meals with processed foods also helps in caloric reduction.
4. In case if your patient travels, or is compelled to eat meals outside use of meal replacers instead of meals themselves helps in reduction of calories.

**Carbohydrates** : A recent meta-analysis found that a low-carbohydrate diet, defined as a diet that contains less than 45% carbohydrates, reduced body mass index (BMI) and total cholesterol and low-density lipoprotein cholesterol in PCOS<sup>10</sup>. Low carbohydrate diets have shown to improve insulin sensitivity and this has been shown to restore the balance of inositol's. It is not just the quantity but the quality of carbohydrates which is also important. Studies have shown that the diets which have low

glycemic index may have beneficial effects for insulin resistance and acne in the PCOS population.<sup>11,12</sup> Glycemic index is the property of carbohydrates to raise blood glucose. High glycemic index foods raise blood sugars faster as compared to low glycemic index foods. The proposed mechanism of this effect is improved metabolic profiles and reduced hyper insulinemia associated with these foods.<sup>13</sup> Most of the foods with low glycaemic index tend to be rich in fibre which is also helpful in increasing insulin sensitivity.

#### Practical Tips

1. Choose coarse grains (unrefined) as compared to refined ones. Millets (unrefined) instead of refined wheat, white rice and their products like poha, semolina etc. Instead of opting for white rice, brown rice is recommended.
2. Eat plenty of vegetables in each meal like greens and other non-starchy veggies. They are a great source of fibre and vitamins and minerals.
3. Have liberal amounts of dal, pulses and sprouts. They are rich in resistant starch, soluble fibre and proteins.
4. Only fill one fourth of your plates with carb rich food like roti, rice, millets or their products.
5. Be careful while snacking. Most of Indian snacks are carb rich even home-made ones like pohachivda, kurmura (mudi) etc. Replace them with protein rich snack like nuts, seeds.

#### **Proteins :**

Proteins have shown to improve satiety and aid in weight loss. They have also been shown to have a positive impact on insulin resistance. Traditionally, Indian diets are very low in protein. The recommendation of 0.8g / Kg BW or 15% of total calories, is rarely achieved. Adding protein especially vegetarian ones have should to aid weight loss and improve insulin resistance which are the main issues in PCOS. Protein is thought to exert effects on weight is through an increased satiety<sup>14</sup>. This is a beneficial dietary option for women with PCOS due to the potential impairment in postprandial satiety.

#### Practical Tips

1. Eat protein in every meal, including breakfast and snack, which are usually lacking in protein.
2. In India pulses are the main source of protein. Include them in every meal.
3. Nuts and oilseeds are also source of protein besides being rich source of fat. Include them in the daily diet.
4. Non vegetarian foods are rich source of protein. They are also rich source of saturated fats. Opt for leaner non veg proteins like egg whites, fish and chicken breast. Choosing right cooking method is important while cooking non veg foods.
5. ¼ of your plate should be full of proteins in each meal of the day.

#### **Meal Planning strategies in PCOS :**

##### **Meal Replacements :**

Meal replacements have also been shown to be an effective weight loss strategy in overweight women with PCOS<sup>15</sup>. They increase flexibility, and help in compliance and adherence to a reduced energy diet. Meal replacements are an effective, nutritionally adequate short-term strategy for reducing weight and improving body composition, quality of life, and metabolic and reproductive variables.<sup>16</sup>

### Practical Tips

1. The key role of an MR is to limit food choices and bad food selections.
2. MRs usually offer a structured, well-measured dietary composition that is easier to use within a diet strategy
3. That aims at controlling portions and high caloric consumption

### **Anti-inflammatory Diets :**

**Obesity** is Pro inflammatory state. This contributes to the promotion of insulin resistance and atherogenesis when present in PCOS.

The inflammatory load from adipose tissue in PCOS is in proportion to body mass.<sup>17</sup>

### Practical Tips

1. The macronutrient composition of such a diet would provide about 150 g of carbohydrates (600 Kcal) per day.
2. The majority of carbohydrates should be from low glycemic - load sources which would lower the production of insulin.
3. This can be achieved by consuming approximately 10 servings of non-starchy vegetables (200 Kcal).
4. Limited amounts of fruits (because of their higher carbohydrate content) per day
5. A relatively rigid (but not total) exclusion of high glycaemic-load carbohydrates such as bread (even naan, parathas), pasta, noodles, rice, and potatoes.

**Conclusion :** Managing overweight or obese women in PCOS can be challenging. The first line of therapy should be weight management and management of insulin resistance. Long term life style modification like diet and exercise have shown to help in improvement in PCOS symptom. For long term benefits these modifications have to be sustainable. Small changes go a long way in modifying the lifestyle.

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# PRE-CONCEPTIONAL NUTRITION



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## **Introduction :**

The preceding three months before a pregnancy is the pre-conceptional period. Some define it as the period 1-2 years before the initiation of unprotected sexual intercourse.<sup>1</sup>

Preconception care is defined as the provision of biomedical, behavioral, and social health interventions before conception occurs, aimed at improving the health status, and reducing behaviors and individual and environmental factors that could contribute to poor maternal and child health outcomes.<sup>2</sup>

The interventions which are necessary in the pre-conceptional period are health education and promotion, vaccination, nutritional supplementation and food fortification, family planning, screening, counselling and clinical interventions for infections, genetic conditions, and chronic conditions such as diabetes and epilepsy.<sup>3</sup>

## **Importance of nutrition in the pre-conceptional period :**

Poor maternal nutrition during fetal development and early life, can induce both short-term and longer lasting effects. There is an increased risk of noncommunicable diseases and obesity throughout the life-course. Programming of the fetus can occur because of maternal nutrition. Epidemiological and experimental studies suggest that the propensity to obesity and diet-related NCDs may be programmed during fetal development and early infancy, and that this susceptibility is partially determined by maternal nutritional status before and during pregnancy.

## **Nutrition and epigenetics :**

In-utero environmental conditions can cause epigenetic changes in the fetus leading to permanent alterations to the metabolic system and an increased susceptibility to chronic diseases. Suboptimal maternal nutrition cause changes in gene expression and are called as nutritional epigenetic changes. Extensive epigenetic reprogramming takes place during embryogenesis and sub-optimal nutrition plays a key role in nutritional epigenetic changes. The hypothesis that adult-onset NCDs have their origins in the early stages of human growth was proposed by Hales and Barker and is known as the “developmental origins of health and disease” hypothesis.<sup>4</sup> In-utero nutritional deprivation or excess can lead to fetal adaptations of the metabolic pathways critical for tissue function and survival in a postnatal environment.

There is a condition called the thrifty genotype. In this when early fetal undernutrition is combined with postnatal nutritional abundance, the response to intrauterine suboptimal nutrition may be irreversible and consist of partial resetting of the metabolic homeostasis and endocrine systems, and down-regulation of growth. The mismatch between pre- and postnatal nutritional environments may partly determine the characteristics and severity of the programmed response and susceptibility to preventable NCDs.<sup>5</sup>

An association between poor fetal growth, early accelerated postnatal so-called catch-up growth in offspring and later development of NCDs has been found in several human studies. Such NCDs include obesity, metabolic dysfunction, insulin sensitivity, T2DM, cardiovascular disorders and renal disorders.

**Effect of maternal under nutrition- the Dutch famine birth cohort :**

The Dutch famine birth cohort consists of 2414 singletons born alive and at term in the Wilhelmina Gasthuis in Amsterdam around the time of the Dutch famine (1943-1947) whose birth records have been kept. In this cohort, prenatal famine exposure had lasting consequences for health in later life. The effects of famine were widespread and affected the structure and function of many organs and tissues, resulted in altered behavior and increased risks of chronic degenerative diseases and increased mortality. The effects of famine were independent of size at birth, which suggests that programming may occur without altering size at birth.<sup>6</sup>

**Maternal over nutrition :<sup>7</sup>**

Maternal over nutrition may cause an increased long-term vulnerability and induce a pathological response. Pre-pregnancy overweight and obesity can lead to impaired fertility, pre-term birth, comorbidities, and even maternal mortality. In the fetus, it can cause macrosomia and alter the glucose and lipid metabolism. The long-term effects of maternal over nutrition are abdominal or generalized obesity across infancy and childhood, which can progress into adolescence and adulthood with related metabolic disorders; and asthma in predisposed children.

**Gestational diabetes mellitus (GDM) :**

The risk of developing GDM increases significantly with increases in pre-pregnancy BMI. The presence of GDM increases the risk of either restricted or excess fetal growth, fetal adiposity, predisposition to obesity throughout life, impaired glucose tolerance, T2DM, and metabolic disorders in the infant.

**Maternal obesity combined with multiple micronutrient deficiency :**

It is paradoxical, but obese pregnant women may have multiple nutrient deficiencies (with undernutrition from intake of micronutrient-poor foods). Micronutrient deficiency and overweight or obesity are likely to overlap, and this conjunction may exacerbate the rise in transgenerational NCDs. This may lead to serious long-term health and societal consequences.

**Anaemia in the pre-conception period :**

One of the most prevalent causes of anemia is iron deficiency, which may be combined with deficiencies of folate, vitamin B12, riboflavin and/or vitamin A. Anemia during preconception and early gestation is associated with impaired fetal development, preterm delivery, and low birth weight. Systemic iron deficiency and hypoferrremia are observed more in obese women compared with women of healthy body weight.

**Folate deficiency :**

Folate deficiency is associated with anemia and neural tube defects (NTDs), intrauterine growth restriction and other fetal malformations, preterm delivery, and low birth weight. NTDs are among the most common congenital anomalies contributing to infant mortality and serious disability. Periconceptual folic acid supplementation can prevent NTDs.

### **Vitamin D deficiency :**

Obese pregnant women are at increased risk of vitamin D deficiency compared with women with healthy body weight. It is also suggested that adipose tissue has its own requirements for Vitamin D (a fat-soluble vitamin) and in pregnancy vitamin D is drawn from maternal reserves. The higher the maternal adipose tissues store, the greater the vitamin D requirements seem to be. Maternal vitamin D status helps regulate fetal skeletal development, and deficiency may affect the offspring's bone trajectory and result in long-term bone disorders, such as osteoporosis, irrespective of the offspring's postnatal nutritional status. Vitamin D deficiency is also associated with pre-eclampsia, preterm birth, and small-for-gestational-age babies.

### **Multiple micro nutrient deficiency :**

A range of multiple micronutrient deficiencies may coexist in the obese, especially in those of low socioeconomic status. Higher the BMI, the greater may be the risk of the presence of multiple micronutrient deficiencies, including: iron, folate, iodine, zinc and vitamins A, -carotene, B12, C and D. Brain development and growth is particularly vulnerable during early pregnancy to low intakes of folate and iodine, and can be harmed by excessive vitamin A intake, and alcohol.

### **Diets in the pre-conception :**

A Mediterranean diet consists of proportioned and diversified macronutrients and is known to prevent congenital anomalies, preterm birth, hypertensive disorders, and GDM. In contrast, a western type of diet which is rich in processed food and low in fruits is a pro-inflammatory diet. It can diminish fertility, increase miscarriage rates, and enhance the risk of neural tube defects regardless of folate supplementation. Diets rich in vegetables, nuts, fish, and cereals can increase fertility and mediated by their antioxidant properties, protect against orofacial clefts, congenital heart, and limb defects in the progeny.<sup>8</sup>

### **Role of health care services :**

Unhealthy diets and physical inactivity are major modifiable risk factors for NCDs and obesity. Professional guidance from health care staff can be helpful in preventing these conditions, by promoting intake of foods such as vegetables, fruit, fish, and rich sources of iron during the reproductive years.

There is a pressing need to ensure adequate and optimum nutritional intakes for all teenagers and women of reproductive age. Waiting until a woman realizes she is pregnant is too late. She needs to be in good nutritional health already, and appropriate body weight should be promoted through a variety of public health measures. Healthy food and meals with an optimum nutritional content, to prevent both under - and overnutrition should be given attention. Services that tackle obesity and NCD prevention need to be integrated with those that tackle micronutrient deficiency. Interventions are needed to adjust the national price and availability of healthy foods in everyday life; and the prevention of marketing strategies which undermine the consumption of healthy diets. Multisectoral interventions implemented simultaneously are likely to prove cost-effective in terms of long-term health outcomes. Appropriate education of health professionals on diet-related issues is needed. Specific guidance should be given on clinical care pathways to manage and prevent underweight, overweight and obesity. There needs to be an incorporation of e-health with shared access among the different groups of health care professionals. Intergenerational impact of nutrition needs to be given

importance. New policy changes are required. There is a need for protecting and promoting public health through maternal and infant nutrition.<sup>9</sup>

Nutrition of the mother in the pre-conceptual period is crucial for health and development. When the mother is nourished well, it results in improvement of maternal and neonatal health, better immunity, safety during pregnancy and delivery, reduced risk of non-communicable diseases (NCD) and increased lifespan. The children born are healthier. Malnutrition poses a threat to health of women and their children. The world is now facing a dual burden in health. It is facing both under and over nutrition especially in low- and middle-income countries.

Malnutrition can occur in various forms ranging from wasting, inadequate intake of vitamins, overweight and obesity. NCDs occur when there are deficiencies in the diet. The impacts of these diseases are felt at the global level.<sup>10</sup>

### **Conclusion :**

Women in the reproductive age group should be counselled before conception regarding nutrition. Many women do not have access to correct information on nutrition. The health care providers need to be well versed with information on nutrition related to the pre-conception period and pregnancy. The provider should initiate the conversation on nutrition in the pre-conceptual period. They need to be advised to take a balanced diet with fruits, vegetables, iron, and calcium rich foods. They are counselled to consume 400 mcg of folic acid daily. Counselling in the pre-conception period provides the best opportunity to give guidance to a woman contemplating pregnancy on healthy eating habits, dietary supplements, and weight maintenance.<sup>11</sup>

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## NUTRITION DURING PREGNANCY AND LACTATION

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The term 'maternal nutrition' focuses attention towards the nutritional status of the women, as it relates to bearing and nurturing the children.

Maternal nutrition comprises of anthropometric factors such as pre-pregnancy BMI and gestational weight gain, as well as intake of balanced diet and micronutrients. A healthy, balanced diet that contains adequate amounts of nutrients is essential for the development of a baby.

During pregnancy and after delivery, a mother's body goes through many physiological changes, including a need for increased nutrients and energy.

Clinical practice guidelines in obstetrics and gynecology and WHO recommend routine dietary and weight management counselling for all women<sup>1,2</sup> Important for maternal and child outcomes<sup>3</sup>.

### Maternal Nutrition - when to intervene?

A life-course perspective from infancy through childhood and adolescence are needed.

Preconception care is the provision of biomedical, behavioural and social health interventions to women and couples before conception occurs. It aims at improving their health status, and reducing behaviours and individual and environmental factors that contribute to poor maternal and child health outcomes.

### Gestational Weight Gain Monitoring.

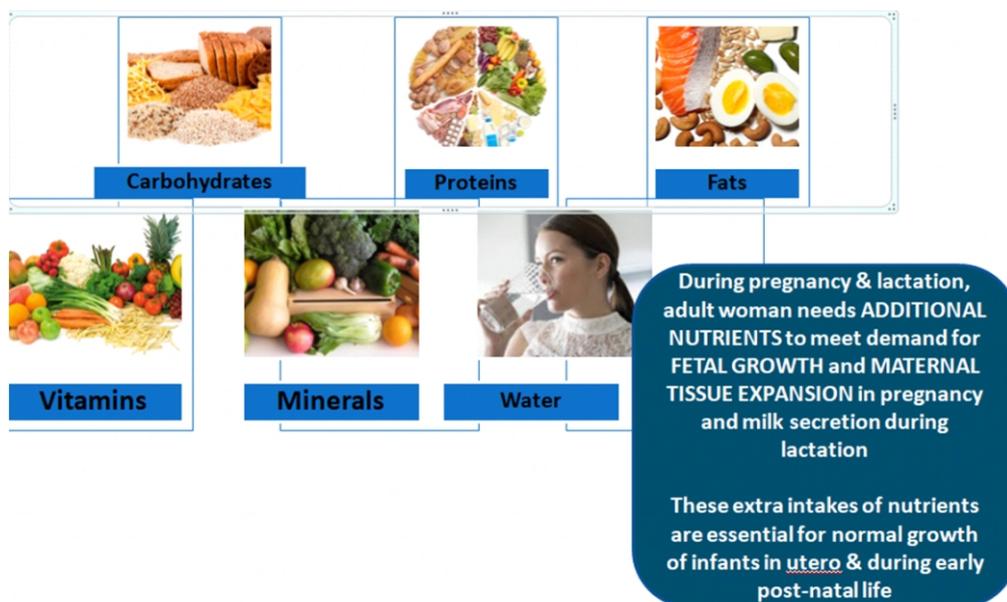
BMI	Ideal weightgain during pregnancy
Underweight < 18.50	13-18
Normal weight 18.50-24.99	11-16
Overweight ≥ 25.00	7-11
Obese ≥ 30.00	5-9

Developed by Institute of Medicine; adopted by WHO and UNICEF.

### Calculation of adult energy requirement.

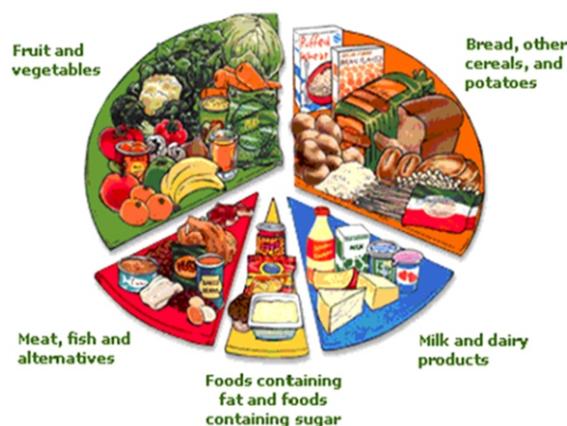
- 1) Energy requirement (kcal/d) = basal metabolic rate x Physical activity level.
- 2) Basal metabolic rate for adult females (18-30 yrs) = 14 X body weight (kg) + 471.
- 3) Basal metabolic rate for adult females (30-60 yrs) = 8.3 X body weight (kg) + 788.
- 4) Pre-pregnancy body to be taken into consideration when calculating the requirement.

## Maternal Nutrition & Supplementation



### Planning healthy meals

- Include all food groups in diet
- Vegetables & fruits
- Milk and dairy foods
- Cereals & Grains
- Meat, beans, and eggs
- Fats and oils



### My Pregnancy Plate

Nutritional Requirement During Pregnancy

#### Carbohydrates

Dietary carbohydrate is broken-down to form glucose. The RDA for carbohydrate during pregnancy is 175 g/day. Carbohydrate/protein intake should be adequate to avoid decrease in gestational weight gain.

#### Not All Carbohydrates Have The Same Effect

Carbohydrate sources are digested and absorbed at different rates. The glycemic index indicates how quickly certain foods raise blood glucose levels compared to glucose, which has a value of 100.

#### Proteins

Proteins consumed should give 10-35% of energy, 71 gm/day Additional 1 gm/day 1st trimester - 8 gm/day in 2nd trimester - RDA 1.1 gm/kg/day 26 gm/day in 3rd trimester - RDA 1.2 gm/kg/day

#### Additional protein is required in pregnancy for fetal growth.

Vegetarian sources of protein : Paneer / yogurt Soya flour / soya chunks / tofu Soya milk / almond milk Nuts like peanut, almonds Green leafy vegetables like spinach Seeds like hemp, tempeh, flax seeds, fenugreek seeds, pumpkin seeds, sunflower seeds. Beans Steamed sprouts Lentils / dhals.

## Lipids and fats

Pregnant women must include enough fats in her diet to meet the needs of her growing baby. There are no separate RDA for fat intake during pregnancy and the recommendations remain 20-35% of total calories 8-14 gm/day during 2nd trimester - 11-18 gm/day during 3rd trimester - Essential fatty acids The EFAs omega-6 and omega-3 are necessary for optimal formation of the brain and eyes. RDA Omega-6 -13 g/day and omega-3 -1.4 g/day Omega 3 fatty acid helps in cognitive development and prevents allergy.

Saturated fat intake (sources-ghee, butter, coconut oil, palm oil, red meat, organ meat, full cream milk etc) should be less than 10% of total calories. Good fats like omega 3 fatty acid are available from nuts and seeds.

Fat can be reduced from diet by : Using less fat in cooking and avoiding frying of foods Using low-fat dairy products in place of whole milk or full cream products Choosing low fat snacks like eating fresh fruit instead of high-fat snacks such as cakes, biscuits, chocolates and pastries. and Using lean meat like fish / chicken in place of red meat.

## Role of DHA

Helps in neuronal development DHA prevents PTB & PE < 34 weeks as per Cochrane review Rich sources are Fish Ocean fish Oily fish Mackerel, Salmon, Herring and Sardine-twice weekly Tuna & sword fish - limited use due to methyl mercury content Should be avoided Non fish eaters - 300 mg -500 mg of omega 3 DHA.

## Fibre

It is important for prenatal diet. Pregnant women needs 28 g/day. Modulates gut micro-biome Reduces respiratory problems like asthma for the new born

## Micronutrients Deficit and Pregnancy Outcome

Folic Acid	Neural tube defect
Iron	Anemia,
Iodine	Cretinism
Calcium	Hypertension,
Zinc	Anemia, Low birth wt, Anencephaly, Neural tube defects
Vitamin A	Infant survival, Maternal anaemia, Infections

## Micronutrients

Iron RDA : 27 mg/day. Supplementation 30-60 mg/day. Essential for fetal growth.

Anemia causes maternal anemia, preterm birth, low birth weight babies and Cardiovascular risk to the offspring during adulthood.

## Folic Acid

Folic acid can help to prevent birth defects known as NTD like spina bifida, congenital heart disease, cleft lip & palate.

Sources Cabbage, green leafy vegetables, legumes, tomato, orange RDA : 600 mcg/day. Supplementation : 0.4 mg/day during preconception and early pregnancy.

## Calcium

RDA for pregnant women is 1-1.3 g/day. Present in milk products-50%, cereals-11%, vegetables-11%. Deficiency results in pre eclampsia.

Magnesium Most prenatal vitamins contains only 10% to 25% of the RDA for magnesium.

**Vitamin C** RDA is 60 mg/day

## Vitamin A

RDA for pregnant women is 770 micro gram/day should be given only in deficient areas. Excess vitamin A results in liver dysfunction & birth defects. Increased risk of night blindness in mothers Low birth weight Miscarriage Still birth Reduced transfer of vitamin A to fetus. Low vitamin A concentration in breastmilk

B Vitamins : RDA for pregnant women is 770 micro gram per day

B1 : RDA for pregnant women is + 0.2 mg/day

B2 : RDA for pregnant women is + 0.2 mg/day

B3 : RDA for pregnant women is 2 mg/day

B6 : RDA for pregnant women is 2.5 mg/day Vitamin B12, also called cobalamin, is a water-soluble vitamin. It synthesized by only microorganisms in the gut.

## Vitamin B12

B12 : RDA for pregnant women is 2.6 micro gram /day.

## Functions

It is needed to absorb iron, Ca, and vitamin A. Plays key role myelinogenesis / brain development / fetal growth. The formation of red blood cells-megaloblastic anaemia. It is involved in the metabolism of every body, especially affecting DNA synthesis, fatty acid and amino acid metabolism Vitamin B12 comes primarily from animal-derived foods. Animal sources include clams, organ meats (especially liver) from lamb, veal, beef, and turkey, fish eggs, mackerel, and crab meat Plant foods do not c Foods for which B12-fortified versions are widely available include breakfast cereals, fruit & vegetable juices, soy products, tofu, non-dairy milk, plant - based meats, energy bars, and nutritional yeast contain vitamin B12 except when contaminated by microorganisms.

Vitamin B12 Deficiency IMPACTION Maternal & Child Health Care Increased risk for adverse pregnancy outcomes for both mother and fetus.

These risks include,

Neural tube defects

Early miscarriage

Pre eclampsia

## IUGR

The neurological and developmental delays are irreversible. Daily requirement during pregnancy and breast feeding is 2.6 to 2.8 micro grams Tablets or syrups (Cyanocobalamin or Methylcobalamin) Sprays & drops Injections.

## **VITAMIN D**

RDA for pregnant women is 600 U/day, up to 2000 U/day in risk group

Sources Sunlight, Cod liver oil, fish, egg, butter, cheese Vitamin D is essential for maternal calcium homeostasis and fetal bone development.

Deficiency of vitamin D leads to IUGR, pre eclampsia, increased risk of LSCS, PTB, abnormal GTT, rickets, osteopenia, neonatal hypo calcemia. In Later life : Asthma, multiple sclerosis, neurological disorders, autoimmune disorder, cardiac failure.

## **DIET & NUTRITION DURING LACTATION**

Mother needs extra nutrition to nourish a rapidly in addition to her own requirements

Any inadequacy in mothers diet influence both the quality & quantity of mother's milk secreted.

### **Nutrition during lactation**

A breast-feeding woman needs 200 more calories per day than she did during pregnancy, and it is important that the calories come from nutritious foods. Breast-feeding women usually loose 1 to 4 pounds per month without restricting their calorie intake. Some important nutrients are as follows  
Proteins.

Breast-feeding mother should eat two to three servings of protein each day. A serving is equal to 3 to 4 ounces of meat, fish or poultry.

### **Calcium**

The suggested daily intake of calcium for breast- feeding mothers is 1,300 milligrams per day.

Iron Breast-feeding mothers should get 10 milligrams of iron per day.

Nursing mothers need slightly more vitamin C than they did during pregnancy. Vitamin C 120 mgm / day.

Breast-feeding mothers need to take some sort of daily multivitamin that contains 100 percent of the recommended dietary allowance (RDA).

While breast-feeding mother should drink at least 8 cups of water each day. Have a glass of water each time she nurses her baby.

Lactating mother must avoid drinking alcohol and smoking cigarettes & must not use any street drugs.

## **SUMMARY**

Pre-pregnancy, pregnancy and post-partum nutrition is critical for women and children's well-being

Poor nutritional status of mothers before and during pregnancy extends throughout the life course and affects the next generation. Lead to intergenerational vicious cycle of under nutrition.

Pregnant women should be screened to identify as nutritionally 'At Risk' i.e. underweight, overweight and obese and should be counselled appropriately for dietary management.





## ROLE OF VITAMIN B12 IN WOMEN'S HEALTH

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### Introduction

Vitamin B12 is an essential water-soluble micronutrient, belonging to the B group of vitamins. Vitamin B12, though required in minuscule amounts, is majorly provided by external sources like diet and supplements because the human body is unable to produce it. Its importance can be briefly stated by its role in various vital biological functions like DNA and RNA synthesis and DNA methylation, hematopoiesis, and neuronal function. The RDA (Recommended Dietary Allowance) of Vitamin B12 in females varies across age groups, starting from 1.8 mcg at the onset of adolescence, to 2.4 mcg till the onset of adulthood. These values increase further during pregnancy and lactation to 2.6 mcg and 2.8 mcg consequent to an increase in demand.<sup>1,2</sup>

In India vitamin B12 deficiency is widely prevalent, ranging from 40-70% as most of the Indian population is vegetarian due to religious, cultural, and socio-economic factors. Prevalence of vitamin B12 deficiency varies across different states of India. It is reported to be 74% in Northern and Western states of India compared to 51% in Southern states like Karnataka.<sup>3</sup> Government programs have focused on interventions related to iron deficiency to combat anemia, however other nutritional deficiencies have not been given required attention. The fact that anemia remains unabated despite free iron and folic acid supplementation under GOI programs points towards the unaddressed problem of vitamin B12 deficiency and other micronutrients in our country. Looking at the magnitude of Vitamin B12 deficiency in women in India and its importance in vital biological functions in them and their newborns, more studies are required on the adverse impact of its deficiency, its diagnosis, treatment and interventions to supplement Vitamin B12 during adolescence and pregnancy.

### Etiology of Vitamin B12 deficiency

There are various causes related to poor intake, poor absorption and increased demand leading to vitamin B12 deficiency in women.

**Decreased intake :** Vitamin B12 is available in foods of animal origin hence deficiency due to decreased intake is common in vegetarians and vegans. Women from poor socioeconomic status cannot afford non-vegetarian food and dairy products and many women in India abstain from non-vegetarian food due to religious and cultural beliefs. This is the commonest cause for Vitamin B12 deficiency in India.

**Poor absorption :** Presence of intrinsic factor produced by parietal cells of gastric mucosa and an acidic milieu is essential for the absorption of vitamin B12 from the small intestine. Absorption can be hampered due to decreased secretion of intrinsic factor consequent to an autoimmune production of antibodies against parietal cells as in Pernicious anemia or defective receptors as seen in Imerslund-Gräsbeck syndrome. It can also be due to certain non-immune..conditions like tapeworm infestation, celiac disease related intestinal inflammation, bariatric gastric bypass surgery, terminal ileum resection as in Crohn's disease. Competitive inhibition of absorption due to pharmacological agents like Metformin, Phenytoin, Proton pump inhibitors, Colchicine, Cholestyramine etc. is also common.

Pathologies of stomach, liver, endocrinopathies (hypothyroidism induced achlorhydria), malignancies, enzyme deficiencies, etc. also lead to vitamin B12 deficiency by affecting absorption of vitamin B12.

**Increased demand :** Increased requirement of vitamin B12 in states of infancy, puberty, pregnancy, lactation, and postmenopausal state as well as other pathological conditions including hyperthyroidism, renal disorders etc. can result in vit B12 deficiency.<sup>4</sup>

### **Pathophysiology of Vitamin B12 deficiency**

Both folic acid and vitamin B12 are important for 1 carbon cycle for DNA synthesis and methylation. Vitamin B12 couples with folic acid and converts 5-methyltetrahydrofolate to tetrahydrofolate (active folate), and releases a methyl group, preventing folate trap. Vitamin B12 acts as an active coenzyme and in the presence of methionine synthase, and aids in the conversion of homocysteine to methionine in the cytoplasm. This function is vital in maintaining genetic stability by S-adenosylmethionine (SAM) in genomic and non-genomic methylation for Deoxyribonucleic acid (DNA) maturation, central nervous system development and nucleotide synthesis. These functioning and repair mechanisms occur at all ages, but maximum neurological development takes place in the initial years of life, hence it is essential that infants and children are vitamin B12 replete. Adenosylcobalamine, acts as an active coenzyme, aids in formation of succinyl coenzyme A from methylmalonic acid, that is a mitochondrial enzyme capable of substrate level phosphorylation for production of Adenosine triphosphate (ATP) even in the absence of oxygen. Other functions include its participation in ketone metabolism, heme synthesis and citric acid cycle.

Vitamin B12 deficiency impedes the function of folate for conversion of d-Uridyl monophosphate to d-Thymidine monophosphate causing a decrease in thymine synthesis. This minimizes and arrests the nuclear maturation, resulting in nuclear-cytoplasmic asynchrony, which results in pancytopenia and ineffective hematopoiesis, with resultant anemia.<sup>4</sup>

Thus, deficiency of either folic acid or vitamin B12 can lead to accumulation of homocysteine and interfere with formation of pyrimidine bases, slowing down DNA synthesis and methylation causing megaloblastic anemia impaired fetal growth and other adverse pregnancy outcomes.

### **Vitamin B12 and Women's Health**

#### **Neuronal Function**

Vitamin B12 is important for maintaining levels of methionine and succinyl Co-A which is responsible for production of myelin sheath and neuronal lipids. In the case of vitamin B12 deficiency, defective myelination occurs in fetuses and newborns. This delays the attainment of milestones in children, causing improper psychomotor and neurological development. In adult's defective myelination results in subacute combined degeneration of the spinal cord (SCDSC), loss of proprioception, ataxia, the development of peripheral neuropathy, and dementia.

Vitamin B12 along with vitamin B6 and folic acid enhance the catalyzation of homocysteine that reduces the severity of migraine with aura, which predominantly affects females. Vitamin B 12 deficient patients are found to have certain psychiatric manifestations such as dementia, delirium, seizures, psychosis, depression, and other behavioral changes.<sup>5,6,7</sup>

#### **Hematopoiesis**

By promoting DNA synthesis, vitamin B12 plays a vital role in red blood cell proliferation. Deficiency of Vitamin B12 and folic acid may halt their differentiation, leading to defective mitotic activity and

regeneration of red blood cells causing macrocytosis, ineffective erythropoietin-induced erythropoiesis, intramedullary hemolysis, pancytopenia, with resultant anemia.

Deficiency gets aggravated in women with increased physiological needs like pregnancy adolescence and in infants because of their physiological faster rates of erythropoiesis. It also leads to typical morphological disturbances in blood and bone marrow cells like multi segmented neutrophils in the blood picture, which are seen in the peripheral blood smears and used as a diagnostic criterion to detect Vitamin B12 deficiency.<sup>8,9</sup>

### **Genetic stability**

It collaborates with folate and maintains genetic integrity. Vitamin B12 deficiency is also responsible for elevated homocysteine levels, which is directly associated with genetic instability and anomalies as it causes micronucleus formation and chromosomal damage.<sup>10</sup>

### **Obstetric health and outcomes**

Chronic Vitamin B12 deficiency in a woman of reproductive age group has shown association with defective implantation on the endometrium during pregnancy, increasing susceptibility to pre-eclampsia and preterm labor.

Levels of B vitamins in early pregnancy have been proven to play a major prognostic role in development of insulin resistance in late trimesters, resulting in gestational diabetes mellitus and related adverse obstetric outcomes. It not only compromises the obstetric outcomes for both mother and fetus but also makes the women's and newborn's overall health vulnerable in future.

Low maternal B12 status makes the newborns vulnerable to this deficiency, adversely affecting their health and development at such an initial stage of their lives. Lactating mothers with low Vitamin B12 levels drastically affect the infants, especially the ones on exclusive breastfeeding. It may present delayed developmental milestones, fatigue, pallor, vomiting, dehydration, halted growth and lowered motor tone.

Adverse outcomes in pregnancy such as spontaneous abortions, small for gestational age babies, postpartum depression, vascular occlusive lesions, infantile tremor syndrome, brain oxidative stress etc. have also been reported in literature with Vitamin B12 deficiency.<sup>11,12,13</sup>

### **Cardiovascular health**

Adequate Vitamin B12 levels is essential for keeping the homocysteine levels under control, especially in women willing to conceive and in post-menopause. High blood homocysteine levels promote hypercoagulation of blood and impaired lipid metabolism, predisposing to cardiac conditions like atherosclerosis and may also lead to spontaneous or recurrent loss of fetus as an immediate outcome.

High blood homocysteine levels in women also predispose degeneration of macula, visual impairment, gait abnormalities and cardiac anomalies like coronary artery disease and myocardial infarction.<sup>14</sup>

### **Fertility**

Vitamin B12 and folate supplementation have been found to be advantageous in improving the fecundability and fertility of females. Prolonged elevated homocysteine induced hypercoagulability of blood can alter the ovulatory cycles or halt the development of ovum leading to infertility in reproductive age group females. All the above correlations easily explain the etiological importance of Vitamin B12 in metabolic syndromes like polycystic ovarian syndrome.

## **Bone health**

Women with adequate Vitamin B12 levels have normal serum methyl-malonic acid levels, which in turn maintains the bone mass density. Noteworthy attention should be paid towards vitamin B12 levels, in postmenopausal women, as they are more vulnerable to osteoporosis.

## **Dermatological health**

Sufficient levels of Vitamin B12 moderate the metabolite-mediated reactions and have shown positive effects in improvement of dermatological conditions like acne, cheilitis, stomatitis, atrophic glossitis, seborrheic dermatitis, brittle and matting of hair, premature grey hair etc.<sup>15,16</sup>

## **Insulin resistance**

Low vitamin B12 levels are known to precede insulin resistance and can lead to development of type 2 DM within years postpartum. Infants born to these mothers may have defective lipid and glucose metabolism and are predisposed to obesity and DM in their adulthood. A known complication of an oral hypoglycemic drug is decrease in vitamin B12 absorption, hence its deficiency. Thus, women on this drug should be screened regularly for vitamin B12 deficiency and given adequate prophylaxis to fulfill their nutritional requirements.<sup>17</sup>

## **Clinical presentation**

Clinical presentation of Vitamin B12 deficiency includes pallor of lower palpebral conjunctiva, nails and tongue, fatigue, knuckle hyperpigmentation, glossitis, angular stomatitis, loss of sensations with tingling and numbness of fingers, disturbed mood and irritability, loss of bone strength and joint pains. (18). The complexion of vitamin B12 individuals is usually sallow. Knuckle hyperpigmentation is an important practical clinical sign especially in women with anemia which can aid in suspecting vitamin B12 deficiency in low resource countries like India where serum vitamin B12 estimation is not freely available.

In an unpublished study conducted in the antenatal OPD of LHMC Delhi on 250 pregnant mothers it was observed that 52% were anemic and 73.2% were vitamin B12 deficient. In anemic mothers with knuckle hyperpigmentation 86.3% were vitamin B12 deficient. In anemic mothers with clinical pallor and knuckle hyperpigmentation 92% were vitamin B12 deficient. In those with dimorphic anemia 94.7% were vitamin B12 deficient.

## **Diagnosis**

A complete blood count showing low levels of hemoglobin (< 12 gm/dL) in a nonpregnant woman and < 11 gm/dl in a pregnant mother and a mean corpuscular volume (MCV) of > 100 fl points towards vitamin B12 or folic acid deficiency. The peripheral blood smear showing presence of macro ovalocytes or a dimorphic picture is suggestive of either folic acid or vit B12 deficiency. In patients with combined iron and vitamin B12 deficiency microcytosis and macrocytosis coexist and MCV reflects the average volume of RBCs hence may be in the normal range. In these cases, the peripheral smear and red cell distribution width helps in the diagnosis of vit B12 deficiency. The peripheral smear shows both microcytes and macrocytes and RDW is increased in vitamin B12 and Folic acid deficiency. The presence of hype segmented neutrophils and coexistence of leukopenia and or thrombocytopenia also points towards vit B12 or folic acid deficiency. To confirm the diagnosis and differentiate between vitamin B12 and folic acid deficiency estimation of serum vit B12 levels, serum folic acid levels and methyl malonic acid levels is useful. serum vitamin B 12 levels (< 200 pg./mL) help in confirming the

diagnosis of vit B12 deficiency. However, in pregnancy vitamin B12 levels between 200-300 pg./ml are considered borderline. Raised levels of methyl malonic acid is diagnostic of Vit B12 deficiency and helps in differentiating vit B12 deficiency from folic acid deficiency.

In low resource settings where serum vitamin B12 and folic acid estimation is not freely available a combination of knuckle hyperpigmentation and MCV > 100 fl or presence of macrocytes in peripheral smear can diagnose vitamin B12 deficiency in an affordable manner.

### **Treatment**

Identification and screening of women at high risk of vitamin B12 deficiency must be screened carefully with a CBC and presence of knuckle hyperpigmentation on examination. Those at high risk include women who are vegetarians or vegans, from poor socioeconomic status, on drugs like metformin, proton pump inhibitors, antiepileptics, with inflammatory bowel disease and post bariatric surgery or small intestinal resection. The diagnosis can be confirmed by serum estimation of vitamin B12 and folic acid levels wherever possible. The dietary deficiency can be improved by incorporating animal based products and preventing parasitic infections by deworming.

Vitamin B 12 supplementation in the form of oral tablets, intramuscular injections or nasal sprays can be prescribed in those with deficiency. As the majority have nutritional deficiency, oral preparations of 1000 -2000 micrograms per day for 2-3 months is sufficient. Although there are no clear guidelines on the dose and duration in vitamin B12 deficient individuals with nutritional deficiency. Parenteral preparation is preferred in those with intrinsic factor deficiency or problems related to absorption from the small intestines. Intramuscular routes are preferred except in those with thrombocytopenia as a significant amount gets excreted by intravenous administration. Those with a platelet count of 50,000 or more may be administered intramuscular injection of 1000 micrograms with a fine 26 G needle and keep pressure on the injection site for 3-5 minutes. There is no consensus as regards the dose and duration of parenteral administration. Usually, 5-7 injections of 1000 micrograms are prescribed on alternate days followed by one every month in those with intrinsic factor deficiency. Same is followed by most clinicians in pregnant mothers with documented Vitamin B12 deficiency.

The response to treatment is evident in the form of an increase in reticulocyte count within 3 to 5 days of replacement. Thrombocytopenia if present improves within 5 to 7 days and full recovery takes within 6-8 weeks. It is important that the Government of India focuses on rampant vitamin B12 deficiency in India and adds vitamin B12 to iron and folic acid supplements to prevent and treat anemia.<sup>3,18</sup> Vitamin B12 is stored in the liver for about 400 days even a single injection of 1000 micrograms in the second or third trimester is likely to be useful in correction of anemia and vitamin B12 deficiency during pregnancy.<sup>19</sup>

According to the National guidelines, there is provision of prescribing folic acid tablets (5 mg) from the preconception phase in the first trimester, and in combination as Iron-folic acid tablets (60 mg elemental iron and 500 micrograms of folic acid) for 180 days antenatally in the second and third trimesters and 180 days in the postpartum period.

Folate plays a vital role in neural tube development of the fetus, thus needs to be administered in early pregnancy. Undoubtedly it has reduced the incidence of neural tube malformations and folate deficiency anemia as well. It requires a dose of 500 micrograms per day for this. But imprudent administration of folic acid 5 mg/day (12.5 times the recommended dose) in the presence of Vitamin B12 deficiency can result in an imbalance between folic acid and vitamin B12 with resultant harmful

effects on the women and the infants. It not only predisposes the risk of developing insulin resistance in women but also increases the risk of low birth weight and adiposity in newborns. Hence the importance of vitamin B12 supplementation in pregnancy as the demand significantly increases specifically in the second half of pregnancy when the fetus is growing.

High blood folate levels tend to mask the deficiency of vitamin B12 in hematological studies. This increases the folate trap and declines the hemoglobin in disguise, causing anemia. This further worsens the neurological functions as folate needs Vitamin B12 in conjugation to develop the central nervous system properly.<sup>13,20</sup>

To conclude vitamin B12 deficiency is a common but unaddressed problem in India with many short term and long term adverse effects on women's health. Vitamin B12 plays an important role in many vital biological processes including DNA synthesis and methylation, neuronal health, and hematopoiesis in our body. Hence its early diagnosis and treatment is essential for the health of the nation.

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# NUTRITION IN MENOPAUSE



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### Introduction

Menopause is defined as cessation of menstruation or permanent cessation of menstrual cycles following loss of ovarian follicular activity.<sup>1</sup> Climacteric is defined as a transitional phase from the signs of ovarian senescence till the loss of ovarian activity. Menstrual irregularity and heavy menstrual bleeding occur during perimenopause due to loss of luteal phase progesterone. This is followed by decrease in E2 levels that will lead to vasomotor changes, urogenital atrophy, bone loss and increased cardio vascular and metabolic risk.<sup>2,3</sup> Menopause transition spans over several years. Menopause is associated with obesity, metabolic syndrome, cardiovascular disease and osteoporosis.<sup>4</sup> Sedentary life, added to menopause, increases obesity.<sup>5</sup>

In postmenopausal women, decreased E2 level leads to metabolic flexibility causing central obesity and cardio vascular symptoms. Hence, exercises, calorie restriction are needed to maintain BMI and reduce metabolic and cardio vascular risk. Integral health care includes life style modification to minimize the risk of metabolic syndrome, bone loss and vascular events.<sup>2,3</sup>

Nutritional modification in post menopause can improve the quality of life and longevity. Maintaining healthy weight can prevent and control many diseases in midlife. Obese women are at high risk of developing cardiac diseases, hypertension, type 2 diabetes mellitus, gall stones, respiratory problems and certain cancers. Life style modification is very important in maintaining a healthy weight. There are 3 steps in the management of menopause which are eat the right food, exercise regularly and take proper medications.

Dietary prescriptions for healthy weight maintenance begins with restricting calorie count, according to the individual's body weight and weight distribution. Total calories are equally important that should be inclusive of 60% carbohydrates, 20% proteins and 20% fat. Proteins can be in the moderate level, because physical activity level decreases and body building is absent and hence taking 0.8 gm/kg body weight should be sufficient.

### Carbohydrate

Complex carbohydrate which includes whole cereals, bran, kidney beans, pulses, barley etc (20-25 gms / day) should be taken.

### Fibre intake

Fair amount of fibre should be consumed each day, as it will keep the stomach full and will not lead to any extra calorie intake.

### Healthy fats

A low fat and plant-based diet can lower the risk for experiencing menopausal symptoms. Animal fat and oil should be minimized. In the women's health initiative, peri-menopausal women following reduced fat diet, showed significantly lower incidence of vasomotor symptoms compared with those

consuming fat beyond 30%. It is important to use combination of fats every day for a good supply of essential fatty acids.

### Protein intake

Whey protein contains abundant levels of leucine (a key stimulator of MTORC1, in skeletal muscle) and is the most potent dietary strategy to increase muscle protein synthesis. Expert consensus group recommend at least 1.2 - 1.5g/kg/ day.<sup>6</sup> Increasing protein intake is more effective when vitamin D levels are in optimal range.

### Sugars

Sugar consumption should be avoided. Carbonated soft drinks contribute to a huge percentage of sugar intake, resulting in massive weight gain.

### Salt

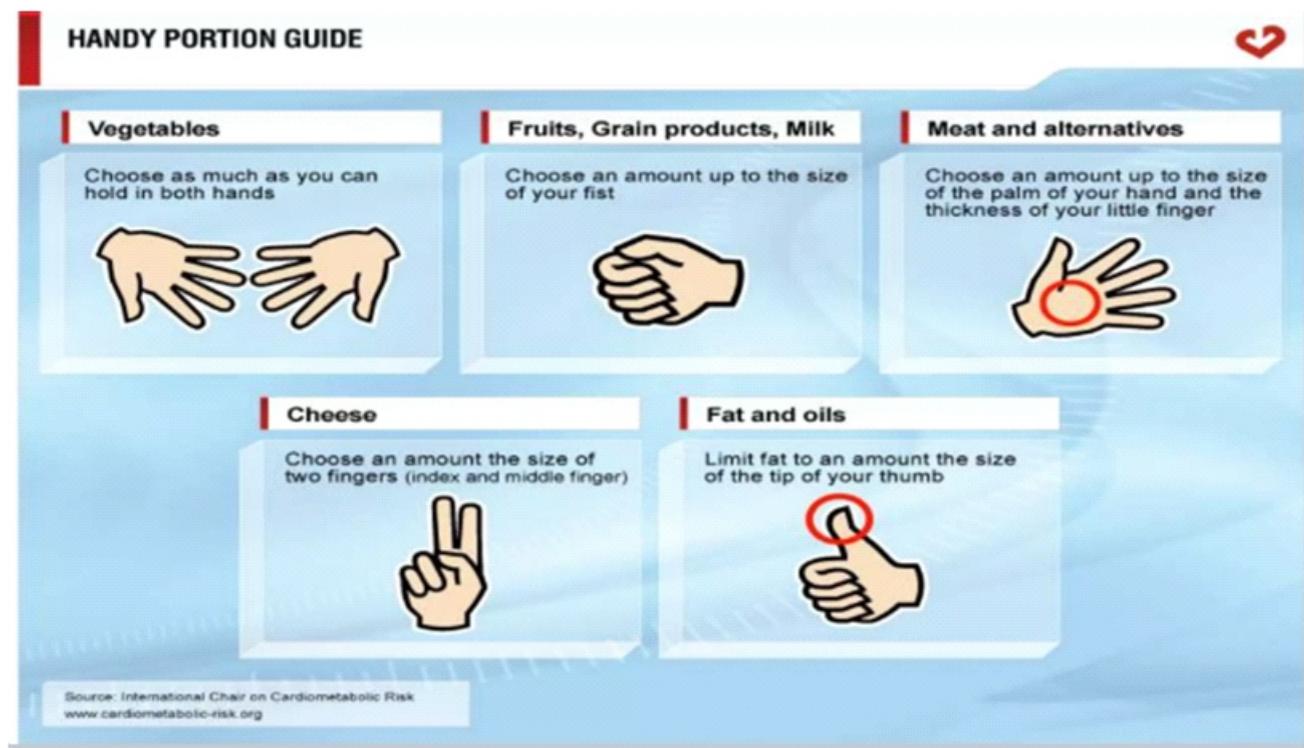
Restrict salt 1.5 tsp or 3-5 gms /day, oil 2 level tbs/day, 8 glasses of water every day and addition of powdered flaxseed, cinnamon, fenugreek, fennel in salads and curds are ideal to reduce hot flashes.

### Tea, coffee and dairy products

Intake of tea and coffee should be restricted to 3 cups a day, 1 cup (150 mL) of brewed coffee is equal to 120 mg of caffeine, 65 mg for 1 cup of instant coffee and avoid more than 200 mg/day of caffeine. Minimum of 500-600 mL of milk or curds (low fat) should be consumed to build on calcium bank in bones and support it with lots of vitamin C rich fruits or vegetables to favor calcium absorption.

### Drink in moderation

It is best defined as the level of drinking that poses a low risk of alcohol related problems, not more than one drink a day but it is ideal to avoid alcohol. Smoking and crash diets should be avoided.



## Micronutrients

2-3 servings of fruits and vegetables (fruit 100 gms /day, vegetables - 300 gms/day) are needed to get the micro nutrients. Required amount of folic acid, zinc, calcium and iron can be obtained from green leafy vegetables taken atleast once in a day. Fat soluble vitamins A, D, E and K should be taken. Calcium 1000-1500mg of /day is recommended through milk and milk products.

### Vitamin E

Vitamin E is a fat-soluble vitamin. It has very marginal efficacy in reducing hot flushes (average reduction of one hot flush/day). 800-1000 IU per day in divided doses taken with food can reduce vasomotor symptoms.<sup>7</sup> Incorporate omega 3 fatty acids regularly such as flax seeds, canola oil, walnuts and soy beans.

### Calcium

The recommended dietary allowance (RDA) of calcium and vitamin D for adult Indian is Calcium 800 mg 1200 mg/day with maximum of 2500 mg/day and vitamin D 1500-2000 IU/day with the maximum of 10000 IU/day.

Calcium requirements for skeletal maintenance fluctuate throughout a woman's life. Calcium absorption averages 20-30%. This efficiency declines slowly with age. By the age of 65, calcium absorption efficiency is typically 50% below that of adolescent peak absorption.

Calcium deficiency occurs in lactose intolerance and limited use of dairy products. Consumption of large amounts of protein or sodium, increases calcium excretion. High oxalate diets, aging, vitamin D deficiency, long-term treatment with corticosteroids, hyperthyroidism, bowel or digestive diseases such as inflammatory bowel disease or celiac disease decrease the ability to absorb calcium.

Assess the total calcium intake from dietary sources and if needed, supplements are used to correct the deficient balance. The intake should exceed > 800 mg/day (Grade B). Risk of CV events and calculi are not observed with the recommended doses of calcium. Prevention of kidney stones is possible if calcium is taken in the prescribed dose with sufficient fluids and preferred salt is calcium citrate.

Common Calcium Supplements	% of Elemental Calcium	Calcium mg/ 1000 mg of salt
Calcium Carbonate	40	400
Calcium Citrate	21	241
Calcium Gluconate	9	93
Calcium Lactate	13	184
Calcium Phosphate Tribasic	38	388

Naturally derived calcium forms like dolomite, oyster shell, bone meal may contain lead and other toxic minerals.

### Calcium carbonate Vs calcium citrate

Carbonate needs acid for absorption but citrate does not need acidity for absorption and as age advances when acidity decreases absorption is not altered. Calcium citrate can be taken at any time unlike calcium carbonate that has to be taken with meals. It is slightly expensive than calcium carbonate. Calcium gluconate, calcium lactate and calcium phosphate have less calcium than the carbonate and citrate forms.

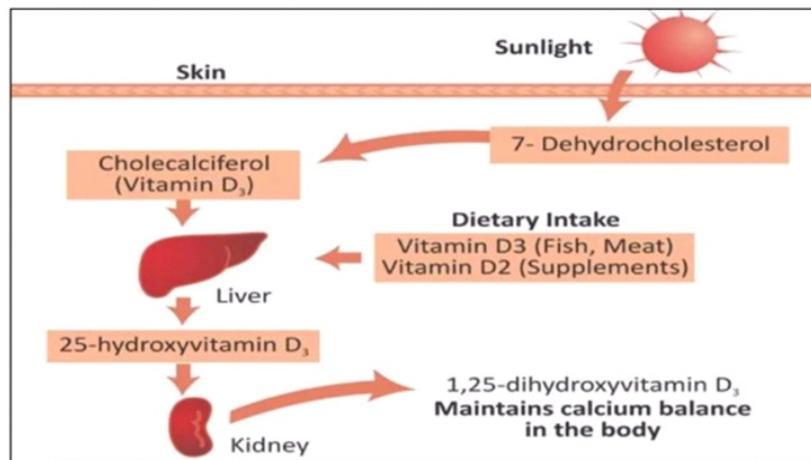
## Calcium supplements

Limit 500 mg calcium at one time from food and / or supplements. Spread calcium sources throughout the day. To reduce the side effects calcium, it can be started with the dose of 500 mg for a week and then it can be increased slowly. Absorption of calcium is decreased when taken with foods rich in fibres, fat, iron, zinc, spinach, coffee, alcohol and antacids.

## Calcium supplements absorption

Thyroid medications, corticosteroids, tetracyclines and anticonvulsants should not be taken along with calcium. Calcium is contraindicated in patients with hypercalcemia, renal insufficiency and used with caution in nephrolithiasis. Excess amounts more than 2500 mg a day affects kidneys and can reduce the absorption of other minerals like iron, zinc and magnesium.

### Vitamin D and Sunlight



Despite the sunny climate there is widespread vitamin D deficiency in Asian Indians of all age groups including children, pregnant women and adult males and females living in urban and rural areas in India.

## Vitamin D from sunlight exposure

Best time to get vitamin D is to expose to the sunlight between 11 am to 2 pm. Clothing, sunscreen, window glass and pollution reduce the amount of vitamin D production.

## Vitamin D deficient population

Above 50 years the skin becomes less effective in vitamin D production. Vitamin D deficiency will occur when dietary intake is low, exposure to sun is reduced, dark skin and pollution. It can also be due to overweight or obesity, gastric bypass surgery, milk allergy or lactose intolerance, liver or digestive diseases, such as Crohn's disease or coeliac disease. Vitamin D is necessary for calcium absorption. A daily combined total of 2,000 IU from food and supplements of vitamin D is safe and excess should be avoided.

## Management of vitamin D deficiency

Cholecalciferol (Vitamin D3) tablet or powder 60,000 IU / once a week for eight weeks preferable with milk or on IM injection of 6,00,000 IU is given to correct the deficiency. It can be repeated only after 3 months after confirmation of persistent low levels of vitamin D). Maintenance therapy (from natural sources or supplements) is advised after correction of the deficiency.

## **Maintenance therapy**

Cholecalciferol tablet or powder 60,000 IU once a month in summer or twice a month in winter or vitamin D supplements by oral spray or oral tablets of 2000 IU/day or injection of Cholecalciferol 3,00,000 IU IM, twice a year or 6,00,000 IU IM once a year. Cholecalciferol, 1,000 IU daily, will raise blood levels, on average, by approximately 10 ng/ml.

## **Vitamin D is important for overall health**

Vitamin D deficiency leads to metabolic syndrome in post-menopausal women. Vitamin D supplementation reduces triglycerides, insulin and HOMA-IR values. It also increases the physical performance and reduces the risk of falls.

## **Benefits of collagen**

Collagen can improve skin health. It slows down aging. It helps in relieving joint pain and reduces inflammation. It could prevent bone loss and improve BMD. It boosts muscle mass and increases muscle growth and strength. Collagen promotes heart health and reduce the risk factors associated with atherosclerosis.

Other health benefits of collagen are it prevents brittleness in hair and nails and stimulate them to grow longer. Collagen also improves gut health and reduces intestinal permeability or leaky gut syndrome. It promotes brain health and improves mood and reduces symptoms of anxiety.

## **Collagen supplementation**

Both vegetarian and non-vegetarian food contain collagen. In vegetarian diet the most abundant amino acids in collagen are glycine, lysine and proline. Plant-based foods that are high in all three amino acids include : soy products like tempeh, tofu and soy protein; Black beans / kidney beans / many other legumes; Seeds especially pumpkin, squash, sunflower and chia; Nuts like pistachio, peanut and cashew.

Non vegetarian diet like chicken skin, pork skin and fish contain collagen. However, its absorption is not as efficient as that of hydrolyzed collagen. Bad taste in the mouth, heartburn and fullness are the side effects due to collagen supplementation. People have reported many benefits of collagen supplements, but these claims haven't been studied much.

## **Physical activity Vs exercise**

Physical activity is any bodily movement, produced by the muscles. Exercise is a type of physical activity that is planned, structured, repetitive and purposeful to improve or maintain some component of fitness or health. Both are important for good health. Physical activity should be maintained. Aerobic and cardio workouts are more helpful. Strengthening, resistance training for muscles, flexibility for muscle and joints will help in balance and posture for prevention of falls which reduces fracture risk. Breathing exercise will improve respiratory health. Kegels exercise for pelvic floor strengthening can be suggested to prevent descent of uterus.

## **Benefits of exercise at midlife**

Helps to maintain a healthy weight, increases BMR, improves bone density, muscle strength and joint mobility. Exercise improves coordination and balance. It also corrects lipid profiles and reduces CVD risk. Pelvic floor exercises can reduce genito-urinary problems. It relieves depression and induces sleep. Over all, exercise improves quality of life.

## Stress reducing techniques

Exercise, stretching, yoga, meditation, periodic vacation with the family, calling a friend, attacking your goal with enthusiasm and focus, slowly indulging in one portion of a favorite food, spending time with a loved one, with pets, watching a funny TV show can reduce stress.

## Management of vasomotor changes

### Phytoestrogens

Dietary or supplementary phytoestrogens modestly improve hot flushes and vaginal dryness. The bean of the soy plant (*Glycine max* L) is used as a phyto-therapeutic supplement. Isoflavones (soy) or black cohosh may relieve vasomotor symptoms. The isoflavones include the biochemical sources like genistein, daidzein, glycitein, biochanin A and formononetin.

### Isoflavones

Isoflavone has been proposed as a natural alternative to hormone replacement therapy (HRT). Isoflavones are identified to decrease bone loss and they favorably alter the insulin resistance, glycemic control and serum lipoproteins in post-menopausal women with T2DM, thereby improving their cardiovascular risk profile.<sup>8</sup>

## Summary

Menopause is inevitable and nearly 1/3rd of women's life is spent in this stage. Nutrition, exercise and medications are important in this golden stage of life. Lifestyle modification is important and should be considered in the treatment plan of menopausal women. Balanced diet is essential to maintain the health of the menopausal women. Adequate daily supplementation of calcium and vitamin D can help to prevent osteoporosis and risk of falls. Physical activity can help to manage some menopause symptoms and decrease the risk of cardiovascular disease and osteoporosis.

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## CALCIUM AND VITAMIN D IN OSTEOPOROSIS

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#### Introduction :

Osteoporosis and osteomalacia are metabolic disorders effecting bone health. **Refer Figure 1.** World Health Organisation defines osteoporosis as “a systemic skeletal disease characterized by low bone mass (measured as bone mineral density BMD) and micro architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fractures involving the wrist, spine, hip, pelvis, ribs, or humerus<sup>1</sup>. The causes are multifactorial calcium and vitamin D deficiency adds to the severity of the disease. **Refer Figure 2**<sup>2</sup>. Vitamin D deficiency accounts for the most common nutritional deficiency among children and adults and presents as rickets and osteomalacia. Osteomalacia in adults is due to prolonged deficiency of vitamin D, resulting in impaired osteoid mineralization<sup>3</sup>. Osteomalacia may be asymptomatic and present radiologically as osteopenia. It can also produce characteristic symptoms, independently of the underlying cause, including diffuse bone and joint pain, muscle weakness, and difficulty walking<sup>4</sup>.

Calcium is an essential element of bone architecture and is required for deposition of bone mineral throughout life. Major (99%) part of calcium is stored in the bones and teeth, and the rest is found in the extracellular fluid (ECF) or plasma which is crucial to maintain bone health. If the plasma level decreases, bone resorption increases to restore plasma levels. Adequate intake of calcium is necessary to maintain this balance. Calcium is absorbed in the small intestines with the aid of vitamin D (Bringhurst et al 2005). Excretion of calcium is primarily through the kidneys, although there is minor fecal loss.

Vitamin D is a fat soluble vitamin, and is a prohormone. Major biological function is to maintain normal blood levels of calcium and phosphorus and more than thirty six tissues like macrophages, prostate tissue also have Vitamin D receptor in the nucleus and plasma membrane. Vitamin D is formed in the skin with exposure to sunlight and from the diet. **Figure 3.** The storage form is 25 OH Vitamin D3 (calcidiol), the active form circulating in the blood is 1,25 (OH) 2 Vitamin D (calcitriol). The available forms of vitamin D supplements are ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3) and calcitriol. Patients with serum 25 (OH)D levels < 12 ng/ml are at risk for developing osteomalacia<sup>5</sup>. Institute of Medicine defined the Safe Upper Limit for vitamin D as 4000 international units / day<sup>6</sup>. Vitamin D excess especially combined with calcium supplementation, may cause hypercalcemia, hypercalciuria, and kidney stones<sup>7</sup>. Chronically raised vitamin D levels have been found in some association studies to be linked to a modest increase in risk of some cancers (eg, pancreatic), mortality, and falls<sup>8</sup>.

#### Epidemiology :

Osteoporosis is an asymptomatic or ‘silent’ disease and generally present as a fragility fracture. Global data indicates that 20% of women with hip fracture die within one year of the fracture and 50% of them never regain their functional independence<sup>9</sup>. Stratification of the risk based on age shows that the prevalence of low bone mass is more than 40% from the age of 40 years and increases to more than 62%

Figure 1 - The pathway from Vitamin D deficiency to falls and fractures

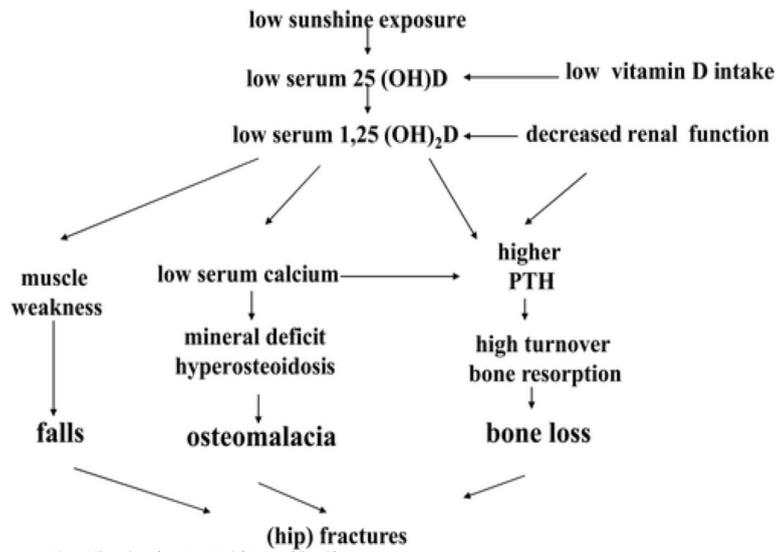


Figure 1 The pathway from vitamin D deficiency to falls and fractures.  
© 2008 American Society for Bone and Mineral Research

Figure 2 - Age versus bones Multifactorial causes

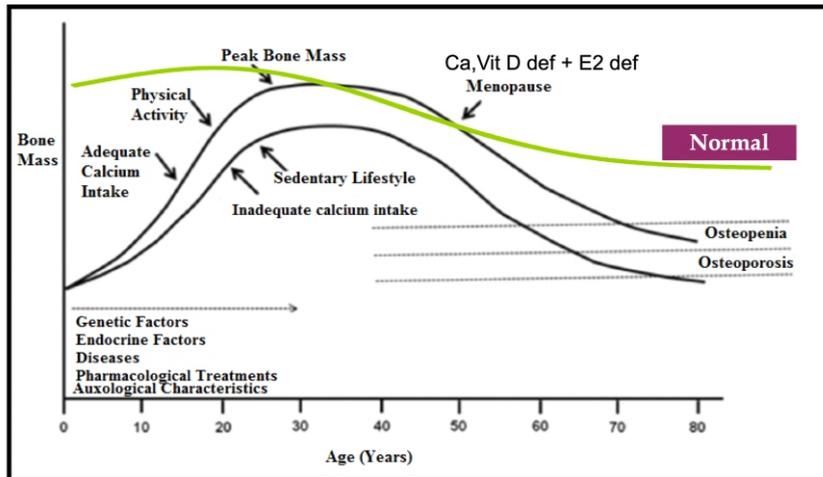
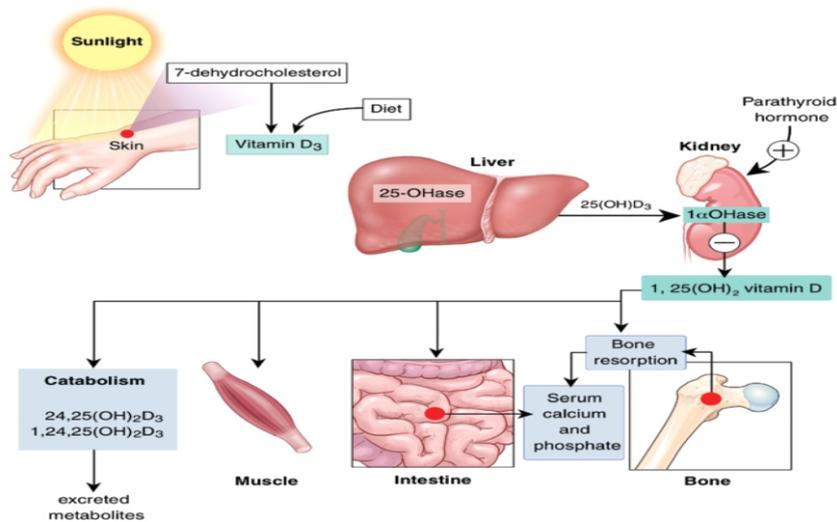


Figure 3

### Metabolism Of Vitamin D



by age 60 and 80% by the age of 65 years<sup>10</sup>. High prevalence of postmenopausal osteoporosis in Indian women may be due to inadequate nutrition, i.e., Low consumption of dairy products, cereals, green vegetables Diets high in oxalates (eg : spinach) or phytates (eg : grains, seeds, legumes) inhibit calcium absorption, rice (poor source), high salt content, caffeine (Increase calcium excretion) low protein (decrease urinary calcium excretion) lactose intolerance, malabsorption syndrome sedentary life style, and early menopause<sup>11</sup>. There is wide prevalence of low dietary calcium intake in Indians of all age groups with majority of postmenopausal women consuming < 400 mg/ day<sup>12,13</sup>. This extends to all the other age groups (infancy, adulthood, postmenopausal women, pregnancy and lactation). Coarse cereals (defined as cereal grains other than wheat & rice) are directly consumed in many developing countries. The nutrient content-kcal, calcium(mg), phytate (mg) per 100 g of edible portion (12% moisture) for various cereals are rice (milled, *oryza sativa*) 356,33,266; wheat (*atta*, *triticum aestivum*) 320,30,632; sorghum (jowar; *sorghum vulgare*) 334,25,549; pearl millet (*bajra*; *pennisetum glaucum*) 348,42,485; maize (zeus maize) 334,26,646; finger millet (*ragi*; *eleusine coracana*) 320,350,306 respectively (74-79). Finger millets contain highest amount of calcium but with high amount of antinutrient-phytates. Phytates inhibit the micronutrient absorption (calcium) and reduce the bioavailability<sup>14</sup>.

About 80% - 85% of population from India are suffering from various degrees of vitamin D deficiency<sup>15</sup>. Studies on bone mineral health from different parts of India indicate wide prevalence of vitamin D deficiency in all age groups, including neonates, infants, school children, pregnant / lactating women, adults, and postmenopausal women. This is due to poor dietary sources, inadequate food fortification, abundant sun-shine but over-clothing, higher skin pigmentation, pollution calcium deficiency, genetic factors, increased metabolic clearance of 25OHD<sub>3</sub>, at age 50 or older the skin becomes less effective as a source.

Nutritional factors probably play a major role as shown in the ICMR studies on three socioeconomic groups at National Institute of Nutrition. They showed that after the age of 50 years, osteoporosis of the spine was only 16% in the high income group (with calcium intake of 1000 mg) compared to the low income group with 65% osteoporosis (calcium intake around 400 mg)<sup>16</sup>. The fracture rate at the neck of the femur was shown to occur 12-15 years earlier in women from low income group as compared to that in high income group<sup>16</sup>. Based on NNMB, Report of Urban Surveys National Nutrition Monitoring Bureau, National Institute of Nutrition (ICMR). Hyderabad 2016. the median milk consumption in Urban and Rural India is 122 ml/Consumption Unit (CU) and 85 ml/CU, respectively. Calcium intakes from the same data show intakes of 402 mg/CU (Urban) and 331 mg/CU (Rural).

#### Impact of lifestyle management on bone health

Maternal nutrition and in utero influences have the potential to influence skeletal development through in utero programming of several hormones. Recent data on vitamin D status in pregnant and lactating Indian women from Delhi, Lucknow and Mumbai reveal a very high prevalence of hypovitaminosis D (84-93%). One study suggested that supplementation with vitamin D during pregnancy could result in better anthropometric indices in the newborns up to 9 months of follow up<sup>17</sup>. Hence, optimization of maternal nutrition and intrauterine growth should ideally be included in the preventive strategies for osteoporotic fracture.<sup>7</sup> There is evidence to support the role of poor maternal nutrition (calcium and vitamin D) on the neonatal bone mineral content and its consequences on adult bone mass, skeletal size, and fracture risk. It is imperative to initiate the management of postmenopausal osteoporosis from in utero<sup>18</sup>. Marwah et al have evaluated the impact of lifestyle on

BMD and osteoporosis in Indian Jawans and Indian sportswomen, and highlighted that good nutrition, better bone biochemical parameters, adequate sun exposure and physical activity from younger age helped to attain better peak bone mass when compared to their age matched sedentary controls<sup>19</sup>.

#### Impact of calcium and vitamin D supplementation on bone health

Supplements of calcium and vitamin D have a vital role in the management of low bone mass osteoporosis, in the elderly and during pregnancy and lactation. Supplements may be needed throughout lifespan in people suffering from non modifiable factors effecting calcium and vitamin D absorption and or inadequate consumption from the diet. A meta-analysis primarily based on the subanalysis by Prentice et al. from the Women’s Health Initiative clinical trial and cohort study indicate that supplementation could decrease the risk of total and hip fractures by 15 and 30 %, respectively, which could decrease the public health burden of osteoporotic fractures<sup>20</sup>. Calcium and vitamin D supplements are highly cost-effective, and expanded use could considerably reduce fractures and related costs. If all adults with osteoporosis in the European Union (EU) and United States (US) used calcium and vitamin D supplements, it could prevent more than 500,000 fractures / year in the EU and more than 300,000 / year in the US and save approximately €5.7 billion and US \$3.3 billion annually.

Although these analyses included individuals aged  $\geq 50$  years, the observed effects are likely driven by benefits observed in those aged  $\geq 65$  years<sup>21</sup>. Optimal intake can be achieved with a combination of diet (**Refer Table 3**) plus supplements, preferably 50% from dietary sources. Calcium appears to be as well absorbed from supplements as from milk<sup>22</sup>. It is important for patients to be aware that calcium and vitamin D alone are insufficient to prevent fracture<sup>23</sup>.

The recommended dietary allowance (RDA) of calcium intake for an adult Indian women is given in **Table 1**. (National Institute of Nutrition, ICMR, Dietary Guidelines for Indians : A Manual. 2011 Annexure 3).

**Table 1**

Daily Requirement of Calcium	
Age Group	Calcium (mg)
Adult Women	600
Pregnancy	1200
Lactation	1200
Post menopausal women	800

**Table 2**

Estimate your daily Calcium Intake from diet			
Source	Calcium (mg)*	Number of servings	Total calcium (mg)
Dairy	300-500/1 glass milk 300/1 katori curds		
Non-dietary	200-300	x	
Total intake of calcium in mg			

**Table 3 : Sources of calcium**

Dietary Product	Serving (gm)	Calcium (mg)
Milk (cows)	1 glass (250 ml)	300
Milk (buffalos)	1 glass (250 ml)	522
Milk low fat	1 glass (250 ml)	300
Curd (cow's milk)	1 katori	149
Butter milk (cow's milk)	1 glass (250 ml)	75
Channa (cow's milk)	25 g	52
Khoa (cow's milk)	25 g	239
Cheese slice	20 g	158
Whole milk powder (cow's milk)	1 katori	155
Paneer	25 g	50
Chapati	1 (25 g)	12
White bread	1 slice	30
Ragi	25 g	7
Rajma	1 katori (25 g)	65
Soyabean	1 katori (25 g)	60
Kale chane (whole bengal gram)	1 katori (25 g)	72
Udad dal (black gram dal)	25 g	50
Palak veg	1 katori	73
Beetroot	25 g	50
Methi veg	1 katori	395
Chaulai	1 katori	397
Beans	1 katori	90
Bathua	1 katori	150
Sarso	1 katori	155
Okara (bhendi)	½ katori	65
Broccoli	½ katori	50
Almonds	1 handful (25 g)	58
Cashew nut	1 handful (25 g)	13
Dried figs	5 whole	95
Gingelly seed (til)	25 g (1 tablespoon)	363
Orange	1 medium sized	50
Fish Hilsa	25 g	45
Fish Rohu	25 g	160

**Table 4 : US Endocrine Society 2011 RDA**

Life stage group	RDA (IU)	Upper limit
Adults (18 years and above)	1,500–2,000	10,000
Pregnancy and lactation	1,500–2,000	10,000
Children and adults at risk*	2–3 times the normal requirement for their age	

\*Obesity, HIV infection, on glucocorticoids, anticonvulsant, antifungal, and antiviral therapy. A desirable range is between 30 and 60 ng/mL, although levels up to 100 ng/mL are unlikely to result in vitamin D toxicity. Except in granuloma disorders, wherein it is advisable to maintain the serum levels of 25 (OH) D upto >30 ng/mL.

The following section is taken from the book Meeta, CV Harinarayan, Raman K Marwaha, Rakesh Sahay, Sanjay Kalra, Sushrut Babhulkar. 2012,2020: Clinical Practice Guidelines of Management of Postmenopausal Osteoporosis - Indian Menopause Society.

- a. Encourage dietary intake supplements are added to correct the deficient balance. The risk of cardiovascular events and calculi are not observed with the recommended doses of calcium
  - Limit 500 mg calcium at one time from food and/or supplements. Spread calcium sources throughout the day
  - Dietary calcium restriction is no longer recommended for patients with hypercalciuria
  - The 2016 NOF guideline on the safety and benefit of calcium supplementation stated that calcium intake below the UL (2,000 - 2,500 mg/d) is not associated with CVD risk in generally healthy adults
  - The data on supplemental calcium intake over and above the RDA is currently controversial. In case where calcium supplementation is medically necessary, patients should be encouraged to take their calcium supplements with a meal and should be monitored for hypercalciuria
  - Absorption of calcium is decreased when taken with foods rich in oxalic acid, phytates and tannins (spinach, fibres, Iron, zinc, spinach, tea, alcohol), vitamin D deficiency, estrogen deficiency, ageing, decreased gastric acid production, and malabsorptive disorders. Thyroid medications, corticosteroids, tetracyclines, and anticonvulsants and calcium should be taken separately.
  - 24-h urine calcium is the best method of evaluating adequacy of calcium intake and absorption.

### **Vitamin D**

Vitamin D deficiency can be considered as a National Nutritional Deficiency pandemic. In the background of widespread Vitamin D deficiency in all age groups, it is prudent to adopt the US Endocrine Society 2011 RDA **Refer Table 4**

- a. It is preferable to get Vitamin D through sunlight by exposing 15%30% of body surface area (face, neck, and both arms and forearms) without sunscreen for at least 30 min between 10 am and 3 pm, depending on the season, latitude, altitude, pollution, and skin pigmentation. This is equivalent to consuming 340-490 IU of Vitamin D every day based on the reports that 100 IU of Vitamin D intake will raise serum 25(OH)D by 1 ng/ml
- b. Dietary sources are limited; hence, the Government of India has permitted fortification of food which would enable population at large to enhance an intake of RDA of Vitamin D by 30% - 50% (200-300 IU). This would be of value if one assumes that the consumption of milk/milk products is 700 ml per day and of oil is 30 ml/day. However, implementing intake from the natural sources has practical limitations. Hence, it is recommended to use Vitamin D as supplements (Grade A)
- c. Recommendations for the management of Vitamin D deficiency and maintenance are given below (Grade B):
  - i. Cholecalciferol (Vitamin D3) is available in the form of oral tablets (conventional morcellized or nanoemulsion formulations), granules, and oral spray. Dosages of 1000, 2000, and 60,000 IU are available

Intramuscular (IM) injections of Vitamin D3 are available in doses of 300,000 and 600,000 IU per ampoule. Injections of cholecalciferol are cost-effective and may be recommended in cases of

malabsorption and also to increase compliance. The disadvantages are painful and erratic blood levels.

- Cholecalciferol is the preferred therapy for correction of deficiency and maintenance.
- Management of deficiency : Cholecalciferol (Vitamin D3) 60000 IU/orally once a week for 8 weeks preferably with milk is given. One IM injection of 600,000 IU is given to correct the deficiency (not to be repeated before three months and may be given after confirmation of persistent low levels of Vitamin D). This is followed by maintenance therapy
- Maintenance therapy : Cholecalciferol 60,000 IU once a month in summer or twice a month in winter is preferred. Vitamin D supplements of 2000 IU/day or injection of cholecalciferol 300,000 IU IM twice a year or 600,000 IU IM once a year is given
- Cholecalciferol, 1000 IU daily, will raise blood levels, on average, by approximately 10 ng/ml
- Upper acceptable limit : The dose for treatment should not exceed 4000 IU/day and hypercalcemia has been reported when the dose exceeds 10,000 IU/day
- Vitamin D derivatives : Calcitriol, the active form of Vitamin D, is reserved only for patients with chronic renal and hepatic disease. Alfacalcidol is a synthetic analog of the active Vitamin D metabolite calcitriol (1,25-dihydroxyvitamin-D3), and it is metabolized to calcitriol by its 25-hydroxylation in the liver. It is less potent than calcitriol. The use of Vitamin D derivatives necessitates monitoring of serum and possibly urine calcium. There is the risk of hypercalcemia and hypercalciuria. Adverse effects of prolonged hypercalcemia include impairment of renal function and nephrocalcinosis
- In postmenopausal women, the intake of Vitamin D should be in addition to sunlight exposure. Vitamin D supplementation ( $\geq 500$ -2000 IU/day) was favorable in the reduction of hip fracture and any nonvertebral fracture in persons aged 65 years of age or older.

### Role of Gynaecologist

1. Preconceptional counselling on bone and muscle health
2. In Utero Adequate RDA of Calcium and Vitamin D
3. Adolescence-Attainment of optimal peak bone mass
4. Reproductive phase Maintain adequate menstrual function
5. Pregnancy and Lactation-Increased RDA of Calcium and Vitamin D
6. Menopause and post menopause - Increased RDA of Calcium and Vitamin D, Screening, maintaining and treating for bone health

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## NUTRITION FOR IMMUNE COMPROMISED WOMAN

**Dr. Anju Soni**

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### Session outline

- Historical background
- Relationship between immune compromised and nutrition
- Effects of nutrition on resistance to infection
- Effects of infection on nutritional status
- Mechanisms of infection-nutrition

### Historical background -

- 1950s textbooks of nutrition-little/no mention of a relation to infection
- Same was true for articles on immune compromised diseases
- Studies in experimental animals and clinical observations were pointing out the role of infection in precipitating nutritional disorders
- Clinicians and nutritionists did not recognize the importance of the relationship
- Late 1950s-field and metabolic studies demonstrated the synergism in humans
- Effects were then extensively investigated
- Experience in knowledge of cell mediated immune mechanisms led to an understanding of how malnutrition lower body resistance
- Infection - leading cause of morbidity and mortality in children - Africa, Asia, Latin America
- Malnutrition - IC complex remains the most prevalent PH problem globally
- Immunocompromised patients are increasingly common in modern surgical practice. Challenges related to their care include identifying the determinants of increased risk and selecting the appropriate therapy for individual patients<sup>3</sup>
- Food restrictions used with immunocompromised patients include a sterile diet, low-microbial diet or modified hospital diet.<sup>6</sup>

### What is our Immune System?

- we are constantly exposed to potentially harmful microbes.
- Our immune system, a network of intricate stages and pathways, protects us against these harmful microbes.

### Types of Immunity

Innate Immunity : is a first-line defense from pathogens that try to enter our bodies, achieved through protective barriers. These barriers include :

- Skin that keeps out the majority of pathogens
- Mucus that traps pathogens
- Stomach acid that destroys pathogens

- Enzymes in our sweat and tears that help create anti-bacterial compounds
- Immune system cells that attack all foreign cells entering the body

### **Adaptive or acquired immunity**

- Learns to recognize a pathogen.
- Regulated by cells and organs
- Spleen, thymus, bone marrow, & lymph nodes.
- Create antibodies and lead to multiplication of immune cells Specific harmful substance

### **Immune Disorders**

**Autoimmune disorders** like lupus, rheumatoid arthritis, or type 1 diabetes are partly hereditary and cause hypersensitivity in which immune cells attack and destroy healthy cells.

**Immunodeficiency disorders** can depress or completely disable the immune system, and may be genetic or acquired. Acquired forms are more common and include AIDS and cancers like leukemia and multiple myeloma.

### **Microbiome area of intense & active research**

- Trillions of microorganisms or microbes that live in our bodies
- Play a key role in immune function
- Gut is a major site of immune activity and the production of antimicrobial proteins.
- Diet plays a large role in determining what kinds of microbes live in our intestines
- A high-fiber plant-rich diet with plenty of fruits, vegetables, whole grains, and legumes
- Microbes break down fibers into short chain fatty acids
- Probiotic foods feed microbes include kefir, yogurt with live active cultures, fermented vegetables, sauerkraut, tempeh, kombucha tea, and miso.
- Prebiotic foods live helpful bacteria include garlic, onions, leeks, asparagus, Jerusalem artichokes, dandelion greens, bananas, and seaweed, a more general rule is to eat a variety of fruits, vegetables, beans, and whole grains for dietary prebiotics.

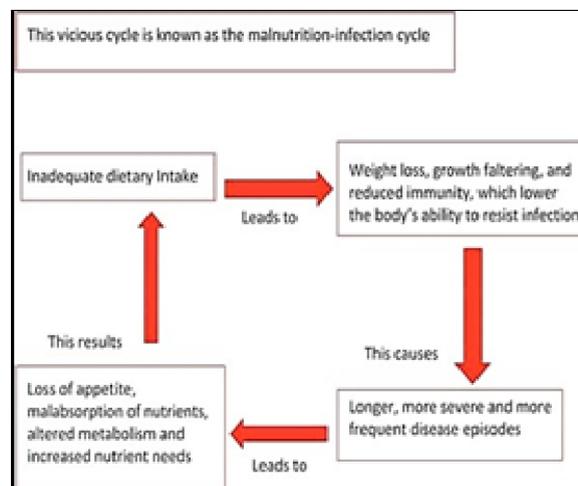
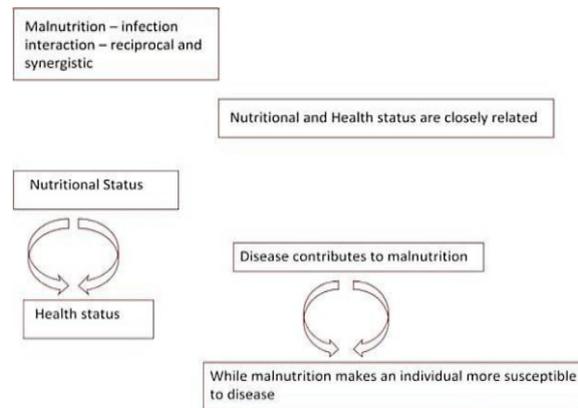
### **3DP Technology :**

Three-dimensional printing (3DP) technology gained significance in the fields of medicine, engineering, the food industry, and molecular gastronomy. 3D food printing (3DFP) has the main objective of tailored food manufacturing, both in terms of sensory properties and nutritional content. Additionally, global challenges like food- waste reduction could be addressed through this technology by improving process parameters and by sustainable use of ingredients, including the incorporation of recovered nutrients from agro- industrial by-products in printed nourishment.<sup>4</sup>

The potential of 3D food printing (3DFP) technology is to improve oral intake and nutritional needs in patients, as its ability to create personalized food that matches the need of consumers. Three aspects of 3DP potential were introduced as a key potential to enhance oral intake in the patients, including the potential to create foods with a variety of textures, the potential to produce a variety of food materials,\* and the potential to design food appearance.<sup>2</sup>

## MALNUTRITION - IC INTRACTIONS

- Relationships is reciprocal and synergistic :
  - ✓ Infection leads to a deterioration in nutritional status and at the same time
  - ✓ Malnutrition increases susceptibility to infections



### Effects of malnutrition on resistance in immune compromised

- Malnutrition immune compromised reduce Body resistance to infection by reducing
  - Antibody formation especially PEM
  - Production of nonspecific protective substances e.g., interference, lysosomes hydrolytic enzymes
  - Phagocytic activity of microphages
  - Non-specific resistance to bacterial toxins
  - Inflammatory responses
  - Wound healing and collagen formation

### Effects

- Examples of effects of micronutrient deficiency
  - VitaminA deficiency reduces leucocyte numbers, lymphoid tissue weights, T-Cell function.
  - Iron deficiency reduces cytotoxic activity of phagocytes and proliferation of t helper cell
  - Vitamin B deficiency reduces lymphocyte number, lymphoid tissue weight, antibody response and depresses phagocyte function and T cell proliferation
  - Zinc deficiency reduces T cell development and function

### **Effects of IC on nutritional status**

- Profound effects on the intake, metabolism and excretion of most nutrients
- Cause protein catabolism
- Increase resting energy metabolism
- Reduces serum vitamin A concentration, precipitating xerophthalmia

### **Effects**

- Metabolic responses to IC-have deep effects on utilization of food and endogenous nutrient stores leading to malnutrition
- Increased energy expenditure, 10-15% per 1°C rise in BT
- CHO stores for energy are rapidly depleted
- Increased fecal losses and/or poor absorption of nutrients
- Increased permeability of intestinal mucosa
- Macroscopic blood loss-certain parasites

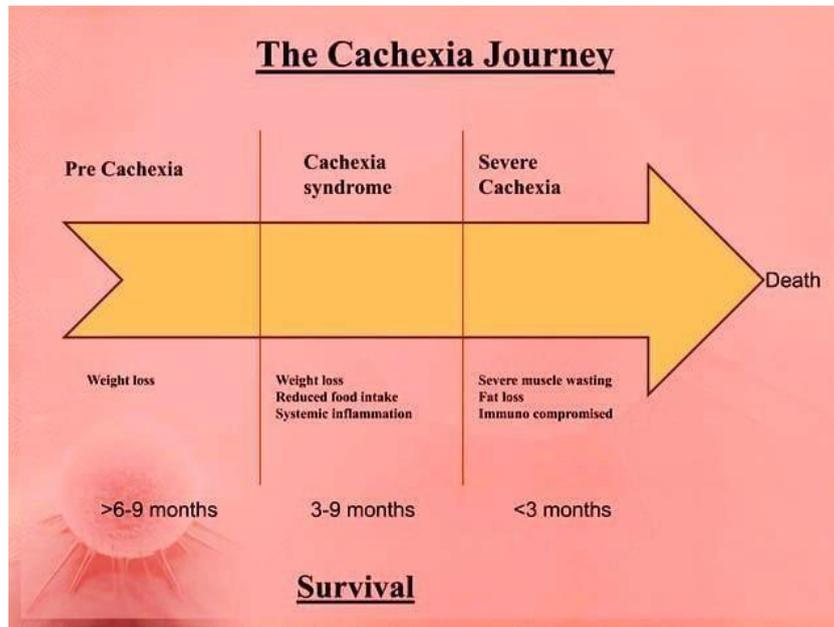
→ IDA

### **Effects of HIV/AIDS on nutritional status**

- Depressed appetite, poor nutrient take and limited food availability
- Fever, nausea, vomiting and diarrhoea
- Depression
- Increased energy requirements -20-30% IN Symptomatic HIV AIDS
- Side effects from drugs-opportunistic infections
- Chronic infections, malabsorption, metabolic disturbances, muscle and tissue catabolism

### **General mechanism-infection-malnutrition**

- 1 shifts in the types and quantities of foods consumed (custom or loss of appetite)
- 2 Adverse effects of treatment on nutrition
  - ✓ Purgatives to children with diarrhoea or worms
  - ✓ prolonged antibiotics may interfere- synthesis of vitamin K and B vitamins
- Impaired absorption-Diarrhoea-proteins, vitamin A, Vitamin B12 and folic acid
- 2 Energy ,protein and micronutrients needs are elevated in order to fight off infection
- 5. parasitic organism malaria or schistosomiasis or intestinal worms divert nutrients for their own use
- 6 Increased urinary loss :
  - ✓ Nitrogen ,vitamin A, ascorbic acid, Fe ,Zn as a result of stress responsefn
  - ✓ Urinary schistosomiasis loss of Fe and proteinfn
- 7 Increased fecal loss :
  - ✓ Leaking gut phenomenon in hookworm infestation leads to loss of nitrogen and Fefn
- 8 Sweat Loss
  - ✓ Loss of amino acids, nitrogen and minerals



#### Changes That Occur In Metabolism Carbohydrate

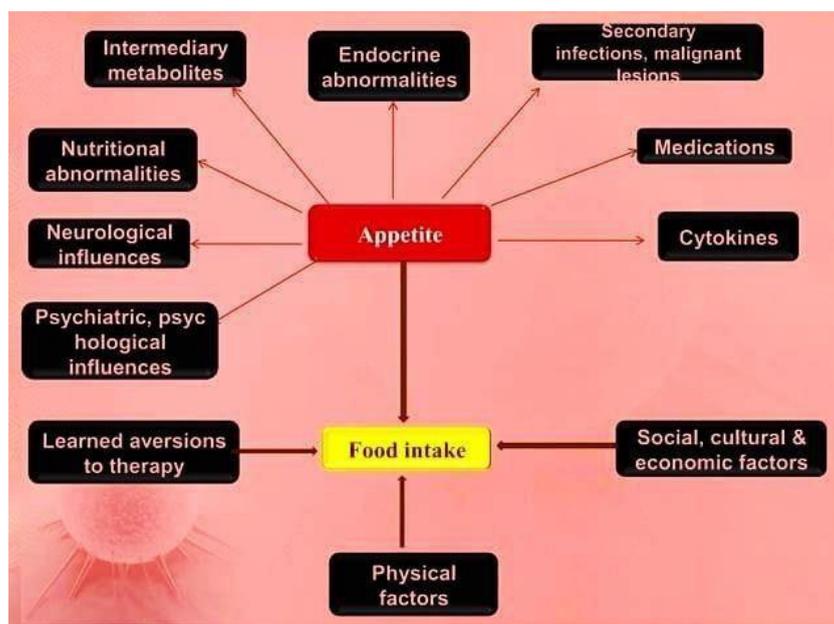
- Insulin resistance
- Increased glucose synthesis
- Gluconeogenesis
- Increased Cori cycle activity
- Decreased glucose tolerance

#### Protein

- Increased protein catabolism
- Decreased protein synthesis

#### Fat

- Increased lipid metabolism
- Decreased lipogenesis
- Decreased activity of lipoprotein lipase (LPL)



## Nutrition support - How to go about?

- Assess** : Patient history, look for signs, weigh regularly and know the lab values
- Plan** : Nutritional requirements set short term and long term goals and individualize needs
- Intervene** : Symptom management- strategies for patients , enteral and parenteral nutrition
- Evaluate** : Effectiveness of intervention, achievement of long and short term goals

## Evaluation : Before beginning intervention

- **Cardinal principle** :  
Individualize to needs of patient
- **Short-term goal** :  
Improve nutritional status
- **Long-term goal** :  
Normalize Nutrient Intake Alleviate disease symptoms
- **Outcomes** :  
Better Quality of life/Vigor  
Fewer Crisis / Improved Treatment Response

## Screening Vs Assessment

### Screening

- Done to detect the possibility of nutrition risk
- All patients in all settings require it
- Required to be stored in the medical file
  
- Patient generated guides

Minimum immediate measurements,  
least expense, concise information

### Assessment

- More intensive and thorough
- Needs intervention, follow up regularly
- Assessment must have weight history, appearance, functional status, diet history, biochemical parameters, medication and planned treatment
- Assessment can include financial and psychosocial aspects is possible
- Has to be done by a dietician or doctor only

Minimum immediate measurements,  
least expense, concise information

## Nutritional Assessment Criteria

### 1. Anthropometry : Weigh regularly

- BMI
- Severe weight loss
- Mild-arm circumference

### 2. Laboratory data : Not always the most accurate when viewed alone

- Serum albumin : Level falls only after significant depletion has occurred
- Serum pre albumin : Can be used for assessment
- Serum transferrin : More sensitive marker for marginal protein depletion
- Total iron binding capacity
- Delayed hypersensitivity skin testing to a recall antigen
- Total lymphocyte count

### 3. Diet history

- 24 hour recall, Food frequency

#### Who is severely malnourished?

- Weight loss more than 10%
- Poor intake for 2 weeks or more
- BMI less than 18.5
- Mid arm circumference : Male < 17.6 cm, Female < 17.1 cm
- Subjective global assessment score - "C"
- Mini nutritional assessment score - < 25
- Albumin on entry < 3 gm%
- Total lymphocyte count < 1500

#### Concept of Low Bacterial Diet in Immunocompromised

- The low-bacteria diet (LBD) is a diet intended to reduce the ingestion of bacterial and fungal contaminants by the exclusion of foods such as uncooked fruits and vegetables, cold cuts, undercooked eggs and meat, unsterilized water, unpasteurized milk products, and soft cheeses. The LBD is also known as a "neutropenic diet," a "low-microbial diet," and a "reduced bacteria diet." By reducing the introduction of potentially pathogenic organisms into the gastrointestinal tract, it is assumed that the risk of bacterial and fungal infections will be reduced<sup>1</sup>
- Neutropenia may be influenced by malignancy type, treatment, age extremes, inadequate nutrition, or psychological stress. Of these five factors, only nutrition and stress are amenable to nursing intervention and management. The increasing trend of providing treatment in the outpatient setting and managing the patient with neutropenia in the home challenges nurses to develop innovative methods of care.<sup>5</sup>

#### Nutrition Requirement Guidelines

Calories (Harris-Benedict formula)

- Obese patients : 21-25 kcal/kg
- Non-ambulatory / sedentary adults : 25-30 kcal/kg
- Sepsis : 25-35 kcal/kg
- Slightly hypermetabolic or those in need of weight gain or those with stem cell transplant : 30-35 kcal/kg
- Hypermetabolic or severely stressed : > 35 kcal/kg

#### Protein needs

- Normal or Maintenance : 0.8-1.0 g/kg
- Non-stressed cancer patient : 1.0-1.5 g/kg
- Bone marrow transplant or HSCT patients : 1.5 g/kg
- Increased protein needs : 1.5-2.5 g/kg
- Hepatic or renal compromised or elevated ammonia : 0.5-0.8 g/kg

#### Vitamins

Folate  
Vit C  
Retinol

#### Minerals

Magnesium  
Zinc  
Copper  
Iron

## Fluid requirements

- 16-30 years, active : 40 ml/kg
- 31-55 years : 35 mL/kg
- 56-75 years : 30 mL/kg
- 76 years or older : 25 mL/kg
- 1 mL/kcal of estimated energy needs

## Managing Symptoms

- Nutrition can help manage symptoms. The key to start early
- Specific diet modifications while minimize nutrition related side effects
- Each side effect has numerous approaches for management
- Strategies for patients include teaching and trial and error pragmatism
- Screening and assessment will identify those who require aggressive intervention
- For other enteral and sometimes parenteral support is a must

### Food safety guidelines - A common sense approach

All patients need to follow 4 basic steps to food safety

**Clean** : Wash hands, surfaces, produce and clean lids for canned produce

**Separate** : Don't cross contaminate. Separate foods and cutting boards.  
Especially true for flesh foods

**Cook** : Cook to proper temperatures. Use a food thermometer to check internal temperature

**Chill** : Refrigerate promptly. Cold temp slows the growth of harmful bacteria.

- While shopping be careful and read all the labels for expiry date
- Be smart while eating out and transport food carefully and go by rules
- Be aware of food borne illnesses and know the symptoms!!

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## ONCOLOGY AND ROLE OF NUTRITION



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Good nutrition is important for all patients and more so in cancer patients. Nutrition is a process by which food is consumed and utilized by the body for growth, to keep the body healthy, and to replenish tissue. Good nutrition is important for good health. A healthy diet includes foods and liquids that have important nutrients (vitamins, minerals, protein, carbohydrates, fat, and water) the body needs.

#### **Healthy eating habits are important during and after cancer treatment.**

A diet with a focus on plant-based foods along with regular exercise will help cancer patients keep a healthy body weight, maintain strength, and decrease side effects both during and after treatment.

#### **A registered dietitian is an important part of the healthcare team.**

A registered dietitian (or nutritionist) is a must in the team of health professionals that plan cancer treatment and recovery<sup>1</sup>. A dietitian will work with patients, their families, and the rest of the medical team to manage the patient's diet during and after cancer treatment. Research has shown that including a registered dietitian in a patient's cancer care can help the patient live longer. Because many times ill health in cancer is due to poor feeding that could be a sequel to the disease itself or the treatment<sup>1</sup>.

#### **Cancer and cancer treatments do cause side effects that affect nutrition<sup>1,2</sup>.**

For many patients, the effects of cancer treatments make it hard to eat well. Cancer treatments that affect nutrition can be anything from treatment to complication :

- Chemotherapy.
- Hormone therapy.
- Radiation therapy.
- Surgery.
- Immunotherapy.
- Stem cell transplant.

#### **Cancer and cancer treatments may cause malnutrition<sup>2</sup>.**

Cancer and cancer treatments may affect taste, smell, appetite, and the ability to eat enough food or assimilation of the food. This can cause malnutrition, which is a condition caused by a lack of key nutrients. Alcohol abuse and obesity may increase the risk of malnutrition.

Malnutrition can cause the patient to become weak, tired, reduce immunity and reduce the capacity to withstand the complications of therapy. As a result, malnutrition can decrease the patient's quality of life and become life-threatening. Malnutrition may be made worse if the cancer grows or spreads.

Eating the right amount of protein and calories is important for healing, fighting infection, and having enough energy.

## **Anorexia and cachexia are common causes of malnutrition in cancer patients<sup>2</sup>.**

Anorexia is the loss of appetite or desire to eat. It is a common symptom in patients with cancer. Anorexia may occur early in the disease or later, if the cancer grows or spreads. Some patients already have anorexia when they are diagnosed with cancer and almost a tell tale sign in many cancers especially when advanced. Anorexia is the most common cause of malnutrition in cancer patients.

Cachexia is a condition marked by weakness, weight loss, and fat and muscle loss. It is common in patients with tumors that affect eating and digestion. It can occur in cancer patients who are eating well, but are not storing fat and muscle because of tumor growth.

Some tumors change the way the body uses certain nutrients. The body's use of protein, carbohydrates, and fat may change when tumors are in the stomach, intestines, or head and neck. A patient may seem to be eating enough, but the body may not be able to absorb all the nutrients from the food.

### **Effects of Cancer Treatment on Nutrition**

#### **Chemotherapy and hormone therapy affect nutrition in different ways.**

Chemotherapy affects cells all through the body. Chemotherapy stops the growth of cancer cells, either by killing the cells or by stopping them from dividing. Healthy cells that normally grow and divide quickly may also be killed. These include cells in the mouth and digestive tract. Hormone therapy adds, blocks, or removes hormones. It may be used to slow or stop the growth of certain cancers. Some types of hormone therapy may cause weight gain.

#### **Chemotherapy and hormone therapy cause different nutrition problems.**

Side effects from chemotherapy may cause problems with eating and digestion. When more than one chemotherapy drug is given, each drug may cause different side effects or when drugs cause the same side effect, the side effect may be more severe.

The following side effects are common with chemotherapy :

- Loss of appetite.
- Nausea.
- Vomiting.
- Dry mouth.
- Sores in the mouth or throat.
- Changes in tastes.
- Dysphagia.
- Dyspepsia.
- Constipation.
- Diarrhea.

Patients who receive hormone therapy may need changes in their diet to prevent weight gain.

#### **Radiation therapy kills cells in the treatment area.**

Severity of side effects depends on the following :

- Portion of the body being irradiated.
- The total dose of radiation
- Type of radiation.

### **Radiation therapy may affect nutrition.**

Radiation therapy to any part of the digestive system has side effects that cause nutrition problems. Most of the side effects begin two to three weeks after radiation therapy begins and lessens few weeks after completion. Some side effects can persist for months or years after treatment ends.<sup>1</sup> Radiation therapy may also cause tiredness, which can lead to a decrease in appetite.

### **Surgery increases the body's need for nutrients and energy.**

The body needs extra energy and nutrients to heal wounds, fight infection, and recover from surgery. If the patient is malnourished before surgery, it may cause problems during recovery, such as poor healing or infection. For these patients, nutrition care may begin before surgery.<sup>1</sup>

### **Nutrition Assessment in Cancer Care**

- The healthcare team may ask questions about diet and weight history.
- Counseling and diet changes are made to improve the patient's nutrition.
- The goal of nutrition therapy for patients who have advanced cancer depends on the overall plan of care.

### **The healthcare team needs to ask questions about diet and weight history.**

Screening is used to look for health problems that affect the risk of poor nutrition. This can help find out if the patient is likely to become malnourished, and if nutrition therapy is needed.

The healthcare team may ask questions about the following :

- Weight changes over the past year.
- Changes in the amount and type of food eaten.
- Problems that have affected eating.
- Ability to walk and do other activities of daily living.

A physical exam is done to check the body for general health and signs of disease. The patient is checked for signs of loss of weight, fat, and muscle, and for fluid buildup in the body.

### **Counseling and diet changes are made to improve the patient's nutrition.**

A registered dietitian can work with patients and their families to counsel them on ways to improve the patient's nutrition. The registered dietitian gives care based on the patient's nutrition and diet needs. Changes to the diet are made to help decrease symptoms from cancer or cancer treatment. These changes may be in the types and amount of food, how often a patient eats, and how food is eaten (for example, at a certain temperature or taken with a straw).<sup>1</sup>

A registered dietitian works with other members of the healthcare team to check the patient's nutritional health during cancer treatment and recovery. In addition to the dietitian, the healthcare team may include the following :

- Physician.
- Nurse.
- Social worker.
- Psychologist.

### **The goal of nutrition therapy for patients who have advanced cancer depends on the overall plan of care.**

The goal of nutrition therapy in patients with advanced cancer is to give patients the best possible

quality of life and control symptoms that cause distress.

Patients with advanced cancer may be treated with anticancer therapy and palliative care, palliative care alone, or may be in hospice care. Nutrition goals will be different for each patient. Some types of treatment may be stopped if they are not helping the patient.

As the focus of care goes from cancer treatment to hospice or end-of-life care, nutrition goals may become less aggressive, and a change to care meant to keep the patient as comfortable as possible.<sup>1</sup>

### **Treatment of Symptoms**

- Anorexia
- Nausea
- Vomiting
- Dry Mouth
- Mouth Sores
- Taste Changes
- Sore Throat and Trouble Swallowing
- Lactose Intolerance
- Weight Gain

When side effects of cancer or cancer treatment affect normal eating, changes can be made to help the patient get the nutrients they need. Eating foods that are high in calories, protein, vitamins, and minerals is important. Meals should be planned to meet the patient's nutrition needs and tastes in food.

The following are some of the more common symptoms caused by cancer and cancer treatment and ways to treat or control them.

#### **Anorexia**

The following may help cancer patients who have anorexia (loss of appetite or desire to eat) : Eat foods that are high in protein and calories. Add extra protein and calories to food, such as using protein-fortified milk.

- Eat high-protein foods first in meal when appetite is strongest.
- Sip only small amounts of liquids during meals.
- Eat foods that smell good.
- Try blenderized drinks that are high in nutrients (check with your doctor or registered dietitian first).

If these diet changes do not help with the anorexia, tube feedings may be needed. Medicines may be given to increase appetite.

#### **Nausea**

The following may help cancer patients control nausea :

- Eat foods that are bland, soft, and easy-to-digest, rather than heavy meals.
- Eat dry foods such as crackers, bread sticks, or toast throughout the day.
- Eat foods that are easy on stomach, such as white toast, plain yogurt, and clear broth.
- Eat dry toast or crackers before getting out of bed.
- Slowly sip liquids throughout the day.
- Suck on hard candies such as peppermints or lemon drops if bad taste in mouth.
- Stay away from food and drink with strong smells.

- Eat 5 or 6 small meals every day instead of 3 large meals.

### **Vomiting**

The following may help cancer patients control vomiting :

- Do not eat or drink anything until the vomiting stops.
- Drink small amounts of clear liquids after vomiting stops.
- After you are able to drink clear liquids without vomiting, drink liquids such as strained soups, or milkshakes, that are easy on your stomach.
- Eat 5 or 6 small meals every day instead of 3 large meals.
- Sit upright and bend forward after vomiting.
- Ask your doctor to order medicine to prevent or control vomiting.

### **Dry Mouth**

The following may help cancer patients with a dry mouth :

- Eat foods that are easy to swallow.
- Moisten food with sauce, gravy, or salad dressing.
- Eat foods and drinks that are very sweet or tart, such as lemonade, to help make more saliva.
- Chew gum or suck on hard candy, ice pops, or ice chips.
- Sip water throughout the day.

### **Mouth Sores**

The following can help patients who have mouth sores :

- Eat soft foods that are easy to chew, such as milkshakes, scrambled eggs, and custards.
- Cook foods until soft and tender.
- Cut food into small pieces. Use a blender or food processor to make food smooth.
- Suck on ice chips to numb and soothe your mouth.

### **Taste Changes**

The following may help cancer patients who have taste changes :

- Eat poultry, fish, eggs, and cheese instead of red meat.
- Add spices and sauces to foods (marinate foods).
- Eat meat with something sweet, such as cranberry sauce, jelly, or applesauce.
- Use sugar-free lemon drops, gum, or mints if there is a metallic or bitter taste in mouth.

### **Types of Nutrition Support**

- Nutrition support helps patients who cannot eat or digest food normally.
- Nutrition support can be given in different ways.
- Enteral Nutrition
- Enteral nutrition is also called tube feeding.
- Parenteral Nutrition
- Parenteral nutrition carries nutrients directly into the blood stream.
- The catheter may be placed into a vein in the chest or in the arm.

### **Nutrition support helps patients who cannot eat or digest food normally.**

It is best to take in food by mouth whenever possible. Some patients may not be able to take in enough food by mouth because of problems from cancer or cancer treatment.

### **Nutrition support can be given in different ways.**

In addition to counseling by a dietitian, and changes to the diet, nutrition therapy includes nutritional supplement drinks, and enteral and parenteral nutrition support. Nutritional supplement drinks help cancer patients get the nutrients they need. They provide energy, protein, fat, carbohydrates, fiber, vitamins, and minerals. They are not meant to be the patient's only source of nutrition.<sup>3</sup>

A patient who is not able to take in the right amount of calories and nutrients by mouth may be fed using the following :

- Enteral nutrition : Nutrients are given through a tube inserted into the stomach or intestines.
- Parenteral nutrition : Nutrients are infused into the bloodstream.

Nutrition support can improve a patient's quality of life during cancer treatment, but may cause problems that should be considered before making the decision to use it. The patient and healthcare team should discuss the harms and benefits of each type of nutrition support.<sup>3</sup>

### **Enteral nutrition is also called tube feeding.**

Enteral nutrition gives the patient nutrients in liquid form (formula) through a tube that is placed into the stomach or small intestine. The following types of feeding tubes may be used :

- A nasogastric tube is inserted through the nose and down the throat into the stomach or small intestine. This is used when enteral nutrition is only needed for a few weeks.
- A gastrostomy tube is inserted into the stomach or a jejunostomy tube is inserted into the small intestine through an opening made on the outside of the abdomen. This is usually used for long-term enteral feeding or for patients who cannot use a tube in the nose and throat.

The type of formula used is based on the specific needs of the patient. There are formulas for patients who have special health conditions, such as diabetes, or other needs, such as religious or cultural diets.

### **Parenteral nutrition carries nutrients directly into the blood stream.**

Parenteral nutrition is used when the patient cannot take food by mouth or by enteral feeding. Parenteral feeding does not use the stomach or intestines to digest food. Nutrients are given to the patient directly into the blood, through a catheter inserted into a vein. These nutrients include proteins, fats, vitamins, and minerals.<sup>3</sup>

### **The catheter may be placed into a vein in the chest or in the arm.**

A central venous access catheter is placed beneath the skin and into a large vein in the upper chest. The catheter is put in place by a surgeon. This type of catheter is used for long-term parenteral feeding. A peripheral venous catheter is placed into a vein in the arm. A peripheral venous catheter is put in place by trained medical staff. This type of catheter is usually used for short-term parenteral feeding for patients who do not have a central venous access catheter. The patient is checked often for infection or bleeding at the place where the catheter enters the body.<sup>3</sup>

### **Medicine may be given with nutrition therapy to treat loss of appetite and weight loss.**

It is important that cancer symptoms and side effects that affect eating and cause weight loss are treated early. Both nutrition therapy and medicine can help lessen the effects that cancer and its treatment have on weight loss.

## **Different types of medicine may be used to treat loss of appetite and weight loss.**

Medicines that improve appetite and cause weight gain, such as prednisone and megestrol, may be used to treat loss of appetite and weight loss. Studies have shown that the effect of these medicines may not last long or there may be no effect. Treatment with a combination of medicines may work better than treatment with one medicine. Patients who are treated with a combination of medicines may have more side effects.

## **Some cancer patients try special diets to improve their prognosis.**

Cancer patients may try special diets to make their treatment work better, prevent side effects from treatment, or to treat the cancer itself. However, for most of these special diets, there is no evidence that shows they work.

### **Vegetarian or vegan diet**

It is not known if following a vegetarian or vegan diet can help side effects from cancer treatment or the patient's prognosis. If the patient already follows a vegetarian or vegan diet, there is no evidence that shows they should switch to a different diet<sup>4,5</sup>

### **Macrobiotic diet**

A macrobiotic diet is a high-carbohydrate, low-fat, plant-based diet. No studies have shown that this diet will help cancer patients<sup>4,5</sup>.

### **Keto diet**

A ketogenic diet limits carbohydrates and increases fat intake. The purpose of the diet is to decrease the amount of glucose (sugar) the tumor cells can use to grow and reproduce. It is a hard diet to follow because exact amounts of fats, carbohydrates and proteins are needed. However, the diet is safe.

Several clinical trials are recruiting glioblastoma patients to study whether a ketogenic diet affects glioblastoma tumor activity. Patients with glioblastoma who want to start a ketogenic diet should talk to their doctor and work with a registered dietitian. However, it is not yet known how the diet will affect the tumor or its symptoms.

Similarly, a study comparing the ketogenic diet to a high-fiber, low fat diet in women with ovarian cancer or endometrial cancer found that the ketogenic diet was safe and acceptable. There is not enough evidence to know how the ketogenic diet will affect ovarian or endometrial tumors or their symptoms<sup>4,5</sup>.

## **Dietary supplements.**

A dietary supplement is a product that is added to the diet. It is usually taken by mouth, and usually has one or more dietary ingredients. Cancer patients may take dietary supplements to improve their symptoms or treat their cancer.

### **Vitamin C**

Vitamin C is a nutrient that the body needs in small amounts to function and stay healthy. It helps fight infection, heal wounds, and keep tissues healthy. Vitamin C is found in fruits and vegetables. It can also be taken as a dietary supplement.<sup>4,5</sup>

## Probiotics

Probiotics are live microorganisms used as dietary supplements to help with digestion and normal bowel function. They may also help keep the gastrointestinal tract healthy. Studies have shown that taking probiotics during radiation therapy and chemotherapy can help prevent diarrhea caused by those treatments. This is true for patients who receive radiation therapy to the abdomen. Cancer patients who are receiving radiation therapy to the abdomen or chemotherapy that is known to cause diarrhea may be helped by probiotics. Similarly, studies are looking at potential benefits of taking probiotics for cancer patients who are receiving immunotherapy.<sup>4,5</sup>

## Melatonin

Melatonin is a hormone made by the pineal gland (tiny organ near the center of the brain). Melatonin helps control the body's sleep cycle. It can also be made in a laboratory and taken as a dietary supplement.

Several small studies have shown that taking a melatonin supplement with chemotherapy and/or radiation therapy for treatment of solid tumors may be helpful. It may help reduce side effects of treatment. Melatonin does not appear to have side effects.<sup>4,5</sup>

## Oral glutamine

Oral glutamine is an amino acid that is being studied for the treatment of diarrhea and mucositis (inflammation of the lining of the digestive system, often seen as mouth sores) caused by chemotherapy or radiation therapy. Oral glutamine may help prevent mucositis or make it less severe.

Cancer patients who are receiving radiation therapy to the abdomen may benefit from oral glutamine. Oral glutamine may reduce the severity of diarrhea. This can help the patients continue with their treatment plan.<sup>4,5</sup>

**Conclusion :** Nutrition plays a crucial role for patients with cancer and is maximum in ovarian cancer. Nutritional Status of cancer patient should be assessed throughout the treatment and post treatment. Nutritional problems are often underprioritized, underdiagnosed, and undertreated. Affects treatment outcomes and quality of life. Focusing on the practical aspects of the daily routine will help improve patient care.

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## ROLE OF PREBIOTICS AND PROBIOTICS IN WOMEN'S HEALTH

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### Prebiotics

Prebiotics are defined as 'non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the colon and thus attempt to improve host health' (Gibson and Roberfroid, 1995).<sup>1</sup>

In 2008, the 6th Meeting of the International Scientific Association of Probiotics and Prebiotics (ISAPP) defined "dietary prebiotics" as "a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health.

The following criteria are used to classify a compound as a prebiotic : (i) it should be resistant to acidic pH of stomach, cannot be hydrolyzed by mammalian enzymes, and also should not be absorbed in the gastrointestinal tract, (ii) it can be fermented by intestinal microbiota, and (iii) the growth and/or activity of the intestinal bacteria can be selectively stimulated by this compound and this process improves host's health.<sup>2</sup>

### Probiotics

The World Health Organization defines probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host"; in order to be labeled a probiotic, scientific evidence for the health benefit would have to be documented.<sup>3</sup>

### Microbiome and its modern understanding

Various types of microorganisms, known as gut microbiota, are inhabitants of the human gastrointestinal tract. It has been reported that there are  $10^{10}$  -  $10^{12}$  live microorganisms per gram in the human colon. The resident microbial groups in the stomach, small, and large intestine are crucial for human health. The majority of these microorganisms, which are mostly anaerobes, live in the large intestine.

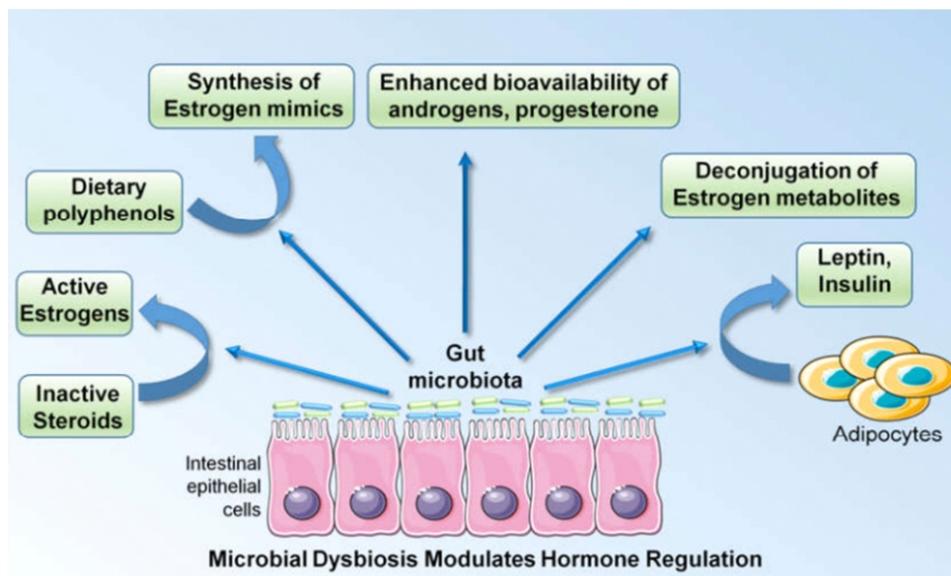
Although some endogenous factors, such as mucin secretions, can affect the microbial balance, human diet is the chief source of energy for their growth. Particularly, non-digestible carbohydrates can highly modify the composition and function of gut microbiota. Beneficial intestinal microbes ferment these non-digestible dietary substances called prebiotics and obtain their survival energy from degrading indigestible binds of prebiotics. As a result of this, prebiotics can selectively influence gut microbiota. On the other hand, the gut microbiota affects intestinal functions, such as metabolism and integrity of the intestine. Moreover, they can suppress pathogens in healthy individuals through induction of some immunomodulatory molecules with antagonistic effects against pathogens by lactic acid that is produced by *Bifidobacterium* and *Lactobacillus* genera.<sup>1</sup>

### Role of microbiome in human health and diseases

The human microbiome comprises bacteria, archaea, viruses, and eukaryotes which reside within and outside our bodies. These organisms impact human physiology, both in health and in disease,

contributing to the enhancement or impairment of metabolic and immune functions. Microorganisms colonise various sites on and in the human body, where they adapt to specific features of each niche. Facultative anaerobes are more dominant in the gastrointestinal tract, whereas strict aerobes inhabit the respiratory tract, nasal cavity, and skin surface. The indigenous organisms in the human body are well adapted to the immune system, due to the biological interaction of the organisms with the immune system over time. An alteration in the intestinal microbial community plays a major role in human health and disease pathogenesis. These alterations result from lifestyle and the presence of an underlying disease. Dysbiosis increases host susceptibility to infection, and the nature of which depends on the anatomical site involved. The unique diversity of the human microbiota accounts for the specific metabolic activities and functions of these micro-organisms within each body site.<sup>4</sup>

**Figure 1 : Microbial Dysbiosis (Cells 2020, 9, 1091; doi:10.3390/cells9051091)**



Caesarean (CS) delivery of neonates has also been identified as a risk factor for allergic diseases. The absence of normal maternal flora during CS predisposes children to such diseases. Molecular-based studies have revealed that CS-delivered children have lower counts of healthy flora (Bacteroidetes) in their gut. This reduces the anti-inflammatory activities of Bacteroidetes and contributes to local tissue inflammation (asthma and allergic rhinitis) triggered by genetic and environmental factors. A recent epidemiological study reported a significant association between dysbiotic gut flora and the production of allergic antigen (IgE) resulting in airway disease in children. Additional studies establish that children with lower microbial diversity of *Bifidobacterium*, *Akkermansia*, and *Faecalibacterium* were susceptible to multiple allergen respiratory sensitivity (polysensitisation) and may contribute to asthma at the age of 4.<sup>4</sup> (???)

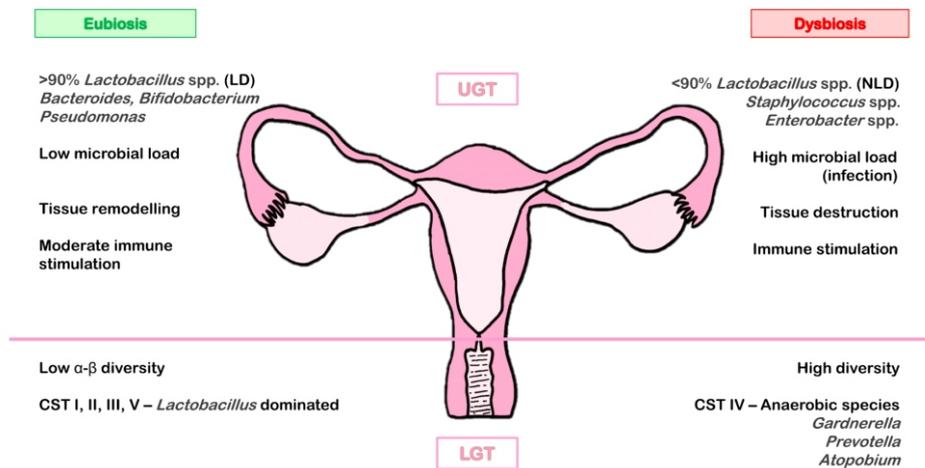
### Vaginal flora in healthy women

The vaginal microbiota is a dynamic system that changes throughout a woman's life, including throughout her menstrual cycle. The most dominant species of the human vaginal flora is *Lactobacillus*, which uses glycogen which is regulated by estrogens, resulting in unique vaginal conditions. *Lactobacilli* and other fermentative bacteria, in collaboration with vaginal epithelial cells, synthesize lactic acid, which acidifies the vaginal environment. This acidic environment provides stability to the vaginal microbiota and prevents foreign bacteria from colonizing, thus preventing

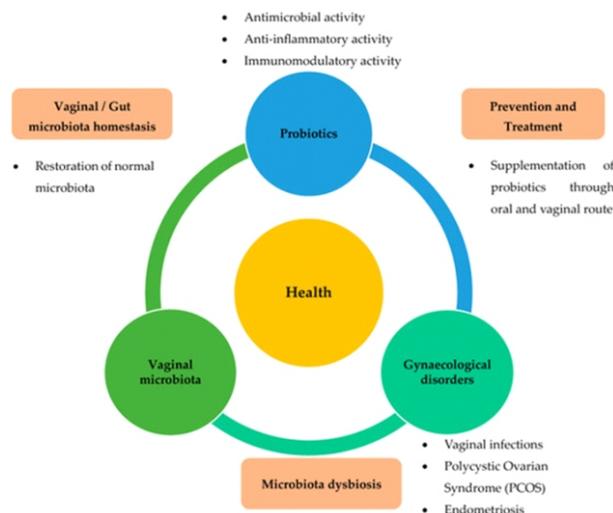
infection. The major population state forms in the vagina are characterized by individual lactobacilli species, primarily *Lactobacillus crispatus*. In addition to lactobacilli, the vaginal microbiota of healthy women is also colonized by non-lactobacillary microbiota, the rate of which is determined by ethnicity (white, black, Hispanic, and Asian) for example, different species of *Lactobacilli* dominate the vaginal microbiota of Asian and white American women, whereas different species of anaerobic bacteria such as *Cryptobacterium*, *Gardnerella*, *Prevotella*, *Porphyromonas*, *Atopobium*, *Peptoniphilus* dominate the vaginal microbiota of a large percentage of Hispanic and black American women.<sup>50</sup> The vaginal microbiota of reproductive-age women constantly exposes physiological changes such as hormonal changes and thus is dynamic.

In terms of the vaginal microbiota, however, there are significant variations between non-pregnant and pregnant women. The richness and diversity of the vaginal microbiome of pregnant women are declining in previous research. Pregnant women have a higher prevalence of *Lactobacillus* spp., *Actinomycetales*, *Clostridiales*, and *Bacteroidales* whereas *Lactobacillus* spp., *Actinobacteria*, *Prevotella*, *Veillonellaceae*, *Streptococcus*, *Proteobacteria*, *Bifidobacteriaceae*, *Bacteroides*, and *Burkholderiales* predominate in non-pregnant women. As a result, the vaginal microbiota varies throughout time in a single person's lifespan. Furthermore, the vaginal microbiota varies greatly across people, and these changes are caused by disparities in sexual activity, douching, chronic stress, geographical disparity, race, and other variables.<sup>5</sup>

**Figure 2 : Eubiosis and Dysbiosis in UGT and LGT : Main factors**  
 (Punzón-Jiménez P, et.al. J Assist Reprod Genet. 2021 Jun 10. doi: 10.1007/s10815-021-02247-5)



### Role of probiotics in Vaginitis



BV is characterized by loss of or significant decline in lactic acid-producing *Lactobacilli* (good bacteria) and higher overgrowth of other pathogenic bacteria such as *Gardnerella* spp., *Atopobium* spp., *Prevotella* spp., and *Mobiluncus* spp. (harmful bacteria). Under this condition, the imbalanced microbiota in the vagina is very typical, resulting in a higher level of pH and lower lactic acid level. When the *Lactobacillus* spp. (*Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus iners*, *Lactobacillus jensenii*, and so on) is lost or reduced in the vagina and the vaginal pH fails to be maintained at the normal range 3.8-4.5, the normal vaginal barrier is destroyed via hydrolytic enzymes (e.g. sialidase and prolidase), and, subsequently, enhanced immune responses will happen, accompanying with a set of proinflammatory chemokines and cytokines (interleukin (IL)-6, IL-8, IL-1, IL-1, TNF-, and so on) were released, which successively contribute to persistent infection potentially caused by a mixture of difficult-to-treat pathogens, especially when some of them possess the ability to form biofilms. Hence, administering probiotics containing high abundance of *L. spp.* could be a possible choice in restoring normal vaginal microflora. For instance, use of probiotic *Clostridium butyricum* WZ001 with vaginal infusion can not only promote the growth of *Lactobacillus* and inhibit the growth of pathogenic bacteria but also reduce the inflammatory response induced by *Escherichia coli*, decrease the increased phosphorylation of nuclear factor-kappa B p65 in vaginal tissue and inflammatory cytokines, IL-1, TNF-, and IL-6 in the serum levels, which is helpful for the restoring of the vaginal microecological environment.

Data suggests role of *Lactobacillus* as a prophylactic therapy in suppressing BV recurrence, after antibiotic treatment. In addition, current evidence indicates that although oral administration of probiotics reduced recurrent BV, however, direct vaginal application may provide more rapid treatment<sup>6</sup>

Probiotics may protect the vagina from pathogen colonization through a number of mechanisms, including blocking potential sites of attachment, production of microbicidal substances, e.g. hydrogen peroxide, maintenance of a low pH and induction of anti-inflammatory cytokine responses in epithelial cells.<sup>7</sup>

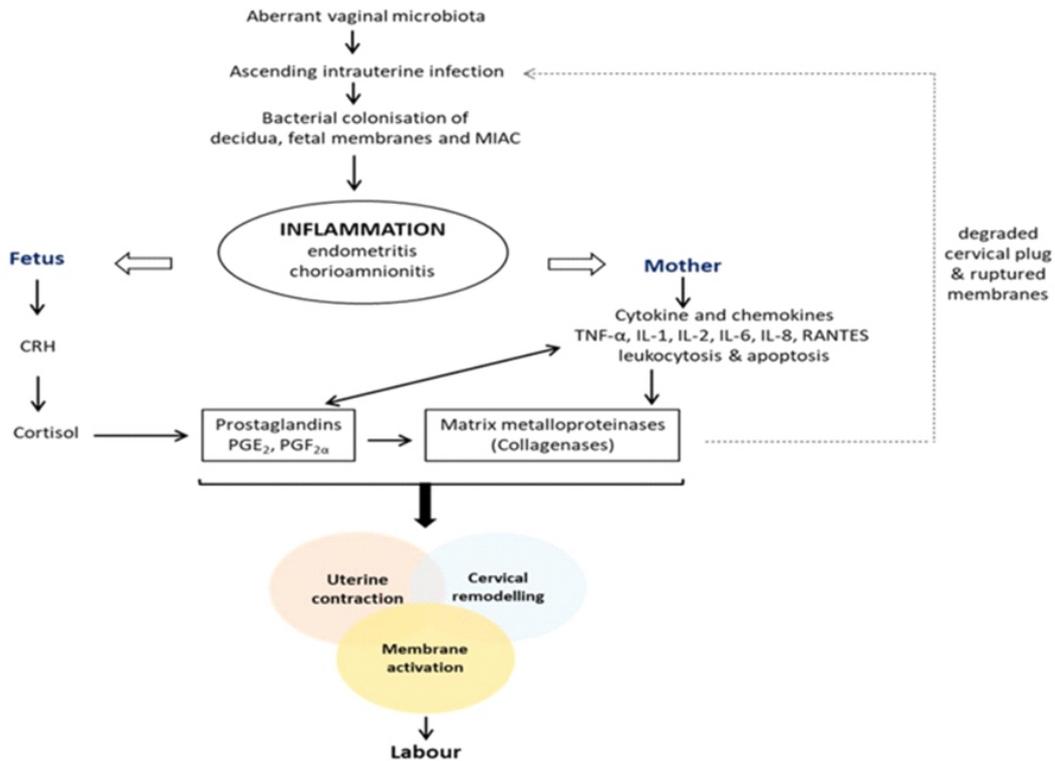
### **Role of probiotics in Pregnancy / Recurrent abortions**

Etiology of preterm birth (PTB) is multifactorial, but it has been estimated that about one third of cases is due to intrauterine inflammation caused by ascending vaginal infections. Infection induced inflammatory pathways are thought to be the causal driver of around 40% of preterm births, and of as many as 80% of early preterm births before 28 weeks of gestation.<sup>8</sup>

It has been shown that probiotic administration to women during pregnancy and lactation can change the composition of breast milk, and consequently, its immunomodulatory molecular composition, bestowing benefits on the child in the form of reduced instances of gastrointestinal disorders. A study conducted in 2013 showed an increase in breast milk of anti-inflammatory molecules such as TGF-B and IL-10 in supplemented mothers compared to the control group. Indeed, maternal probiotic supplementation leads to an increase of the TGF-B, which stimulates gut maturity, influencing IgA production and oral tolerance induction, and that seems to improve gastrointestinal functional symptoms in infants

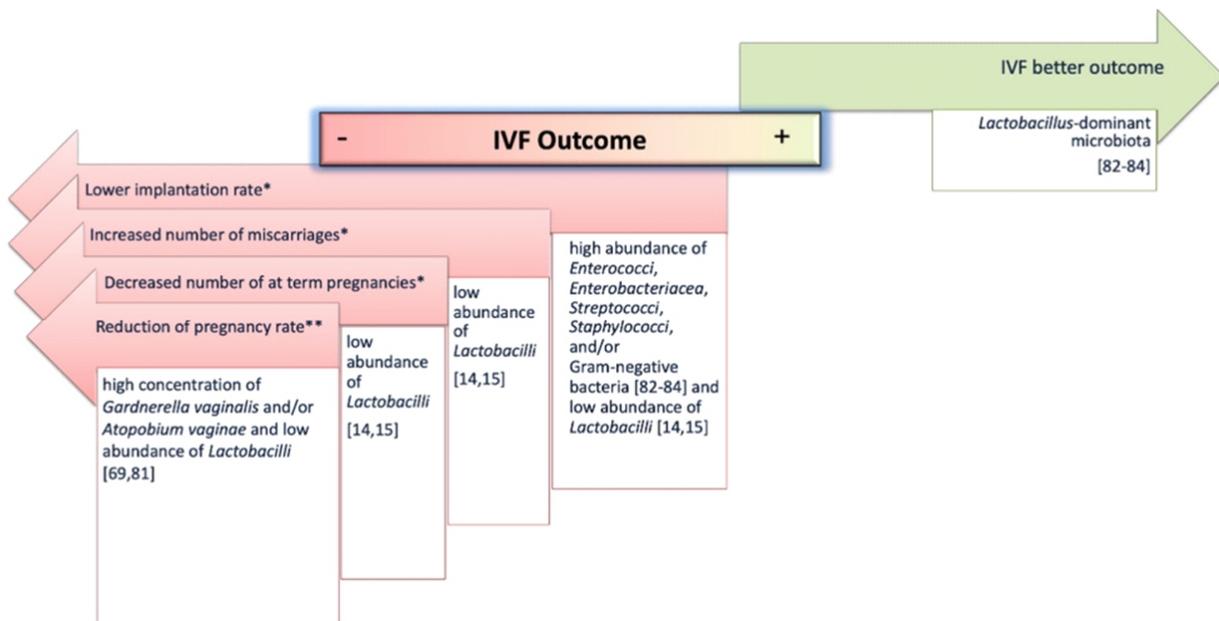
In 2015, the WAO guidelines on the prevention of allergies recommends using probiotics in : (a) pregnant women at high risk for having an allergic child; (b) women who breastfeed infants at high risk of developing allergies; and (c) infants at high risk of developing allergies<sup>9</sup>

**Figure 2 : Preterm birth and dysbiosis<sup>10</sup>**



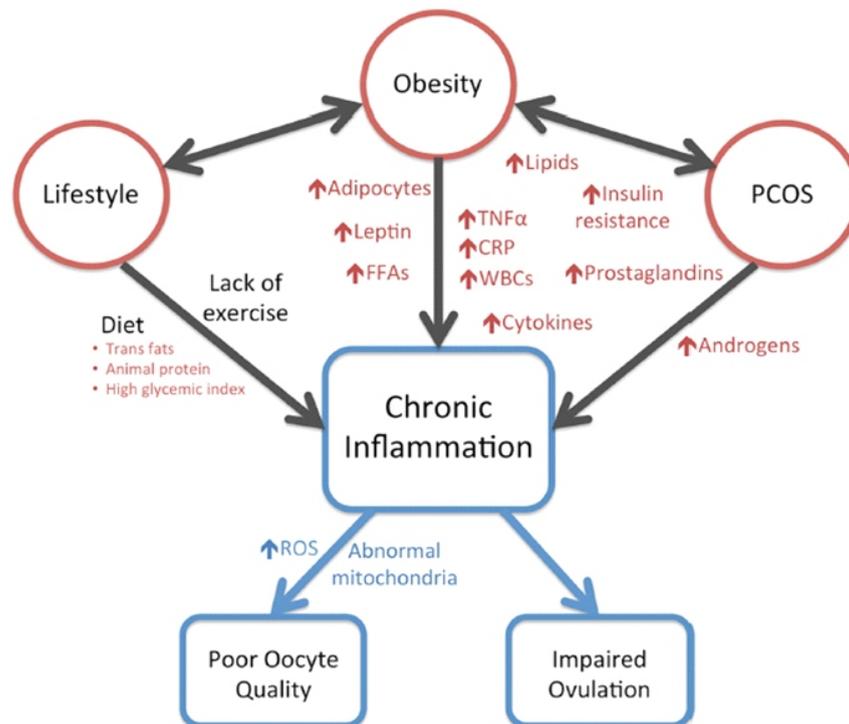
**Role of probiotics in IVF / Recurrent implantation failure**

It is thought that women with diminished Lactobacilli in vagina develop anti sperm antibodies and have failure in in vitro fertilization. A high prevalence of abnormal vaginal microbiome was reported in IVF patients. It is associated with tubal infertility and miscarriage in women following IVF and may negatively affect the clinical pregnancy rate in IVF patients.



## Role of probiotics in PCOS

**Figure 3 : Inflammation and Abnormal Ovarian Physiology<sup>12</sup>**



Studies demonstrated positive effects on the health of women with PCOS, suggesting that probiotics supplementation may be used as an alternative or complementary treatment for PCOS. The studies suggest that probiotic supplementation may influence weight loss, biomarkers of insulin resistance, and lipid profiles in PCOS patients. These beneficial effects could be mediated by host metabolism, modulation of immunological responses and reduction in systemic inflammation.

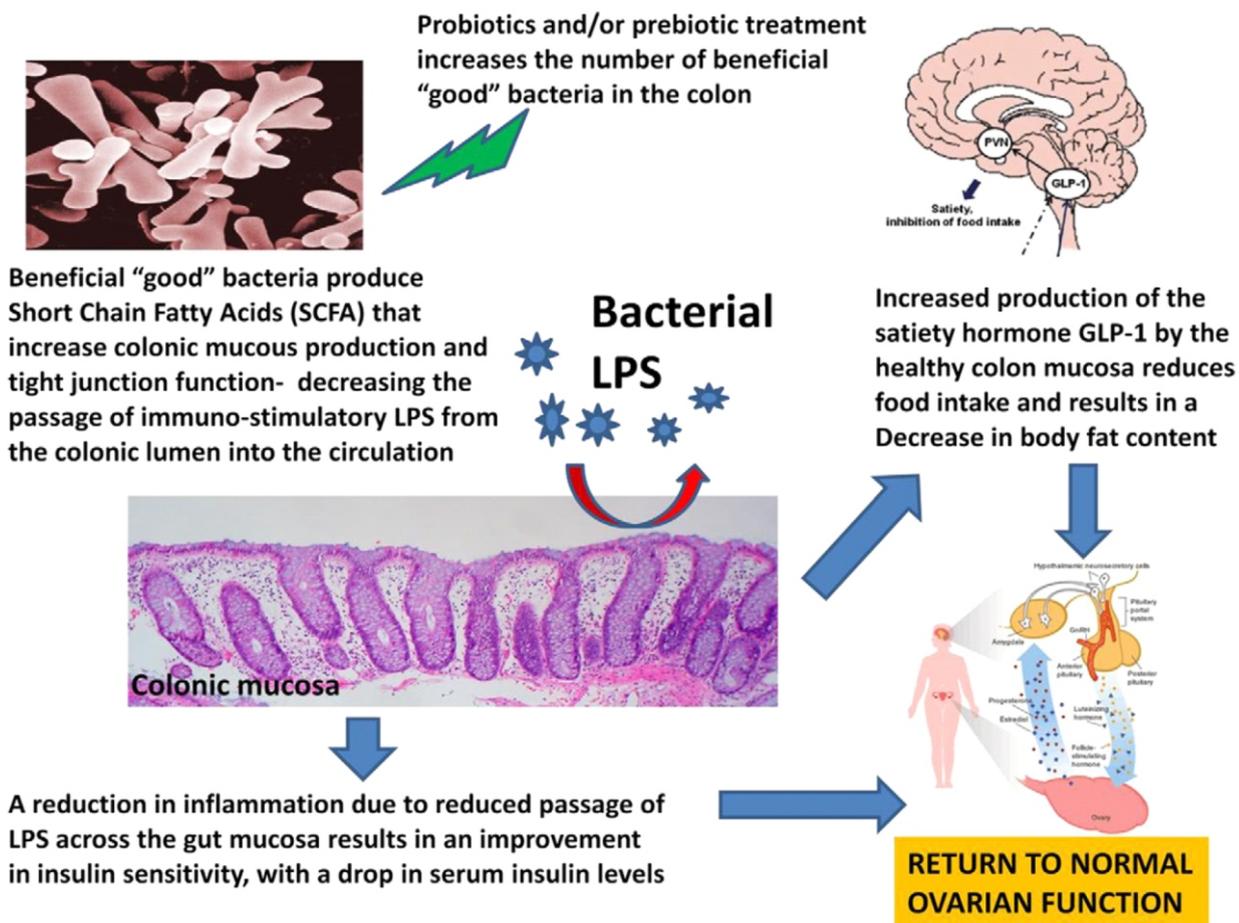
In a clinical trial conducted by Ahmadi et al.<sup>15</sup>, a probiotic capsule, consisting of three viable and freeze-dried strains, *Lactobacillus acidophilus* ( $2 \times 10^9$  CFU/g), *Lactobacillus casei* ( $2 \times 10^9$  CFU/g), and *Bifidobacterium bifidum* ( $2 \times 10^9$  CFU/g), was administered daily to 60 PCOS patients for 12 weeks. The study demonstrated a significant reduction in the weight and BMI of the PCOS patients after 12 weeks of supplementation with probiotics compared to the placebo. The weight loss was associated with a significant decrease in FPG, serum insulin concentrations, HOMA-IR, HOMA-B, serum triglycerides and VLD-Lcholesterol. This could be due to the hypocholesterolaemia effect of the probiotics<sup>13</sup>

A case-control study of 39 PCOS patients and 40 healthy people showed :

- Vaginal microbiota of PCOS patients was significantly different from that of healthy people,
- Characterized by increased diversity and increased relative abundance of *Mycoplasma* and *Prevotella*, and decreased relative abundance of *L. crispatus*

This suggests that vaginal microbiota dysbiosis may participate or contribute to PCOS pathology, and therapies targeted at improving vaginal microbiota are promising<sup>13</sup>

**Figure 4 : Symbiotic approach in PCOD<sup>15</sup>**



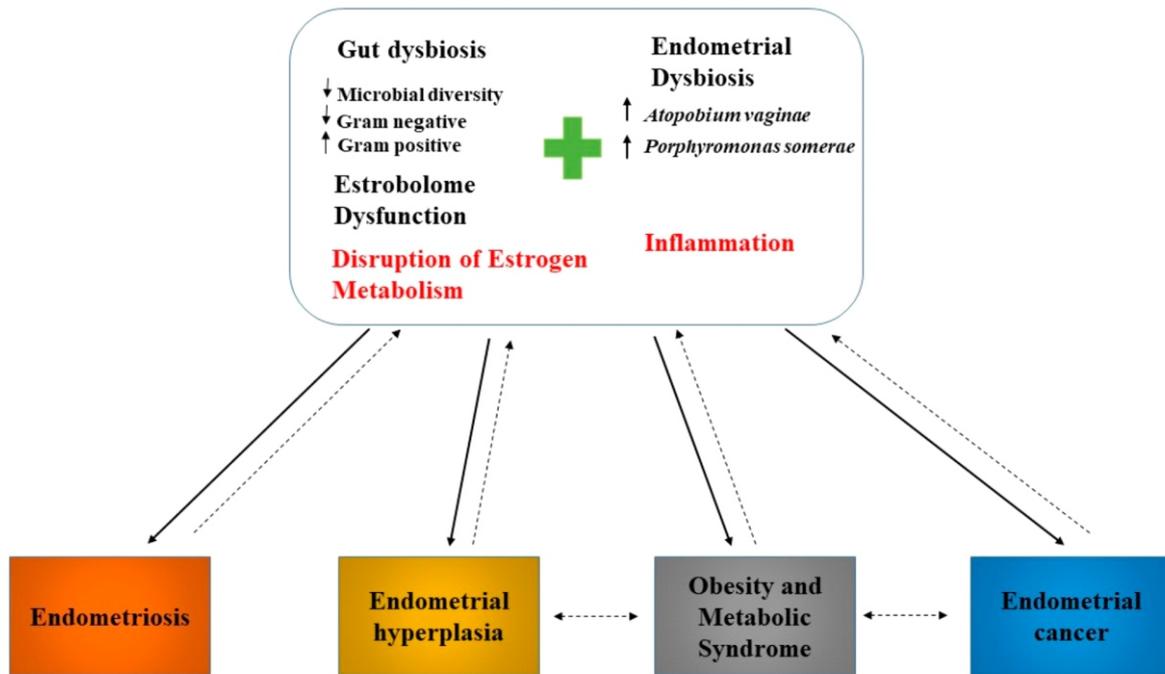
### Role of probiotics in Endometriosis

Recently, research on the involvement of the microbiota in endometriosis has begun to accrue. It is postulated that dysbiosis may be involved in dysregulating the immune system and altering estrogen metabolism. Having discussed the extensive role of the immune system and estrogen signaling in endometriosis, it would seem inevitable that the microbiota plays a critical role in the disease.

Studies have shown that patients with pelvic inflammatory disease (PID), which results from the ascension of vaginal bacteria up into the uterus, fallopian tubes and ovaries, are associated with a threefold increase in risk of developing endometriosis, possibly suggesting that the disease may have an infectious etiology, at least in part.

Researchers have found evidence suggesting the gut and female reproductive tract microbiota may be inextricably linked to the onset and progression of endometriosis. This novel perspective on endometriosis opens the door to many preventative, diagnostic and therapeutic possibilities, and is an emerging area of research.

In randomised, placebo-controlled trials, oral administration of Lactobacillus has been shown to ameliorate endometriosis-associated pain in women, and reduce endometriotic lesions in mice by increasing IL-12 concentration and NK cell activity. Dysbiosis and endometriotic-inflammation leads to impaired NK cell activity, and the probiotic treatment reversed this immune dysregulation. Lactobacillus probiotic treatment not only improved endometriosis, but is also capable of preventing its growth in rats. These impressive frontiers warrant research and testing.<sup>16</sup>

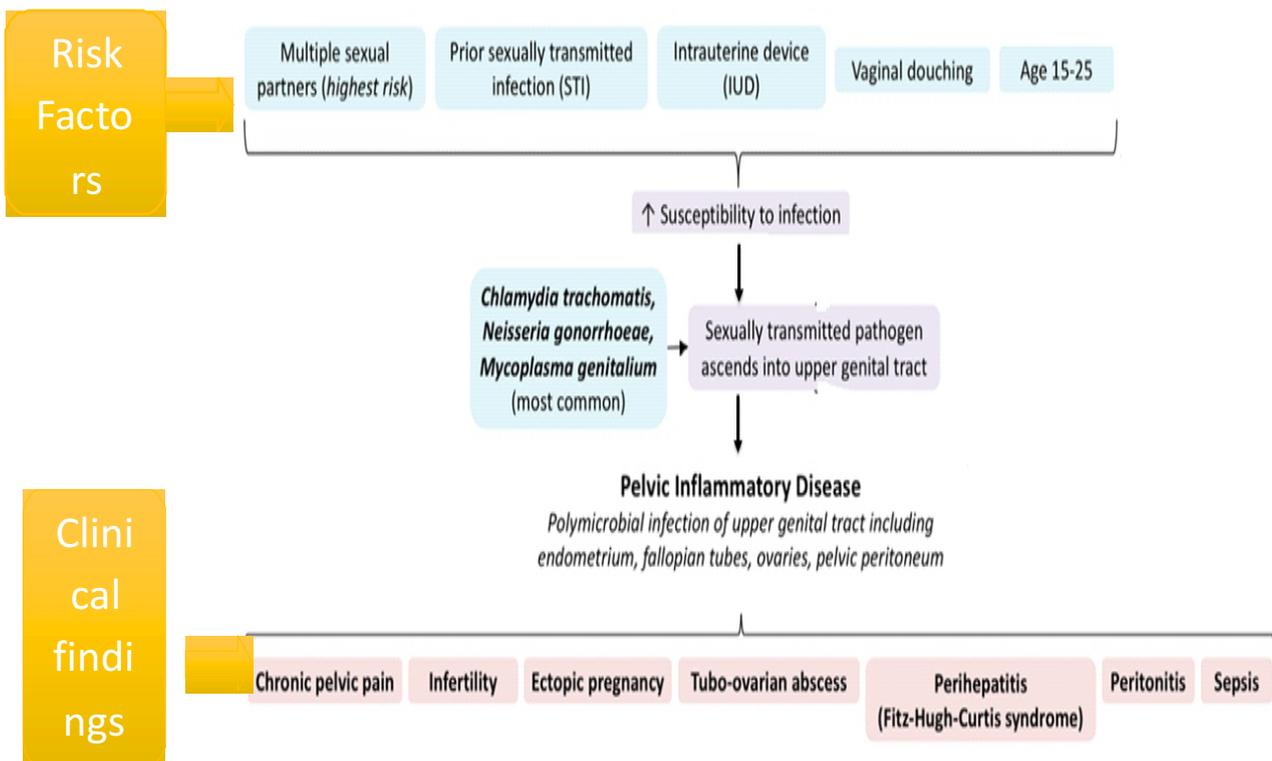


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### Role of probiotics in PID

Infection of upper genital tract occurring predominantly in sexually active young women. Chlamydia trachomatis and Neisseria gonorrhoeae are common causes; However, other cervical, enteric, bacterial vaginosis associated, and respiratory pathogens, including Mycobacterium tuberculosis, may be involved.

An abnormal genital microenvironment facilitates the acquisition of pathogens, the leading cause of bacterial sexually transmitted infections worldwide (source not mentioned in file)

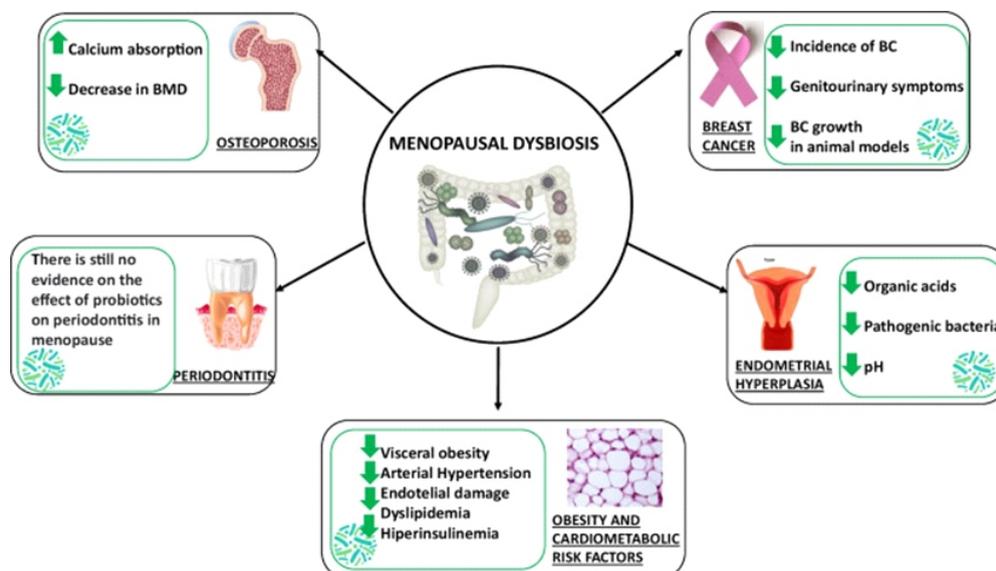


## Role of probiotics in Menopause

Although evidence from human intervention studies is limited so far, probiotic supplementation in postmenopausal women could represent a feasible and safe strategy to manage the menopause-related disease. In particular, oral probiotic formulation - especially those including *Lactobacillus* ssp. casei, helveticus, rhamnosus, and reuteri - might have pleiotropic beneficial effects on health by :

- Promoting intestinal calcium absorption and reducing a further decrease in BMD in women at risk of osteoporosis or with osteopenia, thus potentially delaying bone damage
- Reducing the incidence of breast cancer and by improving the genitourinary symptoms associated with breast cancer therapy
- Promoting the reduction of vaginal pH, through the production of organic acids and the reduction of pathogenic bacteria which are risk factors for type 1 endometrial hyperplasia in in vitro models

Improving insulin resistance, dyslipidemia and inflammation, thus reducing the cardiometabolic risk of the postmenopausal woman<sup>18</sup>



## Role of probiotics in DM

Data analysis showed a significant effect of probiotics in reduction of total cholesterol, triglyceride levels, CRP, HbA1c, fasting plasma glucose, fasting insulin levels and both systolic and diastolic blood pressure values. Supplementation with probiotics increased HDL levels however did not have a significant effect on BMI or LDL levels.<sup>19</sup>

Probiotic supplementation may ameliorate glycemic control in GDM patients. The supplementation of the probiotic capsule that consists of four probiotic strains (*L. acidophilus* LA-5, *L. delbrueckii* bulgaricus LBY-27, *S. thermophilus* STY-31, and *Bifidobacterium* BB-12;  $4 \times 10^9$  CFU in total) for eight weeks hindered the weight gaining process after 6 weeks of the intervention compared to the placebo group in recently diagnosed GDM patients.<sup>20</sup>

## Role of probiotics in Obesity

Obese people's microbiomes are physically and functionally diverse from their healthier counterparts, according to research. Ferrer et al. found that in the gut of obese people, Firmicutes (94.6%) were more numerous than Bacteroidetes (3.2%), whereas the gut of lean people showed a change towards increased Bacteroidetes (18.9%). Additionally, the intestinal microbiome of an obese person is less

diverse than that of lean person. This strongly suggests the possibility of using the microbiome in the therapy of obesity.

### Role of probiotics in GI disorders

There is high-quality evidence that probiotics are effective for acute infectious diarrhea, antibiotic-associated diarrhea, Clostridium difficile-associated diarrhea, hepatic encephalopathy, ulcerative colitis, irritable bowel syndrome, functional gastrointestinal disorders, and necrotizing enterocolitis. Conversely, there is evidence that probiotics are not effective for acute pancreatitis and Crohn disease.

Probiotics are safe for infants, children, adults, and older patients, but caution is advised in immunologically vulnerable populations.

### 1. Common Dietary Sources

PREBIOTICS	PROBIOTICS
<ul style="list-style-type: none"> <li>● artichokes</li> <li>● asparagus</li> <li>● bananas</li> <li>● barley</li> <li>● berries</li> <li>● chicory</li> <li>● garlic</li> <li>● green vegetables</li> <li>● legumes</li> <li>● linseed</li> <li>● oats</li> <li>● onions</li> <li>● tomatoes</li> <li>● wheat</li> </ul>	<ul style="list-style-type: none"> <li>● kefir</li> <li>● kimchi</li> <li>● kombucha</li> <li>● miso</li> <li>● pickles</li> <li>● sauerkraut</li> <li>● sourdough bread</li> <li>● tempeh</li> <li>● yogurt</li> </ul>

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**Table 1**  
**The potential sources of functional probiotic strains.**

Potential probiotic	Isolation source	Ref.
<i>Lactobacillus</i>	Fruits, fermented foods and human origin.	[3]
<i>Lactobacillus</i> , <i>Lactococcus</i> , <i>Leuconostoc</i> and <i>Enterococcus</i> genera,	Artisanal soft cheese.	[86]
<i>L. paracasei</i>	Human breast milk.	[12*]
<i>L. plantarum</i>	Edible farmed snail <i>Cornu aspersum maxima</i> .	[87]
	Rotten fruits and vegetables including grapes, apple, strawberry, tomato, cucumber, cauliflower, and brinjal.	[88]
<i>L. plantarum</i> and <i>L. paracasei</i>	Inulin extracted from Jerusalem artichoke.	[21]
<i>L. plantarum</i> , <i>Enterococcus faecalis</i> , <i>L. paraplantarum</i> , and <i>Weissella paramesenteroides</i>	Food crop plant leaves.	[6*]
<i>L. rhamnosus</i> and <i>Weissella cibaria</i>	<i>Kimchi</i> - traditional fermented product.	[17]
<i>L. brevis</i> , <i>L. curvatus</i> , <i>L. fermentum</i> , and <i>Pediococcus pentosaceus</i> ,	Harbin dry sausages.	[29]
<i>L. acidophilus</i> , and <i>BB. animalis</i> subsp. <i>Lactis</i>	A synbiotic dietary supplement.	[24]
<i>Bacillus</i> spp. Isolates	Hainan aquaculture pond.	[89]
<i>B. subtilis</i>	The Hulong Grouper GI tract.	[80]
<i>B. methylotrophicus</i> , <i>B. amyloliquefaciens</i> , and <i>B. licheniformis</i>	The gut of rohu, <i>Labeo rohita</i> .	[90]
Yeast strains	Food ecosystems.	[91]
	Cucumber <i>jangajji</i> .	[16]
	Traditional kefir grains.	[92]
	Traditional fermented foods.	[59]
Oil-borne yeast strains	Italian virgin olive oil of <i>Leccino</i> and <i>Taggiasca</i> cultivars.	[93]
<i>Candida adriatica</i> , <i>C. diddensiae</i> , <i>Nakazawaea molendini-olei</i> , <i>N. wickerhamii</i> ,	Italian virgin olive oil.	[93]
<i>Wickerhamomyces anomalus</i> , and <i>Vamadazyma terventina</i>		
<i>Pediococcus acidilactici</i>	Raw camel milk.	[36]

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## 2. Common nutritional supplements

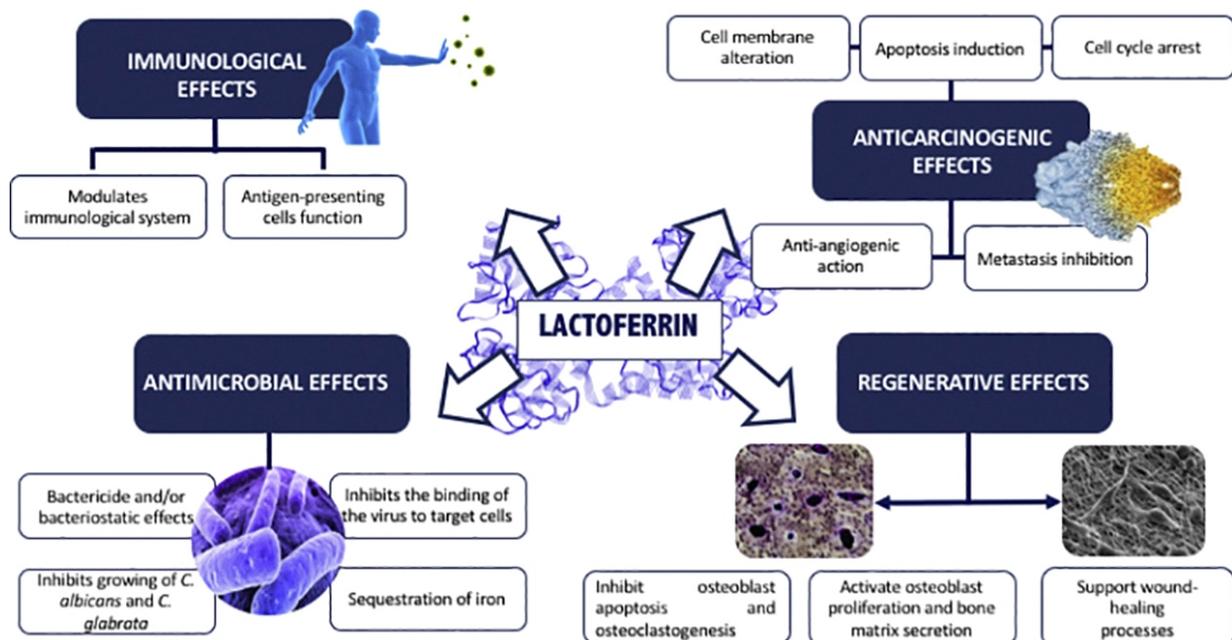
MANUFACTURED SUPPLEMENTS INCLUDE	
PREBIOTICS	PROBIOTICS
<ul style="list-style-type: none"> <li>● cyclodextrin</li> <li>● galactooligosaccharides</li> <li>● lactulose</li> <li>● maltooligosaccharides</li> <li>● ructooligosaccharides</li> </ul>	<ul style="list-style-type: none"> <li>● Bacillus</li> <li>● Bifidobacterium</li> <li>● Enterococcus</li> <li>● Escherichia (beneficial subtypes)</li> <li>● Lactobacillus</li> <li>● Streptococcus (beneficial subtypes)</li> </ul>

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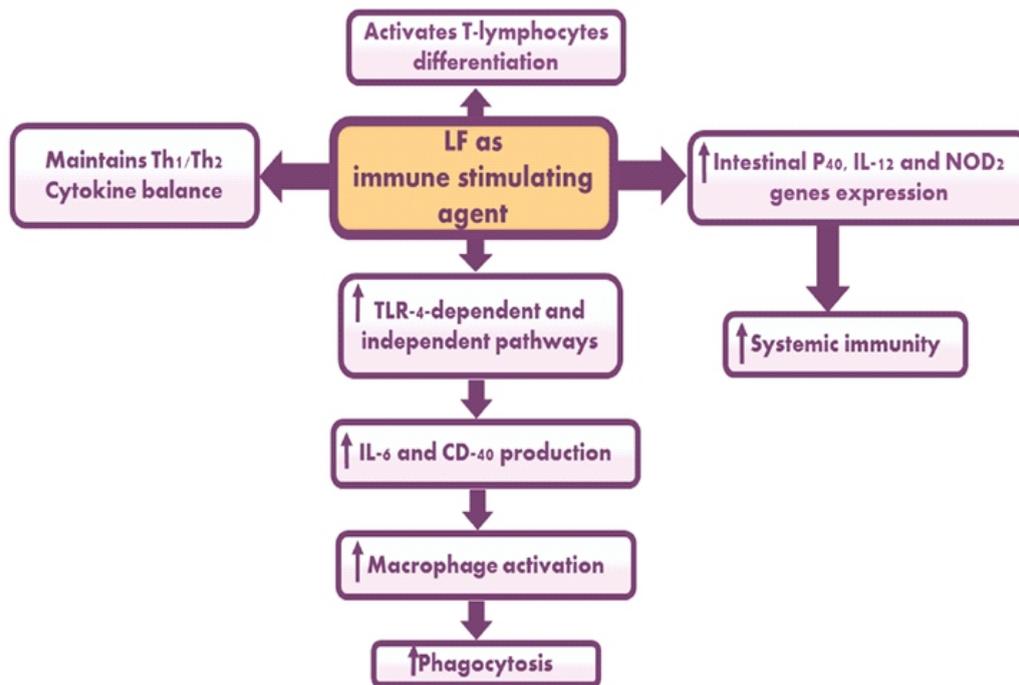
The colonization of vaginal mucosa by probiotics can be done using two different delivery ways: oral or vaginal administration. Probiotics used in oral formulations must be able to survive during gastrointestinal tract passage, to compete with potential pathogens, to reach the rectum and ascend to vaginal tract, colonizing and repopulating the vagina (Barrons and Tassone, 2008; Bolton et al., 2008). This way of administration could decrease the risk of infection by pathogenic bacteria and yeast from the rectum to the vagina (Cribby et al., 2008). Probiotics incorporated into vaginal dosage forms are introduced locally, avoiding all the steps required for oral probiotics. Besides the longer time of the process, oral administration depends on the viability of the strains through the gastrointestinal tract passage and also the number of cells delivered by this way is significantly lower than in vaginal administration way (Cribby et al., 2008)<sup>23</sup>

### Lactoferrin - An Endometrial Prebiotic

Lactoferrin is an iron-binding protein, found in human secretions such as breast milk (especially in the colostrum), seminal fluid, uterine secretions, tears, and saliva. Lactoferrin is a sole glycoprotein able to contemporarily act against microbial multiplication, biofilm formation, iron disorders and oxidative stress, viral and parasitic infection as well as inflammation. Lactoferrin thus has multifunctional capacity as depicted below.



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In an attempt to modify endometrial microbiome lactoferrin a prebiotic agent with favourable prebiotic activity was administered orally during and after treatment with antibiotics among women undergoing infertility treatment. Among non-Lactobacillus dominant patients treated with lactoferrin for three month after the antibiotics therapy, 67% (6/9) of them reached Lactobacillus dominance in the endometrium. Additionally, lactoferrin administration has demonstrated effective result against bacterial vaginosis, leading to pregnancy and full-term birth in women with a previous medical history of preterm birth<sup>26</sup>

### Safety of Probiotics

Probiotics are mostly considered to be safe. Lactobacillus species utility is related to their GRAS status. Elias J, et.al article published in 2011 stating that probiotics do not appear to pose any safety concerns for pregnant and lactating women. Systemic absorption is rare when probiotics are used by healthy individuals, and the current literature does not indicate an increase in adverse pregnancy outcomes<sup>27</sup>

### Conclusion

Probiotics and prebiotics have direct and sometimes indirect effects on a spectrum of clinical conditions. It is important to conclude that the information derived based on clinical trials and review of literature states that probiotic supplementation yields some beneficial effect in women's health issues. Affordability should be kept in mind while prescribing formulations and natural sources should be promoted. While choosing a formulation, it is important to note the content and verify its effectiveness.

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