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چکیده مقالات سخنرانی های چهارمین کنگره سالانه همگرایی در علوم غدد درون ریز

Hormonal therapy in menopausal women

Mahbod Ebrahimi. M.D. Reproductive Gynecologist. Associate Professor, IVF Unit. Yas Complex Hospital. Tehran University of Medical Sciences (TUMS)

Hence the mean age of menopause in human species is 51 years, women spend a third of their life in menopause and beyond. Menopause is associated with a marked decrease in production of ovarian estrogenic hormones as well as the symptoms that negatively impact quality of life such as systemic vasomotor (hot flashes), genitourinary symptoms (vaginal dryness, dyspareunia and other lower urinary tract symptoms) and osteoporosis.

Estrogen is the most effective treatment for relief of systemic vasomotor and genitourinary symptoms , prevention of osteoporosis as well as chronic disease in women with primary ovarian insufficiency (POI).Although hormonal treatment is effective for vasomotor and genitourinary symptoms, the understanding of its impact on cardiovascular disease, cognitive dysfunction, and depression continues to evaluate.

The clinical guidelines published by the Endocrine Societies present individualized approach to treatment based upon calculating a woman's baseline cardiovascular and breast cancer risks prior to initiating therapy.

The guidelines suggest that hormone therapy is indicated for the treatment of menopausal symptoms but not for the prevention of cardiovascular disease, osteoporosis, or dementia. The benefits seem to outweigh its risks for most symptomatic women who are either under age 60 years or less than 10 years from menopause

For women who have contraindications to estrogen therapy, nonhormonal modalities can be recommended to treat systemic and local menopausal symptoms

Metabolomics in endocrine disorders

Farideh Razi
Professor of Pathology
Metabolomics and Genomics Research Center, Cellular and Molecular Institute,
Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences

Metabolomics represents a modernized approach to biochemical analysis, focusing on the systematic exploration and measurement of small metabolites within biological systems. These metabolites encompass a wide array of compounds, from endogenous molecules like lipids, amino acids, and sugars, that are vital for fundamental physiological processes to exogenous compounds originating from the environment or diet. The intricate relationship between metabolites and genes highlights their sensitivity to genetic variations and environmental factors that enables metabolomics to serve as a powerful tool for probing an individual's phenotype, offering dynamic insights into ongoing metabolic processes and serving various fields like biomedical research, drug testing, and nutritional analysis. The application of metabolomics offers a comprehensive understanding of metabolic states and pathophysiological changes, providing a holistic view of biological systems. Notably, metabolomics has gained traction in disease exploration, particularly in the search for biomarkers that elucidate altered metabolic pathways associated with pathological conditions. Technological advancements, including mass spectrometry and nuclear magnetic resonance spectroscopy, combined with sophisticated statistical methodologies, have propelled metabolomics research forward. These advancements enable high-resolution, high-throughput analysis, facilitating the simultaneous detection and quantification of numerous metabolites and the construction of intricate metabolic maps. Such maps are instrumental in highlighting altered pathways, particularly in conditions like endocrine disorders, contributing to advancements in disease understanding and diagnosis.

Traditional approaches to studying endocrine disorders such as diabetes mellitus and thyroid dysfunction, have primarily focused on individual hormones or specific molecular pathways. However, the complex interactions between hormones and metabolic pathways necessitate a more comprehensive analytical framework to unravel their underlying mechanisms.

Metabolomics, as a systems-level approach, offers a unique opportunity to explore the complex metabolic signatures associated with endocrine disorders, thereby enhancing our understanding of their etiology, progression, and therapeutic interventions.

New technique of fertility preservation

F.Davari-tanha, Professor of reproductive endocrinology,Yas Hospital

Treatment of malignant conditions, as well as a few precancerous and benign conditions , may require surgical resection of reproductive organs or gonadotoxic chemotherapy or radiation treatment . This regularly leads to infertility, which may be a major quality of life concer.

With fitting pretreatment arranging and intercession, biologic parenthood is conceivable for numerous men and ladies who will lose their fertility becaude of surgery or gonadotoxic treatment.

The most well-established strategy for conservation of child-bearing is embryo cryopreservation. cryopreservation of oocytes,In vitro development of oocytes,cryopreservation of ovarian tissue is investigational, isn't broadly accessible, and has an dubious viability. Ovarian transposition out of the radiation field may be performed.

Beta cell and immune cell interactions in type 1 diabetes

Mojtaba Malek, MD

Research Centre for prevention of cardiovascular disease, Institute of Endocrinology & Metabolism, Iran university of medical sciences, Tehran, Iran.

During these years, the incidence of type 1 diabetes has increased, its cause remains unknown. Unfortunately, its prevention is still not possible, and its cure is impossible.

The management burden of type 1 diabetes is heavy, and a majority of patients do not reach treatment goals.

Type 1 diabetes is one of the well-characterized autoimmune diseases that destruction of β-cells are caused by T cell-mediated and characterized by a stepwise progression from autoantibody detection to dysglycemia to clinical disease.

It seems immune attack by T cells without proper immune regulation and loss of tolerance leads to imbalance in immune homeostasis and Progressive damage of beta cells

Asymptomatic type 1 diabetes can be identified by islet autoantibody screening. The purpose of screening is to prevent diabetic ketoacidosis at onset and support a smooth progression into diagnosis of clinical type 1 diabetes and Identify opportunities for intervention.

Three stages of type 1 diabetes have been identified. Stage 1 is asymptomatic, and people in this stage have normoglycemia and the presence of two or more islet autoantibodies. Stage 2 is identified with positive antibodies and dysglycemia. Finnaly the indicator of the third stage is clinical diabetes.

Although there is no cure for type 1 diabetes, there is now a treatment to delay the progression from stage 2 to stage 3 of the disease.Teplizumab is the first drug approved to change the progression of autoimmunity in type 1 diabetes. It is an anti-CD3 monoclonal antibody that binds with high affinity to the CD3 and may help to preserve β-cell function in children and adolescents with newly diagnosed type 1 diabetes. It seems the research in this

era is in its early days. Whatever the future brings, it will undoubtedly make a huge difference in the lives of millions of people with diabetes.

Revolutionizing Endocrinology Through Proteomics: Advancements in Diagnostics and Targeted Therapies

Babak Arjmand* (Corresponding Author);

1. **Cell Therapy and Regenerative Medicine Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.**
2. **Student Research Committee, AJA University of Medical Sciences, Tehran, Iran**

   Email: barjmand@sina.tums.ac.ir

   Scopus ID: 24485067100

   ORCID ID: 0000-0001-5001-5006

Abstract

Proteomics can unravel the intricate molecular tapestry underlying endocrine disorders and diseases. Here, the authors delve into the profound impact of proteomic technologies in elucidating the complex web of proteins governing endocrine dysregulations, thereby laying the foundation for targeted therapeutic interventions and precision medicine approaches. In other words, precise examination of proteins, even those with low levels in intricate biological samples will facilitate the application of targeted proteomics in clinical environments and provide valuable insights into biomarker investigations. This narrative also explores the symbiotic relationship between proteomics and regenerative medicine in revolutionizing the treatment paradigm for endocrine disorders. By harnessing the analytical power of proteomic profiling, researchers and clinicians are spearheading the development of personalized regenerative medicine and advanced therapies tailored to individual patients. It can offer a bespoke approach to managing endocrine ailments and improving clinical outcomes.

Keywords: Endocrinology; Protein; Proteomics; Regenerative Medicine; Targeted Therapies

Genetic screening of endocrine related cancers: The future impact of Artificial intelligence

Mahsa M.Amoli

Metabolic Disorders Research Centre, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Iran.

Endocrine cancers have various origins according to the initial endocrine glands they arise from, including the thyroid, parathyroid, pituitary, adrenal, and pancreatic islet cells. Recent advancements in genetic research have shed light on the underlying causes of these cancers, revealing both inherited and somatic genetic alterations as critical contributors to disease pathogenesis.

Hereditary endocrine cancers are associated with germline mutations which segregate through generations, which increase individual susceptibility to tumor development, including multiple endocrine neoplasia (MEN) types 1 and 2, Carney complex, and von Hippel-Lindau syndrome. Genetic testing for these syndromes can aid in the identification of individuals at high risk and inform appropriate surveillance and prevention strategies.

Somatic de-novo mutations occurring within the affected tissues are the main cause of most sporadic endocrine cancers, which account for the majority of cases, and have been characterized by Large-scale genomic studies providing insights into the molecular mechanisms driving tumor initiation and progression. Mutations in genes such as *BRAF*, *RAS*, and *RET* are observed in thyroid cancer, leading to dysregulated signaling pathways involved in cell proliferation and survival identifying them as the most common driver mutations leading to aberrant activation of the MAPK and PI3K/AKT signaling pathways. In parathyroid cancer, alterations in the CDC73 and MEN1 genes disrupt the regulation of cell cycle progression and calcium homeostasis. In adrenal tumors, mutations in genes such as TP53, CTNNB1, and MEN1 contribute to dysregulated hormone production and abnormal cell growth.

Advancements in genomic technologies, such as next-generation sequencing (NGS) and high-throughput genotyping and employment of artificial intelligence (AI) have accelerated the

discovery of novel genetic alterations in endocrine cancers. Large-scale sequencing studies have enabled the identification of additional driver genes and the characterization of mutational landscapes across different tumor types. Moreover, integrated multi-omics approaches have shed light on the complex interplay between genetic alterations, epigenetic modifications, and gene expression patterns, providing a comprehensive view of the molecular alterations driving endocrine tumorigenesis which has influenced clinical practice by their prognostic and predictive significance.

AI can assist in predicting the prognosis of endocrine cancer patients by analyzing various factors, such as tumor size, stage, and molecular markers. By integrating genetic information and clinical data besides examining large-scale genomic datasets using AI algorithms genetic markers and potential therapeutic targets specific to endocrine cancers can be identified. This information can be used to develop targeted therapies and personalized treatment approaches, known as precision medicine.

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Type 2 diabetes mellitus in older adults: clinical considerations and management

Seyedeh Zahra Badrkhahan, MD, Geriatric medicine fellowship, Tehran University of Medical Sciences

Type 2 diabetes mellitus (T2DM) poses particular difficulties in older individuals (65 years and above) because of its rising occurrence and distinct clinical characteristics. A considerable portion of people with T2DM are senior citizens, and they are particularly susceptible to problems related to underlying insulin resistance, dysfunction of β-cells, excessive adiposity, and sarcopenia. The existence of general symptoms often linked to aging can lead to the failure to correctly diagnose T2DM in this particular demographic.

The impact of frailty and multiple medical conditions further complicates the management of T2DM in the elderly, resulting in an increased susceptibility to low blood sugar levels and altered disease progression. Aggressive treatment approaches may not yield their expected benefits in frailty, leading to investigations into the long-term advantages of strict blood sugar control in this group. Lifestyle modifications are particularly effective in older age groups, necessitating a shift in treatment approaches for this population. The elderly display notable disparities in their physical abilities, their ability to care for themselves, and the burden of concurrent illnesses. Consequently, it is vital to thoroughly contemplate medication schedules, taking into consideration the possibility of adverse drug effects, drug interactions, and the heightened susceptibility to low blood sugar.

It is imperative to provide specialized care that is tailored to address the specific requirements of elderly individuals with T2DM, as this plays a pivotal role in optimizing treatment outcomes. It is important to strike a delicate balance between maintaining overall health and quality of life while also achieving blood sugar control. Incorporating factors related to frailty, cognitive function, concurrent illnesses, and the integration of social services, mental health support, and community resources are essential components in the comprehensive management of T2DM in the elderly

Cost-Effectiveness Analysis of Precision medicine

Shokoufe Nikfar

Tehran University of Medical Sciences, Tehran, Iran.

The novel health technology known as precision medicine treatment created a new paradigm in the health system. Precision medicine has fewer adverse effects and improved therapeutic outcomes than conventional treatments. However, access to precision medicine is limited, mainly because of its remarkably expensive prices. Given the limited budgets in health systems, the allocation of resources to a new health intervention must be determined by considering the evidence and evaluating the opportunity costs. Economic evaluation plays a significant role in the decision-making process in healthcare systems and is an essential tool for comparing and evaluating the worth of different interventions, particularly the more costly ones. However, there are challenges in conducting an economic evaluation of a precision medicine intervention due to its distinctive characteristics. Some of the challenges of conducting economic evaluation for precision medicine interventions are as follows:

1. Lack of consistent methods for conducting economic evaluations: Typically, the features and data from clinical trials serve as the foundation for the design and conduct of economic evaluations. In the area of precision medicine, clinical trials are mostly designed and implemented by biomarkers. Participants are selected based on the type of biomarker rather than disease. This heterogeneity in the hypothetical cohort raises challenges in aggregating costs and outcomes. Pharmacoeconomics researchers lack an economic evaluation study on a population with one biomarker, different diseases, and one cost-effectiveness ratio, requiring further research and a specific method.
2. Measuring the real value: It has been determined that QALY must be considered as a standard outcome to evaluate the efficacy of interventions in economic evaluations. However, it is not possible to solely assess the value of more complex interventions, such as precision medicine interventions, through QALY because their benefits are not limited to health.

3. Inadequate available data: The major challenges related to the data needed for conducting economic evaluations of PMI are their availability and reliability.
4. Increasing Complexity: Increasing Complexity: Economic evaluations of precision medicine are associated with considerable complexity because such studies evaluate more than one technology (at least two, one intervention, and one test).

Conducting an economic evaluation of precision medicine provides sufficient evidence applicable to making appropriate decisions about using it in healthcare systems. For more appropriate and precise evidence, it would be necessary to address the difficulties associated with the economic evaluation of precision medicine interventions.

Next-generation probiotics for management of obesity and its-associated complications

Hanieh-Sadat Ejtahed

Obesity and Eating Habits Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Introduction: Obesity is a major health problem which has been known as an important risk factor for many non-communicable diseases, such as diabetes, stroke, non-alcoholic fatty liver disease and depression. A growing body of evidence supports the role of microbiota in influencing host appetite, eating-related behavior, food intake and energy harvest. There is an emerging interest in the use of next-generation probiotics (NGPs), as a microbiota-modulating approach, for weight loss.

Methods: Scopus, PubMed, and Web of Science databases were searched to find relevant preclinical and clinical studies investigating novel probiotic species with anti-obesity effects.
Results: Administration of traditional probiotics, different strains of *Lactobacillus* and *Bifidobacterium,* has shown modest anti-obesity properties. Recent preclinical studies with promising results introduced some candidate NGPs in combating obesity like *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, and *Christensenella minuta*. There are some proposed mechanisms: ameliorating gut dysbiosis, improving the intestinal barrier integrity, modulating the gut-brain axis and reducing chronic inflammation. Translating these exciting observations to humans would be the next necessary step for developing novel food or supplements with anti-obesity effects.

Conclusion: The importance of intestinal microbiota composition has now been shown in obesity. So modulating the gut microbiota by novel microbiome-based biotherapeutic strategies like NGPs could be promising. There are some novel probiotic bacteria as anti-obesity agents.

However, Safety issues have to be clarified and further large-scale studies with longer follow-ups are needed to shed light on their therapeutic potential in obesity and associated complications.

Keywords: microbiota, obesity, probiotics

The effects of various dietary patterns on the management of diabetes and its complications

Nazli Namazi[1]*

[1]Diabetes Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran

Objective: The combination of foods in dietary patterns and the possible interactions among nutrients promote a synergistic effect on health in patients with diabetes. In this overview, we summarized the effects of several popular dietary patterns on diabetes and its complications.

Methods: In the present overview article, we collected relevant systematic reviews/meta-analyses in which the effects of dietary patterns on diabetes and related complications were examined.

Results: Evidence shows that low-carbohydrate diets can improve glycemic status only in a short time and their effects in the long term are not remarkably different from diets containing moderate or high carbohydrates. However, their positive effects on lipid profile were reported in 12-month intervention studies. High protein diets also did not improve glycemic status, whereas their impacts on lipid profile were positive. Type of protein (animal/ plant) can affect diabetes management and other metabolic status. However, the findings are conflicting. Healthy dietary patterns including DASH and Mediterranean diets can prevent cardiovascular diseases (CVDs), stroke, retinopathy, and diabetic foot ulcers alongside their beneficial effects on weight and lipid profile. Studies revealed that such diets can also decrease the risk of metabolic syndrome and mortality from MI, CVDs, and stroke. Vegetarian diets can modulate weight, and glucose level with no considerable effects on blood pressure and lipid status. Positive impacts of a pulse-rich diet and portfolio were also reported on some metabolic parameters and inflammatory factors. Intermittent fasting is another popular dietary pattern suggested for diabetic patients. However, any of the mentioned dietary patents must be recommended considering various aspects of patient status.

Conclusion: Several dietary patterns have been introduced for diabetes management. Positive effects of low-carb diets in only a short period, DASH, Mediterranean, vegetarian, portfolio, and Pulse-rich diets on cardiometabolic outcomes were reported. However, patient status should be considered in choosing the best dietary pattern.

Keywords: Dietary patterns, Diabetes, Healthy diet, Macronutrient, Metabolic Status

Management of Diabetes from the Viewpoint of Complementary & Alternative Medicines (CAMs)

Roja Rahimi (PharmD, PhD)

Department of Traditional Pharmacy, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract

About 51% of diabetic patients use complementary and alternative medicine (CAM) for the management of their diabetes. Thirty types of CAM have been distinguished to be applied by diabetic patients. The Most common CAM types used in diabetes are herbal medicines, acupuncture, homeopathy, and spiritual healing. Among non-pharmacological CAM interventions except acupuncture, meditation and nutrition therapy were the best choices regarding controlling glycemic parameters and diabetes-related problems, as well as increasing quality of life with reducing the risk of cardiovascular complications. Results of various meta-analyzes have revealed the efficacy of acupuncture in controlling glycemic parameters as well as neuropathic pain in prediabetics and type 2 diabetic patients (T2DM). Eight different types of mind-body exercises have been distinguished to be used in T2DM and among them, Yoga, dance, Pilates, and Tai Chi have exhibited the best efficacy in controlling glycemic and cardiovascular parameters. More than 1700 medicinal plants may have been traditionally used for the management of diabetes, more than 1000 were investigated and more than 120 are promising. So, medicinal plants have been used for both developing natural pharmaceutical products and new drug discovery related to diabetes. Amazingly, one of the most used medicines for the management of T2DM has been synthetized by modeling the structure of a plant- derived chemical compound called galegine. Garlic, berberine, fenugreek seed, turmeric and curcumin, black seed, silymarin, and cinnamon are among herbal medicines that demonstrated promising role in the management of T2DM. Conclusively, it seems that applying the potential of CAMs beside conventional treatments, leads to better management of diabetes and its complications as well as increasing patients' quality of life.

Keywords: complementary and alternative medicine, diabetes, acupuncture, herbal medicine, medicinal plant, Yoga, Tai Chi

Title: Commercialization of regenerative medicine-based therapies

Hamid Reza Aghayan, MD, PhD*

***Cell Therapy & Regenerative Medicine Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.**
email: shraghayan@tums.ac.ir

Abstract

Regenerative medicine (RM) is an emerging field in medical sciences that aims to address unmet medical needs. It encompasses gene therapy, cell-based therapy, and tissue-engineered therapy, all of which have the goal of repairing, regenerating, or replacing damaged organs, tissues, and genes in the human body. RM has shown promise in treating chronic, hard-to-treat, or incurable diseases such as diabetes, heart failure, ALS, chronic wounds, progressive MS, osteoarthritis, cancers, hematological disorders, paralysis, Parkinson's disease, and macular dystrophy. Recent advancements in technology and interdisciplinary sciences have improved the outcomes of regenerative therapies. Translation of regenerative therapies from bench to bedside needs passing a long way from proof-of-concept studies to market authorization. To gain approval from regulatory bodies all preclinical and clinical studies (clinical trials) must adhere to the principles of different good practices (GXPs) and relevant regulatory requirements. It is important to address challenges related to safety, efficacy, scale-up, dosing, pricing, and qualification of RM products. Scientists working in this field should be familiar with the commercialization pathways and regulatory frameworks for RM products. This presentation will outline the key elements of commercializing RM products and discuss the current international and national regulatory frameworks for these products.

Keywords: Commercialization, gene therapy, Regenerative medicine, Regulation, Stem cell, Tissue engineering,

Overview and update on anti obesity drugs

Shirin Hasani Ranjbar,

MD, Endocrinologist

Professor/ Endocrinology and Metabolic Research Institute

Tehran University of Medical Sciences, Tehran Iran

Obesity is the fifth leading cause of death worldwide. Being overweight or obese increases the risk of medical, economic, and social problems.

Excessive body weight is associated with cardiovascular disease, stroke, type 2 diabetes mellitus, hypertension, chronic kidney disease, gastro esophageal reflux disease, polycystic ovarian syndrome, infertility, obstructive sleep apnea, cancer, joint problems, and fatty liver disease. Modest weight loss can reduce the risk of chronic diseases.

Recently, there has been an enormous change in the use of anti obesity drugs with high consumption that deserves extensive surveillance for the long-term consequences.

Currently approved anti-obesity medications include liraglutide, naltrexone-bupropion, orlistat, phentermine-topiramate, semaglutide and tirzepatide. When used with lifestyle interventions, these medications result in an average of 5–15% weight loss. These medications may act centrally, act peripherally, or both peripherally and centrally.

In this lecture I will review the literature on approved/non-approved anti obesity medications used for obesity and overweight. Also emerging trials of therapies and evolving remedies will be noted.

Climate Change and Non-Communicable Diseases: Effects and Responsible Sources

Zahra Soleimani, Samaneh Abolli

Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Introduction: The intricate and evolving relationship between climate change and non-communicable diseases (NCDs) forms a compelling narrative at the intersection of public health and environmental sustainability.

Method: This review starts a journey to address the relationship between climate change and NCDs.

Results: Climate change has diverse effects on non-communicable diseases (NCDs), from direct physiological implications to broader socio-environmental determinants. The impacts include rising temperatures and heatwaves exacerbating cardiovascular stress, respiratory compromise due to worsened air quality resulting from heightened forest fires and urban pollution, and escalating allergen exposure amplifying allergic and autoimmune responses. Disruptions in food systems and agricultural productivity, alongside changing disease vectors and waterborne pathogens, directly influence nutritional patterns, infectious disease vectors, and water-related NCDs. NCDs could cost the global economy $47 trillion over the next two decades, with healthcare costs of chronic diseases such as diabetes, kidney, neoplasm, cardiovascular diseases, and respiratory conditions being a significant part of this projection. By 2030, the cumulative economic loss due to NCDs could reach $30 trillion, mostly stemming from factors such as lost productivity and disability. Climate-induced events contribute to heightened rates of psychological conditions such as anxiety, depression, and post-traumatic stress disorder. Both climate change and NCDs are preventable and require a multi-sectoral response. Effective public policies and programs are needed to reduce population risk levels and increase access to treatment.

Conclusion: This study illuminated the multidimensional impact of climate change on NCDs. Mental health impacts, long-term stressors, public health implications, and the intricate web of physiological, ecological, and behavioral are examples of climate change effects on NCDs. The urgent need for integrated public health strategies, climate-resilient policies, and ecosystem protection measures to cope with these conditions is suggested.

"Diet quality and sleep health and mental disorders in diabetic patients"

Leila Azadbakht[1,2], Mohammadreza Moradi Baniasadi[1]

1**. Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran.**

2. Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Type 2 diabetes, an eminent chronic ailment, has been observed to exhibit an escalating trend globally. This disease is associated with a multitude of severe incapacities and complications, encompassing cardiovascular, renal, and ocular disorders, along with sleep disturbances, mood disorders, and mental ailments. Among the complications commonly encountered in diabetic patients, sleep disruptions and psychological disorders, which include aggression, anxiety, stress, and depression, are of significant concern. It has been found that around one-third of individuals suffering from type 2 diabetes experience sub-threshold depression, while over 40% display either minor or major depression along with anxiety disorders. Furthermore, it has been established that diabetic patients generally exhibit poor sleep quality, characterized by lower sleep efficiency and an increased prevalence of sleep disorders as compared to their non-diabetic counterparts. Additionally, the occurrence of anxiety and depression is more pronounced in individuals afflicted with diabetes, as opposed to those with normal glucose tolerance levels.

Diet, being a significant and alterable environmental factor, has the potential to exert an influence on both the regulation of blood sugar levels and the occurrence of psychological disorders and disruptions in sleep. Additionally, the inclusion of nutrients such as zinc, magnesium, and B-vitamins, which are abundantly found in vegetables, can contribute to an enhancement in the quality of sleep experienced, as well as a reduction in the likelihood of developing symptoms of depression. Furthermore, the adoption of dietary patterns that emphasize the consumption of nuts, fruits, and vegetables has been found to be associated with a decreased risk of depression. Furthermore, it has been demonstrated that adherence to a diet that is deemed healthy or of high quality is often correlated with an improved state of mental health,

with the latter frequently being defined as the absence of symptoms related to unipolar depression.

Based on the previous cross-sectional investigation, individuals with diabetes who fell into the highest tertile of ferric reducing ability of plasma (FRAP) and oxygen radical absorbance capacity (ORAC) score exhibited a striking 94% and 87% reduction in the likelihood of experiencing poor sleep, respectively. Additionally, adhering to the highest tertile of FRAP and ORAC was associated with a diminished probability of depression among the diabetic population. Diabetic women in the uppermost tertile of FRAP, when compared to those in the lowest tertile of FRAP score, displayed a noteworthy 59% decrease in the risk of anxiety. In this patient cohort, the likelihood of experiencing stress was inversely correlated with adherence to the highest tertile of FRAP and ORAC scores. Another investigation revealed that individuals with higher dietary acid load (DAL) scores and those who adhered to animal-based diets instead of plant-based diets were more prone to experiencing poor sleep and mental health disorders. A cross-sectional analysis concluded that greater adherence to the Diet Quality Index-international (DQI-I) and Healthy Eating Index (HEI-2010) was associated with a reduced risk of mental disorders and poor sleep among diabetic patients.

In conclusion, a diet with high quality is related to a lower risk of sleep and mental disorders. Furthermore, we need to implement prospective cohorts or intervention studies to confirm this result.

PCOS

effect on Fertility

Dr. Marzieh Vahid Dastjerdi

Tehran University of Medical Sciences, Tehran, Iran.

PCOS should be diagnosed using the revised Consensus Rotterdam Criteria.
In adults this requires the presence of two of i) clinical /biochemical hyperandrogenism, ii) ovulatory dysfunction and
iii) polycystic ovaries on ultrasound or elevated AMH Levels.
Where irregular menses and hyperandrogenism are present, ultrasound or AMH are not required.
In adolescents both hyperandrogenism and ovulatory dysfunction. Are required, with ultrasound and AMH not recommended, due to poor Specificity

once diagnosed, assessment and management should address reproductive, metabolic, Cardiovascular, dermatologic, sleep and Psychological features.
A Lifelong reproductive health plan is recommended including Preconception risk factors, healthy Life style, and prevention of weight gain and optimisation of fertility.
Metabolic risk factors, diabetes, Cardio vascular disease, and sleep disorders are all increased in PCOS and screening and management is recommended.

PCOS should be considered a high risk Condition in pregnancy. An increased premenopausal risk of endometrial Cancer should be recognized.

Supported healthy Lifestyle remains vitd throughout The Lifespan in PCOS, with a strong focus on Overall health, prevention of weight gain and weight management. Combined oral Contraceptive Pills are first Line pharmacological Treatment for irregular Mense and hyperandro - genism. With preference for Low dose preparations and less side effects.

Metformin is recommended primarily for metabolic features and has greater efficacy than inositol. Metformin is not routinely recommended for use in pregnant women with PCOS. Laser Therapy is effective for hair reduction in some subgroups, whilst anti androgens have a Limited role, where other Therapies are ineffective or contraindicated. Anti-obesity agents and bariatric Surgery may be considered based on general population guide Lines, balancing potential for benefits and side effects.

Letrozol is first Line pharmacological infertility therapy, with clomiphene alone or in combination with metformin. gonadotropins or ovarian surgery having a role as Second line Therapy. In the absence of an absolute indication for IVF, women with pros and an ovulatory Infertility could be offered IVF potentially with in vitro maturation as Third Line Therapy where other ovulation Therapies have failed.

Risks and management of hypothyroidism and hyperthyroidism in pregnancy

Mojgan asadi

Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Thyroid disorders are the second most common endocrinologic disorders found in pregnancy. Overt hypothyroidism is estimated to occur in 0.3-0.5% of pregnancies. Subclinical hypothyroidism appears to occur in 2-3%, and hyperthyroidism is present in 0.1-0.4%.

Uncontrolled hyperthyroidism, especially in the second half of pregnancy, can lead to numerous complications. Maternal complications include miscarriage, infection, preeclampsia, preterm delivery, congestive heart failure (CHF), thyroid storm, and placental abruption.
Fetal and neonatal complications include prematurity, small size for gestational age, intrauterine fetal death, fetal or neonatal goiter, and/or thyrotoxicosis. Overtreatment may cause iatrogenic fetal hypothyroidism. When maternal thyroid antibody titers are greater than 300% of the normal upper limit, the fetus is at risk of fetal hyperthyroidism and should be evaluated by ultrasound for evidence of hyper- or hypothyroidism. Fetal hyperthyroidism can include tachycardia, accelerated maturation of bone, goiter, growth restriction, and congestive heart failure.
Maternal complications of untreated hypothyroidism include microcytic anemia, preeclampsia, placental abruption, postpartum hemorrhage, cardiac dysfunction, and miscarriage. Fetal or neonatal complications include prematurity, low birth weight, congenital anomalies, stillbirth, and poor neuropsychological development.

Hypothyroidism during pregnancy should be treated with levothyroxine, with a serum TSH goal of less than 2.5 mIU per L.

Serum TSH should be measured in pregnant women who are being treated for hypothyroidism at four to six weeks' gestation, then every four to six weeks until 20 weeks' gestation and on a stable medication dosage, then again at 24 to 28 weeks' and 32 to 34 weeks' gestation

Propylthiouracil is the preferred agent for the treatment of hyperthyroidism during the first trimester of pregnancy and in women with methimazole allergy and hyperthyroidism. Consideration should be given to switching to methimazole after the first trimester, and the dosage should be adjusted to maintain a serum FT_4 level in the upper one-third of the normal range.

In pregnant women who are being treated for hyperthyroidism, serum TSH and FT_4 should be measured every two weeks until the patient is on a stable medication dosage.

In conclusion, effective management of hypothyroidism and hyperthyroidism during pregnancy is essential to reduce adverse outcomes for both the mother and fetus. Close monitoring and appropriate treatment are key components of care for pregnant women with these endocrine disorders.

The Gut-Brain-Endocrine Axis: Gut Microbiota and Sex Hormones Regulation

Seyed Davar Siadat

Microbiology Research Center, Pasteur Institute of Iran

The precise pathways of microbiota-hormone signaling have been studied a lot in recent years and specific changes in hormone levels centered on intestinal microbiota have been well defined, which provides new insights into the prognosis, diagnosis and treatment of many metabolic and endocrine disorders. Microbiota produces and secretes hormones as well as, responds to host hormones and regulates the level of host hormone secretion. Meanwhile, the gut-brain-endocrine axis is a fascinating research area has entered a golden age that emphasizes the broad influence of the gut microbiota on endocrine function. As the studies continue to unravel the intricacies of this axis, it is becoming clear that a balanced gut microbiota is essential for overall health and may hold the key to control and predicts a wide range of endocrine disorders. Future studies will likely provide further insights into the development of targeted therapies harnessing the power of the gut microbiota to optimize endocrine health. One of the attractive fields in this axis, with an emphasis on hormonal regulation, is sexual health and disorders related to changes in sex hormones related to the microbiome. Steroid hormones shape the structure of the gut microbiota and these bacteria also regulate the level of sex-active steroids. These hormones and bacteria act on gut sensory endocrine cells, which modulate downstream activity in the enteric nervous system, vagus nerve, and brain. The purpose of this lecture is to highlight the recent advances and the potential of new therapeutic approaches targeting microbiota-endocrine interactions in the gastrointestinal axis. Key topics include the effect and role of microbiota on the regulation of sex hormones in physiological states such as age and sex and pathological endocrine disorders, and the regulatory pathway of microbiota through diet, probiotics, prebiotics and fecal microbiota transplantation with emphasis on Person-centered medicine is for more appropriate and effective treatments in endocrine-related diseases.

KEYWORDS: STEROID HORMONE, GUT MICROBIOTA, GUT BRAIN AXIS,..

Frailty Causes Metabolic Syndrome in Elderly Patients

Fatemeh Alsadat Mirzadeh

Department of Geriatric Medicine, Ziaeian Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Although aging is a natural phenomenon nor a disease, it is often challenged by various disorders and co-morbidities. Two important risk factors of developing cardiovascular diseases, diabetes, and all-cause mortality are frailty and Metabolic syndrome (MetS). Frailty is a medical condition where older adults become vulnerable to stressors due to a reduction in their physiological reserve. The prevalence of frailty varied widely in different settings, ranging from 0.9% to 35.6%. MetS is more prevalent in the outpatient clinic setting (47.5%) compared to community-dwelling populations (17.5-41%).

Insulin resistance is believed to be a contributing factor in frailty and metabolic syndromes. When insulin sensitivity decreases, the balance of oxidants and antioxidants is disrupted. This leads to an accelerated inflammatory response, particularly by adipocytes and macrophages in adipose tissue and muscle mass density. Moreover, oxidative stress and pro-inflammatory state have an important role in the pathophysiology of syndemic disorders like metabolic syndrome and frailty syndrome.

Studies showed that MetS in those ≥50 years was associated with an increased risk of pre-frailty or frailty (pooled OR 1.73, 95% CI, 1.41–2.13). After reviewing various metabolic pathways in literature, it has been found that the development of metabolic and frailty syndromes is linked to increased oxidative stress and inflammation acceleration, indicating a common pathogenesis. MetS was associated with low physical activity and unintentional weight loss, which are criteria of frailty.

MetS alone doesn't affect disability-free survival, but pre-frailty or frailty alone does. Co-existing MetS with pre-frailty/frailty doesn't increase the risk of shortened disability-free survival. The study suggests that it is important to screen for frailty in older adults with MetS. It also highlights

the role of managing MetS in preventing frailty in older adults. Frailty assessment is more important than MetS in predicting survival free of dementia or physical disability. MetS is a risk factor for frailty and should be considered during comprehensive geriatric assessment due to frailty's dynamic nature and MetS being potentially modifiable.

Gestational Diabetes Mellitus: Update on Screening, Diagnosis, and Management

Mahbube Ebrahimpur

Elderly Health Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Gestational Diabetes Mellitus (GDM) is a condition marked by elevated blood sugar levels during pregnancy in previously non-diabetic women, affecting approximately 14.0% of pregnancies worldwide and inadequate treatment can lead to serious adverse health effects for the mother and child.

Gestational diabetes exposes affected people at risk of developing gestational hypertension, preeclampsia and Caesarean section. In addition, people with Gestational diabetes mellitus are at greater risk of complications such as cardiovascular diseases, carbohydrate metabolism disorders. Increasing incidence of GDM imposed significant economic burden and deserves more attention and awareness. Screening for GDM involves a glucose challenge test followed by an oral glucose tolerance test (OGTT) if results are abnormal. Recent guidelines advocate lower thresholds for diagnosing GDM to enhance risk identification and management. Management of GDM entails dietary modifications, physical activity, and possibly insulin therapy. Regular blood sugar monitoring and prenatal visits are crucial for monitoring maternal and fetal health. Postpartum screening for diabetes is recommended to assess the risk of developing type 2 diabetes.

In conclusion, the evolving screening, diagnosis, and management strategies for GDM aim to optimize outcomes for mothers and babies by reducing complications and promoting healthy pregnancies. Following current guidelines can help healthcare providers effectively identify and manage GDM to ensure positive outcomes for both mother and child.

The Necessity of Improving Health Literacy in Noncommunicable Diseases (NCD)

Moloud Payab

Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

The necessity of improving health literacy about noncommunicable disease (NCD) prevention and control has been emphasized by the World Health Organization (WHO). The 2030 Agenda for Sustainable Development has identified the NCD as a major challenge of our era. Approximately more than one-third of diseases are caused by NCD. A challenging problem according to these types of pathologies is premature deaths (aged < 40 years old), which can be prevented or at least postponed.

The WHO statistics demonstrate that seven of the ten most common death etiologies are NCDs. The most affected populations are low- and middle-income countries (LMICs) residents, which include 86% of premature deaths by the definition of WHO (deaths occurring in populations between 30 and 70 years old). Annually, more than 15 million deaths in these countries lead to escalating disparity and lower productivity rates among LMICs and high-income countries (HICs).

Another evidence for the importance of preventing NCDs is the fact that healthcare systems are remarkably affected by disabilities that are mostly caused by these pathologies all over the world. Policymakers and politicians should plan to control the prevalence of these diseases and their risk factors. Providing equal availability of healthcare services for all patients with these diseases is another crucial factor that should be considered by them. An important indicator of the effectiveness of WHO member state actions is the improvement of health literacy and the application of the responsiveness approach.

The essentiality of improving NCDs relies on the fact that these diseases and their risk factors are most modifiable before the emergence of the symptoms. Unhealthy behaviors such as tobacco use, drinking of alcohol, lack of physical activity, unhealthy diet, polluted air, and daily life stressors are the most crucial issues that should be emphasized in the planning process for improving the general population's healthcare knowledge.

Considering the remarkable impact of healthcare workers' approaches on the improvement of healthcare literacy, they should try to focus on increasing the general population's awareness about NCDs and their risk factors. Digital devices and opportunities can be enormously influential in the development of health literacy. Enhancing access to healthcare information and backing up the well-being of individuals and communities can be achieved through the application of an interdisciplinary approach.

Herbal medicines to care and management of dyslipidemia; advances and prospects

Ozra Tabatabaei-Malazy

[1]Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

[2]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

tabatabaeiml@sina.tums.ac.ir, https://orcid.org/0000-0003-0188-9721

Objectives: Prevalence of Cardiovascular diseases (CVDs) as the leading cause of global mortality is increasing worldwide. So, their prevention, care and management are one of the main health challenges. Dyslipidemia is one of the modifiable risk factors of CVDs. Current guidelines highlight lifestyle modifications and pharmacologic medications as key issues in the care and management of dyslipidemia. Due to high rates of intolerance to anti-dyslipidemic agents, up to 60% of patients, or side effects, many patients discontinue these medications. Since, herbal medicines have shown lipid-lowering properties, they can be a good alternative treatment in this regard. To counter the growing trend to use and prescribe herbal medicines for management of dyslipidemia, it is crucial to raise awareness about their beneficial effects, side effects, safety and effective dose as lipid-lowering agents. The current lecture will explore above effects.

Methods & Results: Relevant studies regarding the safety and efficacy of the herbal trials based on meta-analysis studies, as the top level of evidence-based medicine, published until Feb 10/ 2024, are extracted from PubMed, and Web of Science databases. Some examples of the most studied natural products are including *Allium sativum* (garlic), *Nigella sativa* (black cumin),

Trigonella foenum-graceum L. (fenugreek), green tea, *Hibiscus Sabdariffa L.* (sour tea) and Resveratrol. Details of the findings will be discussed in the lecture.

Conclusions: Regardless of observed lipid-lowering effects of the plant-derived products, due to lack of sufficient data on their effective dose and appropriate duration of treatment, more well-conducted controlled trials are needed.

Keywords: herbal medicine; dyslipidemia; management; meta-analysis.

Immune system interactions in thyroid diseases

Nooshin Shirzad

Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Autoimmune thyroid diseases (AITD) are the most prevalent organ-specific autoimmune diseases.

They reflect, loss of immunological tolerance and the presence of cell and humoral immune response against antigens from the thyroid gland with reactive infiltration of T cells and B cells autoantibody generation.

The etiology in this context is multifactorial, with a complex interaction of environmental factors in genetically susceptible individuals.

Genetics, epigenetics and environmental factors may trigger activation of antigen presenting cells .The thyroid follicular cells from individuals with AITD can also abnormally presenting cells .The thyroid follicular cells from individuals with AITD can also abnormally express HLA-II (induced by IFN-γ). There is also the thyroid infiltration of B lymphocytes , cytotoxic T lymphocytes(TLs), and TLs (CD4+).

In addition, an attenuated regulatory T lymphocyte response has also been found, which may increase the proinflammatory activity of Th17. These mechanisms involve cytokines/chemokines and/or cytotoxins. Pro-inflammatory chemokines recruit the immune system cells in inflammation site. Then there is thyroid destruction or stimulation, depending on the Th1-Th2 balance.

Title: General Overview of Omics Approaches in Endocrine Disorders

Nekoo Panahi

MD-MPH, PhD

Assistant Professor of Endocrinology

Metabolic Disorders Research Center, Endocrinology and Metabolism Clinical Sciences Research Institute, Tehran University of Medical Sciences

Abstract:

Omics technologies have revolutionized the field of endocrinology by enabling comprehensive molecular analysis of endocrine disorders at the genetic, transcriptional, protein, metabolic, and microbiota levels. These technologies, including genomics, metabolomics, proteomics, and microbiomics, have facilitated a deeper understanding of endocrine disorders, holding promise for personalized diagnostics and targeted therapies. Recent advances in omics technologies have enabled cost-efficient, high-throughput analysis of different types of omics data in large human cohorts. Some recent advances include 1. providing a map of reference values for measures of continuous glucose monitoring (CGM) devices obtained from healthy individuals which can be used in research in the field of diabetes and pathologies associated with glucose homeostasis and glycemic variability; 2. demonstrating metabolic heterogeneity within similar BMI classes and the responses to lifestyle patterns; 3. multi-omics profiling showing gut microbacteria associated with insulin resistance; 4. advancements in mass spectrometry, chromatography, and data analysis methods enabling spatially resolved omics analyses, providing comprehensive insights into the molecular, cellular, and tissue levels of endocrine tumors and offering potential for new biomarkers and therapeutic targets; 5. Using multi-omics approach to identify markers of resistance to endocrine therapy in metastatic breast cancer. These advances have provided insights into the pathophysiology of metabolic disorders, identified key molecular pathways and potential therapeutic targets, and informed the development of targeted therapies for endocrine disorders. Omics technologies have the potential to advance knowledge in endocrinology by

enabling the identification of novel biomarkers, elucidating metabolic pathways, and unraveling the complex interplay between genetic and environmental factors in endocrine diseases.

Osteosarcopenia in the Elderly: An Emerging Challenge in Geriatric Medicine

Shima Raeesi, MD

Geriatrician

Osteosarcopenia, a term combining osteopenia/osteoporosis and sarcopenia, represents a complex and multifaceted health issue in the aging population. As individuals advance in age, the concomitant deterioration of bone and muscle mass poses significant threats to overall health and functional independence. The hallmark feature of osteosarcopenia is the simultaneous decline in bone density and muscle mass. Osteoporosis, characterized by low bone mineral density and increased bone fragility, coexists with sarcopenia, the age-related loss of muscle mass and function. Osteosarcopenia contributes to heightened risks of fractures, falls, and functional decline. The intricate relationship between bone and muscle health is bidirectional, with each influencing the other. Reduced physical activity, a common consequence of sarcopenia, further exacerbates bone loss, creating a vicious cycle that significantly impacts the quality of life for older individuals.

Early detection and screening for osteosarcopenia are essential in geriatric healthcare. Dual-energy X-ray absorptiometry (DXA) scans, traditionally used to assess bone density, are now being explored for their potential in simultaneously evaluating muscle mass. Additionally, functional assessments, such as gait speed and handgrip strength, offer valuable insights into overall musculoskeletal health.

Management and prevention strategies for osteosarcopenia are evolving, emphasizing a multidisciplinary approach. Resistance training, weight-bearing exercises, and adequate protein intake emerge as key components of interventions aimed at preserving both bone and muscle mass. Pharmacological agents, including bisphosphonates and anabolic agents, are also considered in certain cases to mitigate bone loss and enhance muscle function.

As the aging population continues to grow, addressing the challenges posed by osteosarcopenia becomes paramount. A comprehensive approach that integrates lifestyle modifications, exercise regimens, and pharmacological interventions is necessary to mitigate the impact of osteosarcopenia and promote healthy aging in our elderly population.

Personalized Medicine in Clinical Practice

Mandana Hasanzad[1,2], Negar Sarhangi[1], Bagher Larijani[3]

1. **Personalized Medicine Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran**
2. **Medical Genomics Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran**
3. **Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran**

Personalized medicine, a growing field in healthcare, is revolutionizing clinical practice by tailoring medical interventions to individual patients based on their unique genetic makeup, lifestyle, and environmental factors. This paradigm shift from a one-size-fits-all approach to a patient-centered model holds immense promise for improving treatment efficacy, minimizing adverse effects, and optimizing healthcare outcomes. As a key element of personalized medicine, pharmacogenomics provides an interesting opportunity to improve patient care by optimizing drug choice and dosage, reducing the possibility of adverse drug reactions, and thereby implementing the principles of personalized medicine.

Personalized medicine has emerged as a breakthrough technique in cancer, providing tailored treatments based on the genetic profile of each patient's tumor. Oncologists can use genomic sequencing and molecular profiling tools to uncover specific biomarkers and genetic alterations that drive cancer progression, resulting in more precise diagnosis and targeted medication choices. By genomic sequencing and molecular profiling techniques, oncologists can identify unique biomarkers and genetic mutations driving cancer progression, allowing for more precise diagnosis and targeted therapy selection. Several challenges such as regulatory hurdles, cost constraints, and ethical considerations persist, underscoring the need for continued research and innovation. However personalized medicine is reshaping the landscape of medicine, empowering clinicians with the tools and insights needed to deliver more effective and individualized care to patients.

Keywords: Personalized medicine, Precision medicine, Genomics, Pharmacogenomics.

Correspondences

1. Mandana Hasanzad

Personalized Medicine Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran university of Medical Sciences, Tehran, Iran.

Address: No.10- Jalal -e-Ale-Ahmad Street, Chamran Highway, Tehran, Iran

Postal Code: 1411713119

Tel/Fax: +98-21-88220091

E-mail addresses: mandanahasanzad@yahoo.com

Cell Therapy in Diabetes

Sayed Mahmoud Sajjadi-Jazi, MD

- Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

- Department of Endocrinology, Shariati Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Cell therapy holds great potential as a viable method for managing diabetes, a chronic metabolic condition marked by elevated blood sugar levels. Diabetes is a significant public health issue, impacting an estimated 537 million adults (20-79 years) worldwide. Presently, treatment options for diabetes consist of insulin therapy, oral medications and lifestyle modifications. Nonetheless, these treatments do not consistently succeed in regulating blood sugar levels and averting complications associated with the disease.

Cell therapy involves transplanting cells that can produce insulin or regulate blood sugar levels in the body of a person suffering from diabetes. The aim of cell therapy for diabetes is to replace or enhance the function of the insulin-producing beta cells that are destroyed in individuals with type 1 diabetes, or to increase the effectiveness of these cells in individuals with type 2 diabetes.

The transplantation of pancreatic islet cells is regarded as one of the most promising approaches in cell therapy for diabetes. Clinical trials have demonstrated encouraging outcomes in islet cell transplantation, leading to a number of patients achieving long-term independence from insulin and enhanced control over their blood sugar levels. Another method of cell therapy for diabetes is the use of stem cells. Stem cells are cells that have not yet specialized and have the ability to mature into various cell types within the body. Different types of stem cells have been investigated for their potential use in diabetes cell therapy, including induced pluripotent stem cells, mesenchymal stem cells and embryonic stem cells. These stem cells can be differentiated in the laboratory into insulin-producing beta cells and then transplanted into the body of a person with diabetes.

Cell therapy shows great potential for improving blood sugar management, decreasing reliance on insulin injections, and preventing complications associated with diabetes. Nevertheless, there are still obstacles that must be overcome before cell therapy can become a widely accessible treatment option for diabetes. One obstacle is the immune response to transplanted cells, which can result in rejection of the transplanted cells or necessitate the use of immunosuppressive medications. Scientists are currently investigating approaches to protect transplanted cells from immune response, such as encasing them in protective materials or utilizing gene editing technologies to make them less detectable to the immune system. Another challenge is the limited supply of donor cells for islet cell transplantation or the generation of adequate amounts of insulin-producing beta cells for transplantation.

Despite these challenges, cell therapy has the potential to revolutionize the treatment of diabetes and improve the overall health of people with this condition. Continued research and clinical trials are needed in order to improve and optimize cell therapy techniques for diabetes and finally make them available in clinical practice. Continuous advances in cell therapy and regenerative medicine technologies are bringing us closer to a future where cell therapy can provide a definitive cure for diabetes.

Genomics in Endocrinology

Fatemeh Bandarian, MD, PhD

Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Genomics has provided a foundation for understanding of the endocrine disorders. Genetic variations influence the susceptibility to as well as the onset and the severity of endocrine disorders and response to therapy, which underscoring the need to unravel the genetic underpinnings. The human genome, comprised of over 20,000 genes, harbors valuable information about the genetic basis of endocrine disorders. The advent of advanced sequencing and genotyping techniques, such as next-generation sequencing (NGS) and Microchip technology has enabled scientists to perform whole genome (WGS) and exome (WES) sequencing as well as genome wide association studies (GWAS) to decode the human genome more rapidly and at a lower cost. As most of endocrine disorders are polygenic and multifactorial, different genes and their multiple SNPs have been identified to be involved in these diseases susceptibility and severity as well as their response to treatment that most of them are in the metabolic pathways of hormone production and action. However, among them, there are few rare single gene disorders. Here, we will have an overview of the most significant gene and SNPs involved in the endocrine disorders including diabetes (type 1 and 2), obesity, metabolic syndrome, thyroid and adrenal disorders as well as poly cystic ovary syndrome (PCOs). Today, the growing knowledge on the genetic reasons behind various disorders affecting organs and by identifying the genomic loci harboring risk alleles for common traits makes the application of precision medicine in everyday clinical practice imperative.

The convergence of endocrine sciences with planetary health

Iraj Nabipour [1,2]

1-THE PERSIAN GULF TROPICAL MEDICINE RESEARCH CENTER, THE PERSIAN GULF BIOMEDICAL SCIENCES RESEARCH INSTITUTE, BUSHEHR UNIVERSITY OF MEDICAL SCIENCES, BUSHEHR, IRAN
2-FUTURE STUDIES GROUP, THE ACADEMY OF MEDICAL SCIENCES OF THE I.R. IRAN ,

INABIPOUR@GMAIL.COM

The concept of planetary health implies that human health and human civilization depend on the healthy state of natural systems of biosphere. Hence, clinical endocrinologists are increasingly seeking to bring planetary health to health of the endocrine system by clarifying the complex interactions of this system with the health of natural systems of biosphere. Concerns about harmful effects of nearly 1000 known or suspected endocrine disrupting chemicals (EDCs) that can interfere with hormone action began to emerge because of their correlation with non-communicable diseases, endocrine neoplasia, adrenal steroidogenesis dysfunction, neurobehavioral disorders associated with thyroid disruption, immunological malfunctions, reproductive dysfunctions and genital malformations in humans beyond their serious effects on the wildlife and ecosystems. The convergence of endocrinology with the science of planetary health will address social and environmental drivers and disruptors of the human endocrine health and the planet. Therefore, in a transdisciplinary endeavor by integrating public health with environmental care, the effects of climate change, stratospheric ozone depletion, atmospheric aerosol loading, ocean acidification, land-system and fresh water changes, biodiversity losses and imbalances in nitrogen and phosphorus flows in the endocrine system should be precisely investigated in order to save not only our planet but also prevent the global epidemics of obesity, type 2 diabetes mellitus and other metabolic disorders that are going to show their increasingly associations with environmental exposomics.

Keywords: planetary health, endocrine, climate change, exposomics, convergence

Interaction of the Immune System and the Endocrine System

Hamid Reza Aghayi

Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran.

The immune system and the endocrine system are two fundamental systems in the human body that work in tandem to maintain homeostasis and protect the body from various threats. The interaction between these two systems is complex and multifaceted, involving a variety of hormones, cells, and signaling pathways.

The immune and endocrine systems communicate bidirectionally to facilitate optimal host responses and homeostasis. This communication is possible because endocrine organs express cytokine receptors, and cells of the immune system express hormone receptors.

Hormones play a crucial role in the development, homeostasis, metabolism, and response to the environment of cells and tissues. For instance, adrenal and/or ovarian hormones from the endocrine system can affect the secretion of cytokines by cells of the immune system. Conversely, the immune system's products regulate endocrine responses. Major metabolic diseases, such as type 1 diabetes, necessitating the development of a clearer understanding of the immune and endocrine interactions. The imbalance between pro- and anti-inflammatory immune responses plays a critical role in the development of altered endocrine function in the beta cells of the pancreas.

A better understanding of these interactions will expand our knowledge of the mechanisms at play in susceptibility to diseases and may reveal opportunities for the development of personalized therapies. Hormone receptors in immune cells and cytokine receptors over endocrine cells may provide a plethora of targets for this approach.

In conclusion, the interaction between the immune system and the endocrine system is a complex and dynamic process that plays a crucial role in maintaining homeostasis and responding to various threats. Further research into this interaction could lead to new therapeutic strategies for a range of diseases.

Dr.Jan Babayi

Theran medical university

Immunotherapy as new landscape in hematologic malignancy and solid tumors doing use progressively and at now sole treatment in some cancer eg, renal cell carcinoma ,melanoma,…

Immunotherapies include :therapeutic vaccines , Adaptive T cell therapy, Bispecific antibodies, Immune checkpoint inhibitors(ANTICTLA4,ANTI-PDL1,ANTIPD1, ANTI-LAG3,…)

Toxicity vary between type of immunotherapies and all of organs may involve but skin, endocrine glands ,liver and gastrointestinal mostly involve.

We do in this discussion focus endocrinopathies due to immune checkpoint inhibitors(ICI).

ICI induced endocrinopathy(EP) include: Thyroiditis(most common), Hypophysitis , Autoimmune diabetes, Adrenalitis,…

Some characteristics of EP-ICI include:

-Acute onset particulary Hyperglycemia with insulin deficiency without honey moon period

-Irreversibility/permanent complication that need lifelong replacement therapy

-EP-ICI occur unpredictable as days to weeks after initiation of treatment ,even often after stopping of treatment, then these need continuous monitoring with physical examination and laboratory assessment ,also lifelong or permanent hormone replacement therapy.

FUTURE:

-More research need to be done to elucidate diagnosis, prognosis, identify higher risk patients for now risk factors are unknown.-

-possibly HLA typing antigen

-Guideline lag on management for this life threatening situation

-More data needed for withdrawing if ICI as disease progression/ irreversible complication

-other risk factors? /hx of familial endocrinopathy causes initiation/precipitation of this EP.

-Probable effect of other immunotherapy for patient.

New laboratory methods in the diagnosis of endocrine diseases

Ebrahim Kalantar

Tehran University of Medical Sciences, Tehran, Iran.

Inborn errors of metabolism (IEM) are a group of genetic disorders characterized by defects in metabolic pathways, leading to the accumulation of toxic metabolites or the deficiency of essential products. Early detection and diagnosis of IEM are crucial for timely intervention and management. Screening and confirmatory tests play a vital role in the identification of individuals at risk for IEM.

Newborn screening programs have been established in many countries to detect IEM in newborns before symptoms appear. These screening tests typically involve analyzing blood samples for specific markers or metabolites associated with different IEM. Confirmatory tests, such as genetic testing or enzyme assays, are then performed to confirm the diagnosis and determine the specific type of IEM present.

Advances in technology have led to the development of more sensitive and specific screening and confirmatory tests for IEM, allowing for earlier detection and more accurate diagnosis. This abstract highlights the importance of screening and confirmatory tests in the diagnosis and management of IEM, emphasizing the need for continued research and improvement in diagnostic methods to improve outcomes for individuals affected by these rare genetic disorders.

Liquid chromatography-tandem mass spectrometry (LC-MS/MS) plays a crucial role in the diagnosis and management of inborn errors of metabolism (IEM). LC-MS/MS is a powerful analytical technique that allows for the simultaneous quantification of multiple metabolites in a single sample with high sensitivity and specificity. In the context of IEM, LC-MS/MS is used for both screening and confirmatory testing.

1. Screening for IEM: LC-MS/MS is widely used in newborn screening programs to detect a broad range of IEM by analyzing dried blood spots for specific metabolites associated with different disorders. LC-MS/MS can detect abnormalities in amino acids, acylcarnitines, and organic acids, among other metabolites, allowing for the early identification of infants at risk for IEM before symptoms develop.

2. Confirmatory testing: Once an abnormality is detected in the initial screening, confirmatory testing using LC-MS/MS is performed to identify the specific type of IEM present. LC-MS/MS can provide detailed information on the levels of specific metabolites, helping to confirm the diagnosis and guide treatment decisions. Additionally, LC-MS/MS can be used to monitor treatment efficacy and disease progression in individuals with IEM.

3. Expanded panels: LC-MS/MS technology has enabled the development of expanded metabolic panels that can detect a wider range of IEM than traditional methods. These panels allow for comprehensive screening and profiling of metabolites, improving the chances of early detection and accurate diagnosis of rare and complex IEM.

Overall, LC-MS/MS has revolutionized the field of IEM diagnosis by providing a sensitive, specific, and high-throughput method for screening and confirmatory testing. Its ability to detect multiple metabolites simultaneously makes it an invaluable tool in the early detection, diagnosis, and management of individuals with IEM, ultimately leading to improved outcomes and quality of life for affected individuals.

There are hundreds of inborn errors of metabolism (IEM) that have been identified, each involving a specific genetic defect that disrupts normal metabolic processes in the body. Some of the most important and well-known IEM include:

1. Phenylketonuria (PKU): PKU is a disorder caused by a deficiency of the enzyme phenylalanine hydroxylase, leading to the accumulation of phenylalanine in the blood. If left untreated, high levels of phenylalanine can cause intellectual disability and other neurological problems.

2. Maple syrup urine disease (MSUD): MSUD is a disorder characterized by the inability to break down certain amino acids, resulting in the accumulation of branched-chain amino acids in the blood and urine. This can lead to neurological problems, metabolic crises, and other complications.

3. Gaucher disease: Gaucher disease is a lysosomal storage disorder caused by a deficiency of the enzyme glucocerebrosidase, leading to the accumulation of glucocerebroside in cells. This can result in organ enlargement, bone abnormalities, and other symptoms.

4. Homocystinuria: Homocystinuria is a disorder caused by defects in enzymes involved in the metabolism of homocysteine, leading to elevated levels of homocysteine in the blood. This can result in cardiovascular problems, intellectual disability, and other complications.

5. Glycogen storage diseases: Glycogen storage diseases are a group of disorders caused by defects in enzymes involved in glycogen metabolism, leading to abnormal storage or breakdown of glycogen in tissues. Depending on the specific enzyme deficiency, individuals with these disorders may experience hypoglycemia, muscle weakness, and other symptoms.

6. Wilson disease: Wilson disease is a disorder characterized by impaired copper metabolism, leading to copper accumulation in the liver, brain, and other organs. This can result in liver disease, neurological symptoms, and other complications if not treated.

These are just a few examples of important inborn errors of metabolism that can have significant impacts on health and quality of life. Early detection, diagnosis, and management of these disorders are crucial for preventing complications and improving outcomes for affected individuals.

In the United States, newborn screening programs typically include testing for a panel of genetic disorders, including certain inborn errors of metabolism (IEM). The specific disorders screened for can vary by state, but some of the most commonly included IEM in neonatal screening

programs in the USA are:

1. Phenylketonuria (PKU): PKU is one of the most well-known and widely screened IEM. Early detection and treatment through dietary intervention can prevent the development of intellectual disability and other complications.

2. Congenital hypothyroidism: While not a metabolic disorder, congenital hypothyroidism is often included in newborn screening programs due to its impact on metabolism and development. Early detection and treatment with thyroid hormone replacement can prevent intellectual disability and other problems.

3. Galactosemia: Galactosemia is a disorder caused by the inability to metabolize galactose, a sugar found in milk. Early detection and dietary management are essential to prevent liver damage, cataracts, and other complications.

4. Maple syrup urine disease (MSUD): MSUD is a disorder that affects the breakdown of branched-chain amino acids. Early detection through newborn screening allows for early intervention to prevent metabolic crises and neurological damage.

5. Homocystinuria: Some states include screening for homocystinuria, a disorder involving abnormal homocysteine metabolism. Early detection and treatment can help prevent cardiovascular problems and other complications.

6. Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD): VLCAD is a fatty acid oxidation disorder that can lead to hypoglycemia and muscle weakness. Screening and early intervention can help prevent metabolic crises and other complications.

These are just a few examples of inborn errors of metabolism that may be covered in neonatal screening programs in the USA. It's important to check with your state's newborn screening program to see which specific disorders are included in the screening panel. Early detection and intervention for these conditions can significantly improve outcomes for affected infants.

The specific inborn errors of metabolism (IEM) covered in the newborn screening programs in the United States can vary by state, but there are some common disorders that are often included in screening panels nationwide. Some of the IEM commonly screened for in the USA include:

1. Phenylketonuria (PKU)
2. Congenital hypothyroidism
3. Galactosemia
4. Maple syrup urine disease (MSUD)
5. Homocystinuria
6. Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)
7. Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
8. Isovaleric acidemia
9. Glutaric acidemia type 1
10. Citrullinemia

These are just a few examples of the IEM that may be included in the newborn screening programs in the USA. It's important to check with your state's specific program to see the full list of disorders included in the screening panel. Early detection and intervention for these conditions can significantly impact the health outcomes of affected infants.

In the context of inborn errors of metabolism (IEM), enzyme analysis is a key diagnostic tool used to confirm specific metabolic disorders. Enzyme analysis typically involves measuring the activity levels of specific enzymes involved in metabolic pathways that are affected by genetic mutations causing IEM. Some of the enzymes commonly analyzed for confirming IEM include:

1. Acid Alpha-Glucosidase: Deficiency of this enzyme is associated with Pompe disease, a glycogen storage disorder.

2. Hexosaminidase A: Deficiency of this enzyme is characteristic of Tay-Sachs disease, a lysosomal storage disorder.

3. Phenylalanine Hydroxylase: Mutations in this enzyme lead to phenylketonuria (PKU), a disorder of phenylalanine metabolism.

4. Galactose-1-Phosphate Uridyltransferase: Deficiency of this enzyme is seen in galactosemia, a disorder of galactose metabolism.

5. Arylsulfatase A: Deficiency of this enzyme is associated with metachromatic leukodystrophy, a lysosomal storage disorder.

6. Alpha-Galactosidase A: Deficiency of this enzyme is characteristic of Fabry disease, a lysosomal storage disorder.

7. Lysosomal Acid Lipase: Mutations in this enzyme are linked to Wolman disease and cholesteryl ester storage disease, both lipid storage disorders.

These are just a few examples of the enzymes that are commonly analyzed to confirm specific inborn errors of metabolism. Enzyme analysis is an important part of the diagnostic process for IEM, and it helps healthcare providers identify the specific metabolic pathways that are disrupted in affected individuals. In addition to enzyme analysis, other diagnostic tests such as genetic testing, metabolite analysis, and clinical evaluations are often used in combination to confirm the diagnosis of IEM and guide treatment decisions.

Glycogen storage diseases (GSDs) are a group of inherited metabolic disorders characterized by defects in enzymes involved in glycogen metabolism. The specific enzyme deficiencies associated with different types of GSDs include:

1. Glycogen Phosphorylase: Deficiency of this enzyme is seen in GSD type VI (Hers disease), which leads to impaired glycogen breakdown in the liver and muscle.

2. Glycogen Debranching Enzyme (Amylo-1,6-glucosidase): Deficiency of this enzyme is

characteristic of GSD type III (Cori disease or Forbes disease), resulting in abnormal glycogen structure and accumulation in tissues.

3. Phosphofructokinase: Deficiency of this enzyme is associated with GSD type VII (Tarui disease), leading to impaired glycolysis and energy production.

4. Phosphorylase Kinase: Deficiency of this enzyme is seen in GSD type IX, resulting in impaired activation of glycogen phosphorylase and glycogen breakdown.

5. Glucose-6-Phosphatase: Deficiency of this enzyme is characteristic of GSD type I (von Gierke disease), leading to impaired gluconeogenesis and glycogenolysis in the liver and kidneys.

6. Glycogen Synthase: Mutations in this enzyme are linked to GSD type 0, resulting in impaired glycogen synthesis.

These are some examples of the enzymes associated with specific types of glycogen storage diseases. Enzyme deficiencies in these metabolic pathways disrupt the normal storage, breakdown, or synthesis of glycogen, leading to various clinical manifestations depending on the type and severity of the GSD. Diagnosis of GSDs involves enzyme analysis, genetic testing, and clinical evaluations to confirm the specific subtype and guide treatment strategies, which may include dietary modifications, medications, and management of symptoms.

Genomics plays a crucial role in the field of inborn errors of metabolism (IEM) by helping to identify the underlying genetic causes of these disorders. Here are some key ways in which genomics contributes to the understanding and management of IEM:

1. Genetic Diagnosis: Genomic testing, such as whole exome sequencing (WES) or whole genome sequencing (WGS), can help identify the specific genetic mutations responsible for an individual's IEM. This information is important for confirming the diagnosis, understanding the inheritance pattern, and providing personalized treatment and management strategies.

2. Carrier Screening: Genomic testing can also be used for carrier screening to identify individuals who carry a genetic mutation for a specific IEM. This information is valuable for family planning and genetic counseling, as it can help assess the risk of passing on the condition to future generations.

3. New Gene Discovery: Advances in genomics have led to the discovery of new genes associated with IEM. By identifying novel genetic mutations, researchers can gain insights into the underlying mechanisms of these disorders and develop targeted therapies or interventions.

4. Pharmacogenomics: Genomic information can also be used to personalize treatment approaches for individuals with IEM. Pharmacogenomics studies how genetic variations influence an individual's response to medications, allowing healthcare providers to tailor drug therapies based on a patient's genetic profile.

5. Research and Precision Medicine: Genomics has opened up new avenues for research in IEM, enabling scientists to better understand the genetic basis of these disorders and develop innovative treatments. The concept of precision medicine, which aims to deliver personalized healthcare based on an individual's genetic makeup, is particularly relevant in the field of IEM.

Overall, genomics plays a critical role in advancing our understanding of inborn errors of metabolism, from diagnosis and treatment to research and personalized medicine. By harnessing the power of genomic technologies, healthcare providers and researchers can improve outcomes for individuals affected by IEM.

Metabolomics is another important area of study that plays a significant role in the field of inborn errors of metabolism (IEM). Metabolomics focuses on the comprehensive analysis of small molecules, known as metabolites, present in biological samples such as blood, urine, and tissues. Here are some key ways in which metabolomics contributes to the understanding and management of IEM:

1. Biomarker Discovery: Metabolomics can help identify specific metabolites or metabolic

profiles that are altered in individuals with IEM. These biomarkers can be used for diagnostic purposes, monitoring disease progression, and assessing treatment responses.

2. Pathophysiological Insights: By studying the metabolic changes associated with IEM, metabolomics can provide insights into the underlying biochemical pathways affected by genetic mutations. This information can help researchers better understand the pathophysiology of these disorders and develop targeted therapeutic interventions.

3. Nutritional Management: Metabolomics can also be used to evaluate the impact of dietary interventions on individuals with IEM. By analyzing changes in metabolite levels in response to dietary modifications, healthcare providers can tailor nutritional strategies to optimize metabolic function and improve clinical outcomes.

4. Personalized Medicine: Similar to genomics, metabolomics can contribute to the concept of personalized medicine in IEM. By profiling an individual's unique metabolic signature, healthcare providers can design personalized treatment plans that target specific metabolic abnormalities and optimize therapeutic outcomes.

5. Drug Development: Metabolomics can aid in the development of new therapies for IEM by identifying potential drug targets and assessing the efficacy of experimental treatments. By understanding how drugs impact the metabolic profile of individuals with IEM, researchers can develop more targeted and effective therapies.

Overall, metabolomics plays a crucial role in advancing our understanding of inborn errors of metabolism by providing valuable insights into metabolic pathways, biomarker discovery, personalized medicine, and drug development. By integrating metabolomic data with genomic and clinical information, healthcare providers and researchers can improve diagnosis, treatment, and management strategies for individuals with IEM.

The role of personalized nutrition in the control of endocrine disorders

Majid Ghayour-Mobarhan

Department of Nutrition, Faculty of medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

The role of diet in health and disease is well-established, with compelling evidence suggesting that a healthy lifestyle (including diet) can be more effective than pharmacy therapy in preventing disease in susceptible individuals. Despite general dietary and lifestyle advice being a common method to motivate people towards healthy choices, these recommendations have limited impact. Non-communicable diseases account for approximately 70% of all deaths worldwide, incurring high social and economic costs. Due to individual variability, a one-size-fits-all diet approach is ineffective for everyone.

A personalized diet is a strategy that utilizes individual information, genetics, and gut microbiome to provide customized nutritional recommendations, products, or services. This approach could help people achieve sustainable dietary behavior change, which is beneficial to health. Some studies on people with diabetes, cardiovascular diseases, and cancers have shown that personalized nutrition can have beneficial results in the treatment of diseases. However, no large-scale personalized nutrition study has been conducted in an appropriate population group over a sufficiently long time. Due to this reason, and the significance of lifestyle change for large sections of the population, other researchers recommend a universal, rather than targeted, approach to lifestyle intervention for disease prevention and treatment. More research is necessary to fully realize its potential.

Key words: *Personalized Nutrition, Diet, Genetics, Gut Microbiome*

Role of immunohistochemistry in the pathologic diagnosis and management of thyroid neoplasms

Mohammad Tavangar
Professor of Pathology
Endocrine pathology Fellowship
Department of Pathology, Shariati Hospital
Tehran University of Medical Sciences

Role of immunohistochemistry in the pathologic diagnosis and management of thyroid neoplasms

Thyroid carcinoma is the most common malignancy of endocrine organs and accounts for approximately 1% of all cancers.

Based on new WHO classification the neoplasms of the thyroid gland are stratified into the following main categories:

- Follicular cell-derived neoplasms
- C-cell derived neoplasms
- Mixed medullary and follicular cell derived neoplasms
- Salivary gland type carcinomas
- Thyroid tumors of uncertain histogenesis
- Thymic tumors within the thyroid
- Embryonal thyroid neoplasms.
- Even though the majority of thyroid neoplasms can be diagnosed on the basis of cellular and architectural features, difficulties in the diagnosis can occur due to overlapping histomorphologic features between primary and secondary thyroid neoplasms and partial or complete loss of differentiation

Immunohistochemistry (IHC) has proven to be helpful in the diagnosis of the following rare tumors:

- Mixed follicular and medullary thyroid carcinoma
- Salivary gland type carcinomas
- Tumors of uncertain histogenesis
- Intra-thyroidal thymic neoplasms .

There are three main reasons for the application

of immunocytochemistry in thyroid pathology:

- Determining cell and site of origin
- Differentiating benign from malignant neoplasms
- Influencing clinical management.

Determining cell and site of origin

Thyroid follicular cell lineage markers

Is the most specific marker of thyroid follicular cell derivation.

Normal thyrocytes show diffuse cytoplasmic staining by TG; this staining pattern is maintained in well-differentiated follicular-derived thyroid carcinomas, such as papillary thyroid carcinoma (PTC) and follicular thyroid arcinoma (FTC), and is completely absent in medullary thyroid carcinoma (MTC) and metastasis to the thyroid gland.

The use of TG FNA washout evaluation for regional and distant metastasis and the role of serum TG

measurement for the follow up of patients with thyroid

carcinomas.

Thyroid transcription factor 1

TTF-1 is diffusely expressed in PTC, FTC, high-grade follicular-derived non-anaplastic thyroid carcinoma and MTC.

TTF-1 expression is retained in less than 20% of ATCs. TTF-1 is expressed in more than 80% of lung adenocarcinomas, a subset of squamous cell carcinoma of pulmonary origin, small cell carcinoma, neuroendocrine carcinomas, and also rarely in adenocarcinoma of genitourinary and gastrointestinal tracts and breast.

TTF-1 can be useful in confirming the diagnosis of a thyroid primary lacking a well-differentiated growth pattern (papillary or follicular) or unusual cytology, such as poorly differentiated thyroid carcinoma.

PAX8

With IHC, its expression is seen in thyroid, renal, and urinary bladder neoplasms and malignancies of Mullerian origin, including ovarian primaries**.**

Gives a nuclear staining in normal and neoplastic thyrocytes, and usually maintains this expression pattern also in cases of high grade follicular-cell-derived carcinoma, anaplastic carcinoma, and its squamous subtype .

Parafollicular C-cell specific markers

Parafollicular C-cell specific markers

Medullary thyroid carcinoma (MTC) originates from

parafollicular C-cells of the thyroid gland. The C-cells mainly secrete calcitonin hormone, which plays a minor role in calcium metabolism compared with parathyroid hormone (PTH).

Most MTCs (>95%) secrete calcitonin and show patchy to diffuse cytoplasmic expression of this biomarker with IHC.

Owing to its architecture and cellular features, MTC can be difficult to distinguish from metastases to the thyroid from neuroendocrine carcinoma arising in other organs, especially the lung and gastrointestinal tracts .

It is well known that calcitonin is also expressed in other neuroendocrine tumors besides MTC.

MTC also shows cytoplasmic expression of

monoclonal carcinoembryonic antigen (mCEA), which can also serve as biomarker for disease surveillance in addition to calcitonin

Differentiating benign from malignant thyroid neoplasms

Most thyroid neoplasms are diagnosed based on architectural and cellular features and a lack or presence of invasive features.

In some instances, it may be difficult to distinguish between follicular adenoma and non-invasive follicular tumor with papillary-like nuclear features (NIFTP), an encapsulated follicular variant of papillary thyroid carcinoma, follicular carcinoma, and follicular adenoma with papillary architecture from papillary thyroid carcinoma.

The combination of HBME-1, GAL-3, and CK19 is by far the most common panel for distinguishing benign from malignant thyroid neoplasms, as no individual biomarker has sufficient sensitivity or specificity to accomplish this task.

Markers that influencing clinical management

- Ki67
- PDL1

Molecular immunohistochemistry

Modern immunohistochemistry has proven to be an easily practiced approach in the everyday practice of histopathology to triage advanced tumors for further mutation testing.

Specific IHC is available for BRAFV600E mutation, RASQ61R mutation, NTRK rearrangement, and ALK rearrangement. Of note, among the IHC for these altered proteins

derived from molecular changes, only IHC for BRAFV600E is approved to be of value in the clinical management of malignant thyroid neoplasms.

Conclusion

Currently, immunohistochemical and molecular analysis are integral to the diagnosis and management of thyroid neoplasms.

Accurate diagnosis and classification of thyroid tumors

according to the recent classification scheme can be achieved by employing specific immunostains in both histologic and cytologic specimens.

Reference:

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The association between the serum concentration of uric acid and Gestational diabetes

Mahdi Shadnoush

Tehran University of Medical Sciences, Tehran, Iran.

Gestational diabetes is one of the common complications in pregnancy, affecting approximately

14% of all pregnancies. It may be associated with adverse outcomes such as macrosomia, cesarean section, and neonatal hypoglycemia, manifested in both mothers and newborns. Additionally, it may be linked to disruptions in glucose metabolism in mothers and childhood obesity during later stages. Maternal obesity, older maternal age, and a family history of diabetes, among other conventional risk factors, have been identified for gestational diabetes. A novel risk factor suggested for this condition is elevated serum uric acid (hyperuricemia), considered a potential marker for predicting risks associated with pregnancy-related complications like GDM. Serum uric acid is the end product of purine metabolism, and its higher concentration can serve as an indicator for the pathological mechanisms of various diseases. Evidence suggests that alongside obesity, diabetes, hypertension, and dyslipidemia, serum uric acid should be recognized as a marker of the metabolic syndrome. Nevertheless, studies have shown that hyperuricemia can lead to endothelial dysfunction and insulin resistance. In normal pregnancy, serum uric acid levels decrease until the 20th week of gestation due to increased glomerular filtration and reduced reabsorption of uric acid from renal tubules, gradually returning to normal levels. However, hyperuricemia may also be implicated in the pathogenesis of GDM. Studies have shown that women with GDM have higher serum levels compared to healthy women. However, there is no consensus on the specific week of pregnancy when this hyperuricemia increases the risk of GDM. Substantial evidence suggests that elevated serum uric acid levels between weeks 13 and 18 of pregnancy are associated with an increased risk of GDM. A systematic review revealed that young pregnant women are more sensitive to the association between hyperuricemia and the risk of gestational diabetes compared to older women. Therefore, assessing uric acid levels before the

20th week of pregnancy could be a potential indicator for predicting the risk of gestational diabetes.

Various mechanisms may elucidate the association between serum uric acid and GDM. Uric acid can inhibit insulin signaling and directly induce insulin resistance. Additionally, it reduces nitric oxide production by endothelial cells, disrupting endothelial function. Since glucose uptake in some tissues relies on nitric oxide, the diminished induced nitric oxide by uric acid increases insulin resistance. On the other hand, hyperuricemia increases the production of free

radicals, which weakens insulin secretion. Moreover, studies have indicated that the use of uric acid- lowering medications such as benzbromarone or allopurinol enhances insulin sensitivity. Nevertheless, there is still a lack of studies to assess the effectiveness of these medications in women with GDM.

It should be noted that foods rich in purines increase the concentration of uric acid, and their high consumption is considered a potential risk factor for diseases such as gout. Purine-rich foods include organ meats, red meat, lentils, etc., and should be restricted in individuals with hyperuricemia. To date, there is no study examining whether high consumption of these foods during pregnancy increases the risk of GDM due to elevated uric acid. Additionally, it has not been investigated whether limiting the intake of these foods in women prone to GDM enhances insulin sensitivity. Therefore, there is a need for clinical studies to determine whether the consumption or restriction of these foods during pregnancy has an impact on the risk of GDM.