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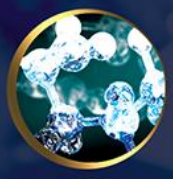
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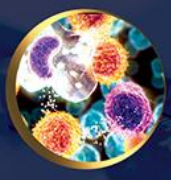
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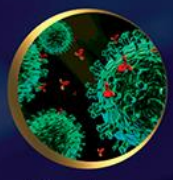
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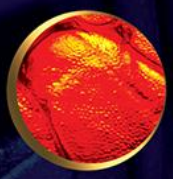
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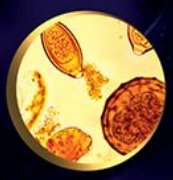
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Immunology Pannel

Name of Speaker: Dr. Saeid Abedian

Position of Speaker:

Immunogenetics Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

Title of Speaker:

HLA and HLA-typing in transplantation

Major histocompatibility complex antigens is most polymorphism genes in the human antigens.
The human leukocyte antigen (HLA) gene family is the human from of the major histocompatibility complex (MHC).In humans, the HLA is located on the short arm of chromosome 6 and including a large portion of DNA.
The dynamics, duration, and nature of immunity produced in the most immune response are clear and noticeable. HLA molecules have high polymorphisms in population that many factors have been linked to genetic mutations disrupting the regulatory lineage development. Reasons of HLA polymorphisms are point mutation, Gene conversion and infectious diseases. HLA molecules have key role in autoimmune diseases and immune response condition. Cell immunity response mechanisms depend to HLA molecules that these molecules are important key regulators of the immune defense to improve lymphocyte's response and saving immune homeostasis. -On the other hand, the regulation and development of lymphocytes cells are tightly modulated by several mechanisms such as HLA molecules. There are several methods for HLA typing such as serology, DNA-based Methods and SBT,
HLA molecules have high polymorphisms in population that many factors have been linked to genetic mutations disrupting the regulatory lineage development. Reasons of HLA polymorphisms are point mutation, Gene conversion and infectious diseases. In addition, HLA molecules have key role in autoimmune diseases and immune response condition.
Key words. HLA; HLA-typing; Transplantation

Immunology Pannel

Name of Speaker: Dr. Mozhgan Esmaeili

Position of Speaker:

Immunogenetics Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

Title of Speaker:

In The name of GOD

The human leukocyte antigen (HLA) is one of the most polymorphic genes in the human genetic system. Matching for HLA at the allele level is crucial for stem cell transplantation. There are several methods used for HLA typing tests, serological (micro-lymphocytotoxicity) and DNA-based methods, such as Sequence-specific primer (SSP) –PCR, Sequence-specific oligonucleotide probe (SSOP)-PCR, and sanger Sequence-based testing (SBT).

SBT is a high-resolution HLA typing method. In this method, the alleles are separated by group-specific amplification using low-resolution typing. Next, PCR Product is purified, and Sequencing determines the full nucleotide sequence of the alleles present.

Immunology Pannel

Name of Speaker: Dr. Pooria Gill

Position of Speaker:

Immunogenetics Research Center, Mazandaran University of Medical Sciences

Title of Speaker:

HLA-typing Nanodiagnostics

Using nanomaterials for molecular detection of biomarkers or cells were called "Nanodiagnostics". However, employing nanodiagnostic methods for molecular HLA-typing of cells were so-called HLA-typing nanodiagnostics. Using some binder molecules such as antibodies, aptamers, and aphibodies have been employed for nanomolecular detection of biomolecules. Gold nanoparticles were the most important nanomaterials for making nanoprobes in detection of biomarkers. Quantum dots were the most known nanomaterials that those have fluorescent. Diagnostic methods could be developed using nucleic acids or proteins. Nucleic acid-based diagnostics could be used RNA/DNA aptamers for detection of the ligands. Protein-based diagnostics could be employed antibodies or aphibodies for detection of biomarkers. Gold nanoparticle-conjugated antibodies rather than the enzyme-antibodies could be employed for colorimetric assay of antigens. Hence, design and development of antibody-based nanoprobes from gold nanoparticles are one of the most novel colorimetric nanodiagnostics of HLA molecules. Quantum dot probes have also been reported for fluorescent detection of PCR amplicons. Recently, a new NGS technology has been introduced based on a Short Range (SR) PCR using Nano and Microfluidic technologies for nanomolecular HLA-typing. Commercializing of these nanodiagnostics confirmed an important role of nanotechnology for high resolution typing of HLA molecules.

Immunology Pannel

Name of Speaker: Dr. Alireza Mardomi

Position of Speaker:

Immunogenetics Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Title of Speaker:

APPLICATION OF VIRTUAL CROSS MATCHING IN TRANSPLANTATION

Organ transplantation still stands as the gold-standard treatment for most end-stage organ failure diseases.
Iran always have had an increasing statistics regarding the transplanted organs either from live, deceased, and cadaveric donors except in COVID-19 pandemic that there was a global drop Transplantation statistics. The pre-transplant monitoring and matching of donor and recipient is of high importance even in low risk patients who are generally the mid-age or elderly patients without history of transfusion,
pregnancy, and previous transplantation.
This importance has roots in the considerable sensitization upon experiencing an unsuccessful transplantation.
Sensitization is a phenomenon in which the recipient contains allo-antibodies against a vast category of HLA molecules rendering them unsuitable candidates for the majority of available organs.
The cross-reaction of HLA molecules stands as the chief underlying mechanism for developing anti-HLA antibodies known as "donor-specific antibodies (DSAs)
The Pre-transplant tests stand as the main preparative tools for selecting proper donor and recipients
Besides to serologic and complement-dependent cytotoxicity (CDC) assays, novel approaches provide more precise comprehension on the immunologic status of the donor and recipient.
The routine tests for kidney transplantation include PCR based (SSP) assessment of the HLA haplotypes of donor and evaluation of panel-reactive antibody (PRA) in recipient in first step. In fact, PRA demonstrates the sensitivity of the patient in terms of the percentage of PRA antibody.
In high-risk patients the physical cross-match has indication too. This test could be conducted in CDC and flowcytometric platforms.

Immunology Pannel

Name of Speaker: Dr. Elham Hasdanzadeh

Position of Speaker:

Immunogenetics Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Title of Speaker:

The development of cell and tissue engineering therapy and combinational treatments

Spinal cord injury (SCI) is a central nervous system (CNS) devastate event that is commonly caused by traumatic or non-traumatic events. The reinnervation of spinal cord axons is hampered through a myriad of devices counting on the damaged myelin, inflammation, glial scar, and defective inhibitory molecules. Unfortunately, an effective treatment to completely repair SCI and improve functional recovery has not been found. In this regard, strategies such as using cells, biomaterials, biomolecules, and drugs have been reported to be effective for SCI recovery. Furthermore, recent advances in combinatorial treatments, which address various aspects of SCI pathophysiology, provide optimistic outcomes for spinal cord regeneration. According to the global importance of SCI, the goal of this article review is to provide an overview of the pathophysiology of SCI, with an emphasis on the latest modes of intervention and current advanced approaches for the treatment of SCI, in conjunction with an assessment of combinatorial approaches in preclinical and clinical trials. So, this article can give scientists and clinicians' clues to help them better understand how to construct preclinical and clinical studies that could lead to a breakthrough in spinal cord regeneration.

Immunology Pannel

Name of Speaker: Dr. Narjes Jafari

Position of Speaker:

Immunogenetics Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Title of Speaker:

MicroRNA in transplantation

Nowadays, although the use of powerful immunosuppressive therapies decreases the incidence of rejection in transplant recipients, there is a critical need for potent immunosuppressive agents for improvement of graft survival rates as well as noninvasive biomarkers for early diagnosis of graft injury and treatment response.

MicroRNAs (miRNAs, miRs) are regulatory non-coding RNAs (with ~ 22 nucleotides in length) which usually inhibit translation of target mRNAs. They are stable in tissues and different biological fluids and can be measured using cost-effective technologies. Several studies suggested the potential use of miRNAs as novel biomarkers for graft quality assessment and targets for therapy in transplantation. For instance, miR-142-3p, miR-886-3p, and miR-132 showed the predictive value for acute rejection in small-bowel transplant recipients. Potential use of miR-150-5p as biomarker to diagnose acute rejection in peripheral blood of kidney transplant patients has been reported. Circulating miR-181a-5p was suggested as a new biomarker for detection of acute cellular rejection in heart transplantation. Urinary miR-210 levels can serve as a novel biomarker for acute kidney rejection in transplant patients.

Collectively, further functional studies could help us to validate the miRNAs potential as reliable biomarkers and promising targets for therapy in transplantation.

Key words: MicroRNAs; Transplantation; Biomarker; Immunosuppressive agents

Immunology Pannel

Name of Speaker: Dr. Manizhe Faghih

Position of Speaker:

Department of Immunology, School of medicine, Mazandaran university of medical science

Title of Speaker:

Stem Cell Transplantation

Stem cells are found throughout the body and can be defined as a population of undifferentiated cells capable of indefinite self-renewal and generation of a functional progeny of highly specialized cells. Stem cells have different proliferative properties and functions depending on their physical location or tissue compartment. Cell-based therapy, especially stem cells, provides new hope for patients suffering from incurable diseases where treatment approaches focus on management of the disease not treat it. Stem cell-based therapy is an important branch of regenerative medicine with the ultimate goal of enhancing the body repair machinery via stimulation, modulation, and regulation of the endogenous stem cell population and/or replenishing the cell pool toward tissue homeostasis and regeneration.

Stem cells for cell-based therapy can be of (1) autologous, also known as self-to-self therapy, an approach using the patient's own cells, and (2) allogeneic sources, which use cells from a healthy donor for the treatment.

Stem cell-based therapy, including human pluripotent stem cells (hPSCs) and multipotent mesenchymal stem cells (MSCs), has recently emerged as a key player in regenerative medicine. MSCs are multipotent progenitor cells possessing self-renewal ability (limited in vitro) and differentiation potential into mesenchymal lineages, according to the International Society for Cell and Gene Therapy (ISCT). recent clinical applications indicated that either hPSCs or MSCs derived from bone marrow (BM), adipose tissue (AT), or the umbilical cord (UC) were used for the treatment of human diseases, including neurological disorders, pulmonary dysfunctions, metabolic/endocrine-related diseases, reproductive disorders, skin burns, and cardiovascular conditions.

Many researchers consider the transplantation of mesenchymal stem cells (MSCs) to be the most effective tool for cell therapy, due to the simultaneous activation of multiple mechanisms (paracrine, trophic, immunomodulatory, and differentiation), affecting all stages of the regeneration of damaged tissues. Bone marrow-derived MSCs

Immunology Pannel

Name of Speaker: Dr. Bahareh Hasani

Position of Speaker:

Immunogenetics Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Title of Speaker:

CROSS-DRESSING IN TRANSPLANTATION

MHC proteins were initially identified as the main antigens recognized in transplantation reactions

MHC genes are highly polymorphic. They code for a large family of cell-surface glycoproteins (MHC molecules) that bind peptide fragments of foreign proteins and present them to T cells to induce an immune responses. There are two classes of MHC, class I and class II Both classes of proteins share the task of presenting peptides on the surface of professional antigen-presenting cells (APCs) for recognition by T cells.Cells, in particular leukocytes, exchange cell surface MHC molecules and other glycoproteins, and intracellular components through mechanisms that have been named cross-dressing

MHC cross-dressing refers to the acquisition by leukocytes, in particular APCs, of foreign intact MHC molecules loaded with peptides. The transferred pMHCs must remain on the surface of the acceptor APC with the right topology, to be presented directly without further Ag processing to cognate T cells. The transferred pMHCs can be provided by cells from the same individual or not (i.e. allo- or xenogeneic MHC from grafts). Mechanisms of Cross dressing is trogocytosis, exosomes and tunneling nanotubes.

In most cases, trogocytosis in immune cells requires ligand–receptor interactions.TCR–MHC interaction is a well-characterized one that triggers trogocytosis. Upon stimulation of TCR on T cells by peptide–MHC complexes on APCs, an immunological synapse is formed between T cells and APCs. The formation of an immunological synapse results in the internalization of TCR and the transfer of peptide–MHC (pMHC) complexes, together with membrane fragments of APCs, onto the surface of T cells.

Biochemistry Pannel

Name of Speaker: Prof. Libin Yuan

Position of Speaker:

University of Toronto, Canada

Title of Speaker:

Inborn Errors of Sphingolipid Metabolism: Advanced Laboratory Diagnosis of Activator Protein Defects

Sphingolipids are essential components of cell membrane and named from its building block, a sphingoid base. Sphingoid base and its derivatives, ceramides, phosphosphingolipids and glycosphingolipids are common types of sphingolipids. Sphingolipids are degraded in the lysosomes by various specific lysosomal hydrolases. Genetics defects of the lysosomal hydrolases underlie a subgroup of lysosomal storage disorders, named sphingolipidoses.

Sphingolipid activator proteins (SAPs) are small glycoproteins assisting lysosomal degradation of sphingolipids by their respective hydrolases. Specifically, SAPs are required for the degradation of glycosphingolipids with short oligosaccharide chains. There are five known activator proteins: GM2 activator protein (GM2AP), saposin A (SAP A), saposin B (SAP B), saposin C (SAP C), and saposin D (SAP D). In addition, all four saposins have a common precursor protein, prosaposin (PSAP). The deficiencies of activator proteins and their precursor cause atypical sphingolipidoses, including GM2-gangliosidosis, Krabbe disease, metachromatic leukodystrophy and Gaucher disease.

Diagnoses of activator protein deficiencies are challenging, mainly because of the discrepancy between classic clinical symptoms and normal lysosomal hydrolase activities. In addition, saposin A and prosaposin deficiencies damage hydrolase activities. The laboratory findings mimic classic sphingolipidoses and, thus, can lead to misdiagnoses. Therefore, correlation with various laboratory investigations is required for the diagnoses of activator protein deficiencies.

Biochemistry Pannel

Name of Speaker: Dr. Jessie Cameron

Position of Speaker:

University of Toronto, Canada

Title of Speaker:

Approach to diagnosis of mitochondrial disorders

Mitochondrial Disease is a group of disorders affecting energy production in 1 in 5000 Canadian children. The symptoms are so variable that the spectrum covers simple exercise intolerance, mild or severe neuromuscular disease or neurodegenerative disease (Leigh Syndrome), cardiomyopathy, liver disease, nephropathy, autistic behaviour, Sudden Infant Death Syndrome and diabetes. Despite major advances in the understanding of these diseases in the past 30 years, less than 40% of children with suspected mitochondrial disease are given a definite genetic or biochemical cause for their problem. Therapies available usually involve dietary and nutritional intervention, coupled with administration of high doses of vitamins and cofactors.

Disease diagnosis is complicated by the fact that over 1000 nuclear genes encode mitochondrial proteins, as well as a number of crucial genes encoded by the mitochondria's own DNA. This DNA is inherited maternally, and is present as many copies in each cell, such that manifestation of disease phenotype can actually be variable in different tissues and between affected family members. For this reason, biochemical testing of enzyme activities in key energy-requiring tissues (such as muscle) is still a vital part of the mitochondrial diagnostic odyssey. The approach to diagnosis of mitochondrial disorders requires an integration of genetic, biochemical, pathological and clinical investigations.

In this talk I will introduce how these different disciplines can be integrated, and give an overview of biochemical enzyme testing carried out at The Hospital for Sick Children in Toronto, Canada.

At the conclusion of this session, participants will be able to:

1. Understand that mitochondrial disease can be caused by mutations in nuclear or mitochondrial DNA
2. Understand why clinical phenotypes are so variable in patients with mitochondrial disease: between tissues, with age, and between family members.
3. Understand how different disciplines can come together to diagnose mitochondrial disease
3. Understand what mitochondrial enzyme testing is offered at The Hospital for Sick Children, Toronto, Canada.

Biochemistry Pannel

Name of Speaker: Dr. Sarang Younesi

Position of Speaker:

Doctor of Clinical Laboratory Science (DCLS), SeniorTechnical Manager of Nilou Medical Laboratory

Title of Speaker:

Improve positive predictive value (PPV) rate in newborn metabolic screening program by using second-tier tests

Background

Nowadays, neonatal screening has become an essential part of routine newborn care in the world. This is a non-invasive evaluation that evaluated inborn errors of metabolisms (IEMs) using tandem mass spectrometry (LC-MS/MS) for the evaluation of the baby's risk of certain metabolic disorders.

Methods

This retrospective study was conducted on 39987 Iranian newborns who were referred to Nilou Medical Laboratory, Tehran, Iran, for newborn screening programs of IEMs. We incorporated second-tier tests and secondary biomarkers to improve positive predictive value (PPV).

Results

Statistical data were recorded via call interviewing in 6–8 months after their screening tests. The overall prevalence of IEM was 1:975. The mean age of all participants was 3.9 ± 1.1 days; 5.1% of participants were over 13 days and 7.7% were preterm or underweight. A total of 11384 (29.4%) of the cases were born in a consanguineous family. The type of delivery was the cesarean section in 8332 (51.3%) valid cases. The neonatal screening results had an overall negative predictive value (NPV) of 100% and the overall PPV of 40.2%. The false-positive rate was 0.15%.

Conclusion

This study showed a high incidence of metabolic disease due to a high rate of consanguineous marriages in Iran and indicated that incorporation of second-tier tests and secondary biomarkers improves PPV of neonatal screening programs.

Keywords: mass spectrometry, neonatal screening, second-tier biomarkers

Biochemistry Pannel

Name of Speaker: Dr. Maryam Razzaghy Azar

Position of Speaker:

Hazrat Aliasghar Children Hospital, Iran University of Medical Sciences

Title of Speaker:

Methanol accumulation due to alcohol dehydrogenase deficiency

Methanol is physiologically produced in human body but is efficiently metabolized and eliminated by alcohol dehydrogenase (ADH) enzyme. Physiologic levels of methanol in human body have been attributed mainly to the metabolism of pectin in fruits and vegetables and the metabolic activity of intestinal flora. In a healthy person, methanol is eventually omitted and kept at a low physiological level via different clearance mechanisms. The main pathway for methanol elimination from the body is via its oxidation to formaldehyde and then to formic acid, which are subsequently excreted in the urine or further oxidized to carbon dioxide. Increased concentration of methanol in human body, initially causes a narcotic effect. In methanol poisoning, toxicity is related to the production of toxic metabolites, formaldehyde and formic acid, primarily by ADH and then by aldehyde dehydrogenase.

ADH is an NAD-dependent enzyme, which is expressed primarily in the stomach and the liver. There are 7 different ADH's isoenzymes. ADH contains four zinc atoms, two of which are involved in the catalysis and the other two are necessary for the structural stability of the molecule.

Here we present A new entity of inborn error of methanol metabolism as a result of mutation in the gene of one of the ADH isoenzymes. This disorder was discovered in an 11.58 yr old boy. During 9-months hospital admission, he had periodic crises of 1-4-day coma and between attacks he was verbose and euphoric but had ataxia, dysarthria and drunken behavior. There was no organomegaly and organ damage in the liver, eyes, heart and brain by clinical and Paradinical investigations. All of the routine laboratory tests and metabolic workups were normal. Hemodialysis twice a week made him awake. Toxicological evaluation of his blood, showed high methanol level (12.2 mg/dL, normal range up to 3.5) while formaldehyde level was zero. Because of normal eyes and liver as well as zero formaldehyde level, insufficiency of alcohol dehydrogenase activity was suspected. Adding zinc to drug regimen 20 mg/daily, could completely eliminate methanol which reached to 0.1 mg/dL; speech and walking with drunken behavior became completely normal. Then zinc decreased to 15 mg/d as daily recommended allowance. Phenobarbital and probiotic which were first administered, were discontinued and it is about 5.5 year that he is normal. During this period, he became comatose and needed hemodialysis twice when he discontinued zinc by himself. Homozygous mutation in ADH1C gene located at exon 3 was found, and both parents were heterozygous for this mutation.

Conclusion: Insufficiency of alcohol dehydrogenase activity can result in accumulation of methanol without producing formaldehyde and formic acid and cause drunkenness, ataxia and sleep and if it is not recognized can result in convulsion and death due to its complications. This disorder can be easily managed by administration of zinc.

Biochemistry Pannel

Name of Speaker: Dr. Mohammad Abdi

Position of Speaker:

Department of Clinical Biochemistry, School of Medicine, Kurdistan University of Medical Sciences, Sanandaj-Iran

Title of Speaker:

Pre-analytical consideration in the laboratory measurement

Ammonia is produced from amino acids deamination during protein metabolism (1). The main source of circulating ammonia is the GI tract. Plasma ammonia concentration in the hepatic portal vein is five to ten-fold higher than that in the systemic circulation (2) and made from microbial metabolism, deamination of amino acids, nucleic acid degradation, and protein catabolism (3). Circulating ammonia is converted to urea in the hepatocytes through the urea cycle. Free ammonia is highly toxic; however, blood ammonia is remained in low level (3). Total blood ammonia has a direct correlation with the pH (2). In addition, ammonia freely passes from the blood–brain barrier where it combines with H+ to form ammonium and inhibits the transport of potassium across neuronal membranes (2). Therefore, hyperammonemia is a life-threatening state and its symptoms include lethargy, irritability, vomiting, and poor feeding in children, as well as hyperventilation, seizures, coma, and eventually death. The major causes of hyperammonemia are urea cycle disorders (defective or decreased urea cycle enzymes), liver failure (hepatocyte destruction and reduced urea cycle enzymes), drug reactions (e.g., inhibition of the urea cycle by valproic acid), hemolytic disease (release of ammonia from red blood cells), and gastrointestinal bleeds (increased ammonia generation due to microbial catabolism of hemoglobin) (4). Urea cycle disorders are inborn errors of metabolism that normally present with severe hyperammonemia in the first few weeks of life, although less severe forms can manifest at any age (5). Early diagnosis and treatment is important to avoid delays in mental development (2).

is two to three times higher than plasma; therefore, hemolysis should be avoided. The next main source of ammonia contamination is cigarette smoking by the patient and it is recommended that patients do not smoke for several hours before sampling (2). There are also some substances that can increase blood ammonia include ammonium salts, asparaginase, barbiturates, diuretics, ethanol, hyperalimentation, narcotic analgesics, and some other drugs. On the other hand, diphenhydramine, Lactobacillus acidophilus, lactulose, levodopa, and several antibiotics decrease values. The main approaches to measure ammonia in body fluids are enzymatic and chemical methods. Enzymatic assay is performed using glutamate dehydrogenase and is the most commonly used method. The accurate laboratory measurement of ammonia in plasma is complicated by its low concentration, instability, and pervasive contamination. For the enzymatic method, the reference interval is 15 to 45 µg/dL (11–32 µmol/L) (2).

Here, a 10-year-old girl presented with non-specific symptom and a very high plasma ammonia will be discussed in detail

Biochemistry Pannel

Name of Speaker: Dr. Mohammad Miryounesi

Position of Speaker:

Department of Medical Genetics, Shahid Beheshti University of Medical Sciences

Title of Speaker:

Glycine N-acyl transferase deficiency; biochemistry and mechanisms; diagnosis and treatment; genetic analysis and novel

Glycine is an important amino acid and has various roles in metabolism and normal cellular physiology. It acts as an inhibitory neurotransmitter similar to γ-aminobutyric acid in the central nervous system (CNS). It is also involved in the metabolism of numerous xenobiotics, especially benzoic acid. Therefore its compromised metabolism leads to several adverse effects on CNS, as well as liver. Glycine may also exert toxic effects on the kidneys due to the ensuing Hyperoxaluria. The balance between synthesis and degradation of glycine is an important factor in the prevention of hyperglycinemia and its devastating effects. One of the main mechanisms for maintaining the homeostasis of glycine is through the reaction catalyzed by glycine N-acyltransferase (GLYAT) enzyme. This enzyme also has an important role in the detoxification of endogenous and xenobiotic compounds, which contain a carboxylic acid group, particularly benzoic acid. Here we present for the first time a case of GLYAT enzyme deficiency sue to a mutation in its gene, and the management of the disease according to biochemical aberrations.

The patient was a 2 year-old-girl with complaint of walking and speech delay. Hyperglycinemia was first diagnosed with the administration of benzoic acid as the treatment of choice in hypergycinemia, which led to generalized seizure and deterioration of her condition. Whole exome sequencing (WES) was performed on the affected individual and identified a homozygous mutation (NM_201648.3: c.322C>T: p.Q108X) in the GLYAT gene. Sanger sequencing was performed to confirm the detected mutation. Treatment was designed according to biochemical abnormalities. After 6 months of treatment, the symptoms as well as walking and speaking improved.

Conclusions: The convergence of endocrinology and metabolism, clinical biochemistry and genetics evaluation led to the diagnosis and management of this novel disorder. The same setting is suggested for various cases of novel hereditary metabolic disorders.

Hormonology Pannel

Name of Speaker: Dr. Maryam Razzaghy-Azar

Position of Speaker:

Professor of Pediatrics and Pediatric Endocrinology and Metabolism, Iran University of Medical Sciences

Title of Speaker:

Congenital Adrenal Hyperplasia and Review of

Congenital adrenal hyperplasia (CAH) is a family of autosomal recessive disorders of cortisol and aldosterone biosynthesis. Cortisol deficiency increases secretion of corticotrophin (ACTH) which in turn leads to adrenocortical hyperplasia and overproduction of intermediate metabolites depending on the deficient enzymatic step. The most prevalent type of enzymatic defect is 21 hydroxylase deficiency (21-OHD) that is reported in more than 95% of the cases. According to the grade of deficiency there are three types of this disorder: classic salt wasting (SW), classic simple virilizing (SV) and non-classic (NC) forms. Clinical manifestations in classic SW form due to aldosterone and cortisol deficiencies are dehydration, poor feeding, failure to thrive, vomiting, lethargy and sometimes cyanosis and shock that begins at 10 – 14 days of life. Hyperpigmentation is caused by increased ACTH. Disorder of sex development development in female and pseudo precocious puberty with small testes in male during childhood are due to hyperandrogenism while acne, muscular hypertrophy and deepening of the voice occur later. Diagnostic laboratory tests include; low serum sodium, high serum potassium and high plasma renin activity (PRA), ACTH excess with high 17-OH Progesterone and androgen levels. In classic SV type there is no salt wasting but hyperandrogenism and virilization of genitalia exists. In NC type, genitalia is normal but premature adrenarche occur in childhood period and hirsutism and poly cystic ovary syndrome in adult females. In 11 hydroxylase deficiency (11-OHD), instead of salt wasting, hypokalemic hypertension exists although it may manifest by salt wasting in neonatal period and hypertension usually does not exist in the first year of life. 3 β-hydroxysteroid dehydrogenase (3β-HSD) converts pregnenolone to progesterone;
17-OHPregnenolone to 17-OHP and DHEA to androstenedione. So, in its deficiency, aldosterone is not synthesized and salt wasting occurs, DHEA is high but androstenedione and testosterone are low so there is under-virilization in male genitalia and no or low-grade ambiguity in female. In spite of this enzyme deficiency17-OHP is high due to periferal conversion of the precursor. Patients who have 17-hydroxylase deficiency(17-OHD) also have 17-20 lyase deficiency in gonad and at the age of puberty they do not have secondary sexual characteristics. Males have female genitalia without uterus and fallopian tubes. Their testes should be removed because of cancer risk. Females have normal genitalia. The patients have hypokalemic hypertension, high progesterone, low estradiol and testosterone, high follicle stimulating hormone (FSH) and luteinizing hormone (LH) at the age of puberty, low cortisol, high ACTH, high desoxycorticosterone (DOC), low PRA and normal aldosterone.
StAR deficiency or congenital lipoid adrenal heperplasia is a failure of transport of cholesterol from the outer to the inner mitochondrial membrane in steroidogenic tissues. StAR-independent cholesterol transport occurs only at a low rate. As a result, there is deficiency of all adrenal and gonadal hormones. The adrenal glands are often massively enlarged and full of lipid. StAR deficiency severely but incompletely abolishes pregnenolone synthesis. Cholesterol esters accumulate under the increased tone of ACTH stimulation. Consequently, the lipid accumulation worsens the dysfunction and leads to adrenal cell destruction.
There are salt-wasting manifestations in the neonatal period with low sodium, high potassium and

Hormonology Pannel

Name of Speaker: Dr. Mona Nourbakhsh

Position of Speaker:

Ali Asghar Children Hospital, Iran University of Medical Sciences

Title of Speaker:

Congenital hypothyroidismthe Patients

Congenital hypothyroidism (CH) is the most common endocrine disorder during the neonatal period. It occurs when the thyroid gland is unable to produce sufficient thyroid hormone at birth. The thyroid hormone is an important hormone essential for a fetus's development, especially since it plays a crucial role in the development of the brain, muscles, and skeletal system. The most common cause of CH is the absence of normal development of the thyroid gland (dysgenesis), i.e. complete absence of the thyroid gland (agenesis), reduction of the thyroid gland (hypogenesis), and displacement of the thyroid gland (ectopic). The second most common cause of CH is dyshormonogenesis, in which the various steps of thyroid hormone production or action are disturbed. CH may be due to maternal thyroid disease or medication, iodine deficiency or excess, and abnormalities of TSH production in the pituitary gland (secondary hypothyroidism). Infants with certain chromosomal abnormalities such as Down syndrome, Turner syndrome, or Wiliams syndrome are at risk for CH. Newborns may be normal at birth, and symptoms may develop later in life. Common symptoms include persistent jaundice, dry skin, cold extremities, large fontanel, large tongue, hypotonia, feeding difficulties, growth retardation, and constipation. CH can be diagnosed by newborn screening in the first 3 to 5 days of life using dried blood samples collected via skin puncture on the mound. Since primary hypothyroidism is ten times more common than secondary hypothyroidism, screening is done by TSH determination. The TSH cut-off value is varied according to birth weight and gestational age. According to the Iranian thyroid screening protocol, TSH > 5 mIU on filter papers is considered abnormal, and the baby is recalled for the second sample. The confirmatory test consists of measuring serum T4 and TSH. If hypothyroidism is diagnosed, treatment with levothyroxine (LT4) should be started immediately. In a proportion of patients, imaging by ultrasound or scintigraphy with or without perchlorate delivery may be required. To assess the severity of intrauterine hypothyroidism, the guidelines recommend radiography of the knee.

Hormonology Pannel

Name of Speaker: Dr. Majid Aminzadeh

Position of Speaker:

Pediatric Department, Ahvaz Children Medical Center, Ahvaz

Jundishapur University of Medical Sciences, Ahvaz, Iran

Title of Speaker:

Growth hormone disorders

Growth hormone-insulin like growth factor 1 axis (GH-IGF1 axis) is a collaboration of different organs and glands to control and induce physical growth. It begins with GHRH (growth hormone releasing hormone) produced by hypothalamus followed by GH (growth hormone) secreted by hypophysis and lasts with IGF1 (insulin like growth factor) made by liver. The last one acts on growth plates in bones to stimulate linear growth. Each product has negative feedback on the previous grand to control and prevent axis over activity.

Higher activities of GH-IGF1 Axis in a growing child can make an oversize tall adult (gigantism) but if this disorder happen in a person after fusion of epiphyseal plates it results in acromegaly.

Hypo-function of GH-IGF1 Axis in other hand, can be due to genetic disorders (congenital) or be acquired (begin in a healthy child). Genetic GH deficiency can be isolated (GHRH receptor, GH1, GH receptor) or be a part of multiple pituitary hormone deficiencies (POU1F1 (Pit1), PROP1, LHX3&4, HESX1, SOX2 . , .).

Some genetic disorders can happen in a collection of variable structural and phenotypical abnormalities like: septo-optic dysplasia, rieger syndrome, Hall-Pallister syndrome.

Few findings are also known as red flag indicating possible defect in pituitary function such as any mid-line defect like cleft lip and/or palate, umbilical hernia, micropenis, bifid epiglottis, imperforate anus ….

Finally acquired GH-IGF1 Axis insufficiency can occur in different processes like autoimmunity, malignancies, chemotherapy, radiotherapy, trauma, systemic chronic illnesses, malnutrition, anorexia nervosa, and even inappropriate psychosocial environment. Early diagnosis and treatment of each disorder and finding the other possible congenital dysfunctions can make a better outcome and even be lifesaving.

Hormonology Pannel

Name of Speaker: Dr. Hossein Babaahmadi-Rezaei

Position of Speaker:

Department of Clinical Biochemistry, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz

Title of Speaker:

Growth hormone disorders: laboratory evaluations

The main use of growth hormone measurement is to diagnose GH deficiency or GH over secretion. There are some problems to accurately measure GH, including: GH is a heterogeneous molecule and there are different isoforms in circulation. Human GH cluster contains five genes. (GH1, GH2, CS1, CS2 and CSL). GH1 is the main isoform secreted by pituitary gland and the molecular weight is 22 KD but also with missing 15 amino acids the 20 KD isoform also present in circulation. It is known that Physical activity, stress, and fasting are major effects on increased secretion 22KD isoform. Immunometric assay (sandwich assay) used excess antibodies against epitopes on GH. In the sandwich method, the polyclonal/monoclonal or polyclonal/polyclonal format detects more circulating GH forms than the monoclonal/monoclonal. Standard preparation and growth hormone binding proteins (GHBPs) are other challenging factors in GH measurement. Serum is the best sample and GH is stable for 24 hours at room temperature.

Virology Pannel

Name of Speaker: Dr. Soad Ghabeshi

Position of Speaker:

Virology Department, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Title of Speaker:

Lecture title: An overview of Maternal Viral infections

Over the past 20 years, we have gained in-depth knowledge of intrauterine infection and viral transmission pathways. This presentation will focus on human viruses that multiply in the placenta, infect the fetus and cause birth defects, and viruses that are important during pregnancy. On the other hand, some viruses are associated with pregnancy outcomes, fetal development, and maternal health. Since 1941, there have been reports that rubella virus (RV) infection during early pregnancy is associated with congenital disease. Today, the medical community knows that maternal infections can pass to the fetus and cause life-threatening illnesses. Viruses that cause congenital disease include rubella virus, varicella-zoster virus, parvovirus B19, human cytomegalovirus (CMV), Zika virus (ZIKV), and hepatitis E virus type 1 (HEV 1). Some viruses also infect newborns at birth, such as herpes simplex virus 1 and 2, human immunodeficiency virus, and hepatitis A-C virus. In addition to herpesviruses, human papillomaviruses HPV6, -11, -16, -18, and -31 can also infect extravillous trophoblasts. HPV16 and HPV62 were identified in chorionic villi at 12 weeks of gestation, and HPV16, -6, -83, and -39 were characterized in the placenta. Several other emerging viruses, such as the Ebola virus, Rift Valley fever virus (RVFV), and West Nile virus (WNV), may also threaten maternal and fetal health through underappreciated mechanisms. Basic research to develop effective antiviral treatments and vaccines without safety concerns in the pregnant population should be prioritized as a powerful weapon to fight the next epidemics and pandemics.

Virology Pannel

Name of Speaker: Dr. Hossein Keyvani

Position of Speaker:

Department of Virology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Title of Speaker:

Lecture title: Diagnostic methods for maternal viral hepatitis infections

In the definition of hepatitis, acute viral hepatitis was found to be the most common cause of jaundice in pregnancy. Maternal viral hepatitis is an important health problem in relation to the risk of pregnancy-related complications. Acute and chronic liver disease are also seen in both mothers and infants as a result of mother-to-child transmission (MTCT). What is needed, therefore, is a comprehensive and multidisciplinary approach to the management of viral hepatitis during pregnancy.

Hepatitis A virus (HAV) usually has little effect on pregnancy. Acute disease tests include serum anti-HAV immunoglobulin M (IgM) antibodies. Also, RT-PCR is used for detecting the hepatitis A virus RNA.

In treating HBV, the World Health Organization recommends reducing an infant's hepatitis B surface antigen (HBsAg) to 0.1% to eliminate hepatitis B virus (HBV) as a public threat by 2030. Prevention of MTCT is therefore an important step in an elimination strategy. Serological tests for detecting HBV infection consist of Surface antigen (HbsAg) and antibodies (Anti-HBs), Core antigen (HBsAg) and antibodies (anti-HBc), and "e" or pre-core antigen (HBeAg) and antibodies (anti-HBe). Also, PCR is used for detecting HBV DNA. There is a small chance (2.27 %) of developing fulminant hepatitis with Hepatitis D infection during pregnancy. Pregnancy outcomes do not seem to be affected by HBV/HDV infections, and vertical transmission of HBV is more likely to happen in women with high levels of HBV DNA.

Hepatitis E virus (HEV) infection rates are much higher in developing countries such as Southeast Asia than in developed countries such as the United States and Europe. Although the risk of fulminant hepatitis and acute liver failure (ALF) in HEV increases during the second and third trimesters of pregnancy, during pregnancy an acute disease is usually asymptomatic and self-limiting.

Virology Pannel

Name of Speaker: Dr. Ahmad Piroozmand

Position of Speaker:

Department of Microbiology and Immunobiology and Autoimmune Diseases Research Center, Kashan University of Medical Sciences, Iran

Title of Speaker:

Lecture title: Diagnosis of HSV infection in pregnancy

Viruses are one of the factors that cause dangerous consequences for pregnant women during pregnancy for mother and fetus and after delivery. Herpes virus infection, which exists in two main types, HSV-1 and HSV-2, is one of the most common sexually transmitted infections. The risk of transmitting this virus to the fetus has become a health concern. During pregnancy, the risk of transmission of herpes virus to the fetus is not very common, but the most transmission of this virus is in the third trimester and before delivery. Intrauterine transmission of the virus is highest in the first 20 weeks, leading to miscarriages, stillbirths, and congenital malformations in babies who survive. Fetal and neonatal complications caused by the transmission of this disease are mostly in the first three months of pregnancy, which include the death of the mother and the fetus. The infant infections (most often caused by HSV-2) are rare, but can be quite serious or even fatal. In 85 % to 90% of neonatal HSV, HSV lesions are acquired at the time of delivery and 5 and to 10% result from early postnatal viral acquisition. Caesarean section is recommended instead of natural delivery for people who have genital symptoms at the time of delivery. Infants born to seronegative mothers with primary genital HSV-2 infection are at greater risk than infants born to seropositive mothers with recurrent primary genital herpes infection (especially in late pregnancy).

Herpes serology is not helpful in determining whether a cesarean delivery should be performed in a mother with probable herpes lesions. Also, herpes serology is not helpful in diagnosing very weak babies suspected of having congenital herpes. In this case, virus culture and PCR are preferred, but the treatment should not be delayed until the test results are ready. In general, the most valuable application of serotyping methods will be the determination of HSV-2 specific antibody in pregnant women to predict the risk of transmission to the newborn. All suspected herpes virus infections should be confirmed through (1) viral detection techniques - Direct methods and (2) antibody detection techniques- Indirect methods. Thus, a positive genital culture provides conclusive evidence of genital HSV infection; however, a negative result does not exclude the presence of infection. Herpes infections Classify to Primary Infection,Non-primary first occurrence ,and Recurrent infection. Primary HSV infection can be differentiated from the first non-primary episode by observing the positive viral detection and the negative second-generation serological test.

Virology Pannel

Name of Speaker: Dr. Niloofar Neisi

Position of Speaker:
Infectious and Tropical Diseases Research Center, Health Research Institute, Department of Medical Virology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Title of Speaker:

Lecture title: Laboratory tests in congenital CMV

Cytomegalovirus (CMV) is a double-stranded DNA virus and belongs to Herpesviridae family. CMV is also a major cause of morbidity and occasional mortality in neonates. cCMV (congenital CMV) contributes to a high burden of disease and is the leading non-genetic cause of sensorineural hearing loss (SNLH) and an important cause of neurodevelopmental disabilities in children. Intrauterine CMV transmission may occur as primary infection or non-primary infection. The risk of congenital infection is approximately 40% in babies born to mothers who acquire a primary (initial) CMV infection. The established link between primary CMV infection during pregnancy and congenital infection makes identification of primary CMV infection an important goal in maternal and neonatal health care. 95% of pregnant women with primary CMV infection are asymptomatic. The majority of cCMV-infected children are born to CMV IgG-seropositive women (non-primary maternal infection). Primary maternal infections can be identified by serologic testing using IgG and IgM serology: IgG avidity testing should be used only if CMV-specific IgM antibodies are positive. CMV IgG avidity is better than CMV IgM for identifying primary CMV infection. Following primary CMV infection, IgG antibodies have low binding strength (low avidity) then over 2-4 months mature to high binding strength (high avidity). A challenge for the clinician may be the discovery of low levels of CMV-IgG antibodies in maternal serum samples in the absence of IgM because this may be due to a true positive or a false-positive result. Amniocentesis to perform PCR for CMV DNA is the best available prenatal diagnostic tool since the infected fetus excretes urine containing the virus into the amniotic fluid. Virus isolation by culture from urine or saliva has long been the standard method for diagnosing cCMV infection. RT-PCR analysis on DBS (Dried-blood-spot) had low sensitivity for identifying newborns with cCMV infection since up to 80% of infants with congenital CMV infections could be missed; therefore, it could not be recommended as a mass screening tool for the diagnosis of cCMV.

Virology Pannel

Name of Speaker: Dr. Alireza Tahamtan

Position of Speaker:

Department of Microbiology, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

Title of Speaker:

Lecture title: Rubella, diagnosis and laboratory investigations

Rubella is generally a mild and self-limited disease in children. During pregnancy, rubella can have potentially devastating effects on the developing fetus. Generally, clinical diagnosis of rubella is unreliable because the clinical manifestations can be mild and non-specific especially in young children. In addition, there are many other viral infections having similar clinical features. Laboratory confirmation of rubella virus infection is therefore essential. The diagnosis of a recent postnatal rubella infection can be based on a positive serological test for rubella-specific IgM antibody in a single sample or a four-fold or greater increase in rubella-specific IgG titres between acute and convalescent sera drawn 2 to 3 weeks apart. Among all the serologic tests available, ELISA are most commonly used to measure rubella-specific IgG and IgM because they are very sensitive, highly specific, technically easy to perform, rapid, and relatively inexpensive.

Virology Pannel

Name of Speaker: Dr. Leila Mousavizadeh

Position of Speaker:

Department of Virology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Title of Speaker:

Lecture title: CRISPR-Based Diagnosis of Maternal Viral Infections

CRISPR (pronounced "crisper") stands for Clustered Regularly Interspaced Short Palindromic Repeats which containing diverse among the different species of archaea and bacteria as a component of prokaryotic adaptive immunity and enables prokaryotes to target any foreign DNA and then destroy it. The CRISPR-Cas9 system consists of two key molecules that introduce a change (mutation) into the DNA; CRISPR-associated (Cas) nuclease (endonuclease activity) and a piece of RNA (guide RNA or gRNA). CRISPR has capacity in a variety of applications related to Genome editing and genetic engineering. Some application such as treating genetic causes of disease, diagnostic of DNA or RNA pathogens. The mechanism of CRISPR system is to use its trans-activating crispr RNA (tracrRNA) and crispr RNA (crRNA) in order to recognize specific site of DNA target and by its endonuclease domains cleaves both DNA strands three bases upstream of the protospacer-adjacent motif (PAM) sequence. The final step would be to repair the double-strand break (DSB) in DNA either by a homology directed repair (HDR) pathway or by non-homologous end joining (NHEJ). The most widely explored area for CRISPR-based diagnostic systems is within the field of viral infection. Methods has been developed based on the CRISPR-Cas12a and Cas13a families, dubbed DETECTR and SHERLOCK, respectively. Once bound to its viral genetic target, a single-stranded DNA molecule bound to a quencher molecule and a reporter fluorophore are cleaved indiscriminately by the Cas12a enzyme. This "collateral" cleavage is detected as a fluorescent signal released from the fluorophore and quencher. SHERLOCK and DETECTR are so sensitive that they are capable of single copy viral detection. They are rapid and do not require expensive thermal cyclers. Viruses such as Ebola, Zika, Dengue, SARS-CoV-2, HCV, CMV, and HBV has been detected by CRISPR CaS system.

Mycology Pannel

Name of Speaker: Dr. Abdolmajid Fata

Position of Speaker:

Dept. Parasitology & Mycology, Mashhad University of Medical Sciences, Mashhad, Iran

Title of Speaker:

Clinical and Paradinical differences between Actinomycetoma and Actinomycosis

Actinomycetoma & Actinomycosis are two different diseases which caused by Actinomycetes.

The Actinomycetes genera which are responsible to cause Actinomycetoma are Nocrdia spp. Actinomadura spp., Streptomyces spp. and rarely Actinomyces spp. but the only cause of Actinomycosis is A. israelii. Actinomycosis can be seen in 4 different clinical forms, named cervico-facial (62%), abdominal (20%), thoracic (15%) and urogenital (3%). The latter clinical Form is only observed in adult females.

The skin lesions of actinomycetoma are mostly observed on foot, in which fistules produce granules in different colors: white, yellow, pink, red, brown, while in actinomycosis, the granules are yellow in color, known on sulfur granules.

To differentiate Actinomycosis from actinomycetoma, it is necessary to pay attention on clinical presentation the result of culture. Histopathology Direct microscopy are not always perfect Tests.

The routes of treatment &type of medicines used in the latter diseases are also different. Discussion about the difference between actinomycetoma and actinomycosis in Mycology session will answer the questions.

Hematology Pannel

Name of Speaker: Dr. Soudabeh Hosseini

Position of Speaker:

Doctoral of cilinical Laboratory medicine, Hematology laboratory director at Aliasghar childeren Hospital

Title of Speaker:

WHO dassification of Myeloid Neoplasm, 5th edition AML with defining genetic abnormalities mutation

The classification of AML in now days is revolutionized in to more risk stratification AML classification integration of clinical, molecular/genetic, and risk stratification and best patient management

In this classification the separation of AML with defining genetic abnormalities from AML defined by differentiation is more obvious Acute myeloid leukemia with defining genetic abnormalities are PML::RARA RUNX1::RUNX1T1 , CBFB::MYH11 ' DEK::NUP214 , RBM15::MRTFA ,BCR::ABL1 ,(KMT2A , Another key change is this classification is the elimination of the 20% blast cutoff for AML with defining genetic abnormalities (with the exception of AML with BCR::ABL1 fusion and AML with CEBPA mutation). The third component of the new classification is the introduction of a section on AML with other defined genetic alterations, which could be a platform for uncommon AML subtypes which might be defined in the future editions of Who classification .

According to WHO B-lymphoblastic leukemia/lymphoma 2022 classification, chromosomal translocations (BCR::ABL1,ETV6::RUNX1, , TCF3::PBX1, TCF3::HLF ,IGH::IL3, KMT2A rearranged) as well as aberrations in chromosome number such as high hyperdiploidy (HeH) and Hypoploidy have refined the conventional risk stratification guidelines in pediatric BCP-All . in this classification ETV6::RUNX1,High hyperdiploidy, and ETV6::RUNX1(ER) like have been considered to have favorable outcome but BCR::ABL1, KMT2A rearranged ,Hypodiploidy, and iAMP21 ,TCF3::HLF and BCR::ABL like entity are considered as high risk subgroup with poor outcome if treated with standard risk protocols. another subtype named "B-ALL with other defined genetic abnormalities "have been also further classified to BCP_ALL with DUX4 , MEF2D , ZNF384 or NUTM1 rearrangements, IG::MYC fusion , and PAX5alt ,PAX5 p.P80R aberrancies which could give a more refined risk stratification guideline when incorporated in to the cytogenetic subtypes

Hematology Pannel

Name of Speaker: Prof. Amir Ali Hamidieh

Position of Speaker:

Pediatric Cell & Gene Therapy Research Center, Gene, Cell & Tissue Research Institute, Tehran University of Medical Sciences

Title of Speaker:

History of HLA Registry in Iran

Hematopoietic stem cell transplantation (HSCT) has been done for 32 years in Iran as a curative treatment but up to 12 years ago except autologous HSCT and sibling donors no other types of HSCT have been done. However, more than two decades ago, more than 70 percent of allogenic HSCT in the would have been done form unrelated donors.

That's why we stablished first HLA Registry in Middle East and Eastern Mediterranean Region in 2007 by proposal presentation to Tehran University of Medical Sciences.

After that, The HLA Registry and its establishment became as important as HSCT ward establishment and the importance of issue became clear for Ministry of Health and Medical Universities so that more than 13 centers of HLA Registry and 3 Cord Blood Bank with more than 92000 donors and cord blood are providing services to patients in Iran.

On the other hand, as everyone knows if all the population of the country being the HLA registry member, compatible donor for 100 percent of patient will not be found. To solve the problem, World Marrow Donor Association (WMDA) is established to exchange donor information since 30 years ago and we have succeeded in connecting Iran to WMDA since 2010. What happen these years' Iranian national stem cell donor network (INSCDN) was stablished in Iran that caused whole donor registry information are accessible in network and are recorded in WMDA uniquitly.

In laboratory context, Education and Research in HLA Typing and HLA Matching are needed and The significance of Immunogenetic issue in HSCT is undeniable. HLA Typing is first lab test for referred patients to HSCT ward to determine match donor. HLA system as most complicated histocompatibility system with three class and 12 loci has most important point in HSCT and organ transplantation.

Finding match donor decreases complications after HSCT and on the contrary overall survival will increase. Up to now more than 35000 alleles of HLA have been defined and because of allele ambiguity, HLA Typing is really difficult test to analysis. so Experienced technician is main part of accurate results. Quality control as a guaranty of quality assurance is another important part of determining accuracy in this test. So external control has vital role in this process.

Hematology Pannel

Name of Speaker: Prof. Nakysa Hooman

Position of Speaker:

Professor of Pediatric

Title of Speaker:

Thrombotic microangiopathy in children

Clinical and laboratory criteria of hemolytic uremic syndrome are microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury. Clinical and pathological manifestation diagnosed as thrombotic microangiopathy (TMA).
The pooled prevalence is 28% (95% CI: 15 to 44) and 18.38 pmp (0.55 pmp/y) in Iran. In children less than 15 years, the prevalence is 79.82 pmp (2.41 pmp/y). TMAs classified as secondary, and primary forms can occur in multiple clinical settings.
A study of complement in all TMA patients, immediately after diagnosis and before any specific treatment is suggested. Genetic study should be done in case of suspicious. A study in Iran revealed the assessment of complement regulatory factors revealed that the B and H factors levels were normal except in two cases but the level of factor I was higher than normal.

The management is directed to the underlying disease, stop causative medication, in case of complement dysregulation infusion of FFP or plasma exchange and ecluzimab help to maintain remission.

Question:
What are the laboratory criteria for TMA?
Low hemoglobuin
Low platelet
Increase serum creatinin
All of the above

What is the pooled prevalence of HUS in Iran?
8%
18%
28%
48%

Hematology Pannel

Name of Speaker: Dr. Akbar Dorgalaleh

Position of Speaker:

Specialized doctorate (Ph.D) in laboratory hematology and blood bank (laboratory hematology and blood bank)

Title of Speaker:

Diagnosis of Factor XIII Deficiency

Factor XIII deficiency is one of the rarest hemorrhagic disorders with an estimated incidence of one per 2,000,000 in the general population. Because of the autosomal recessive pattern of inheritance, the disease is more common in areas with a high rate of consanguineous marriages. Deficiency of factor XIII is associated with a high rate of life-threatening hemorrhage such as umbilical cord bleeding, intracranial hemorrhage, and recurrent miscarriage. Primary prophylaxis is mandatory for all patients with severe factor XIII deficiency (FXIII:C < 5%) from the time of diagnosis. Diagnosis can be made on the basis of family history, clinical presentation and appropriate laboratory tests. Umbilical cord bleeding is a hallmark of the disorder and can be seen in approximately 80% of patients. ICH is another manifestation of the disorder that is more common in factor XIII deficiency than in any other congenital bleeding disorder. Because of the inheritance pattern of the disorder, a positive family history is a strong diagnostic clue. Although the clot solubility test is the most common diagnostic test, it is not further recommended by experts for the diagnosis of factor XIII deficiency. According to the Scientific Committee on Fibrinogen and Factor XIII of the International Society of Thrombosis and Hemostasis, the factor XIII function test should be used as the initial screening test. The factor XIII -Ag assay should be used to classify the disorder and molecular testing should be used for confirmation. Factor XIII function test can be performed based on two principles: Amino incorporation and ammonia release assays. Although amine incorporation assays are highly sensitive, they are time-consuming, poorly standardized, and cumbersome and cannot be used for routine clinical laboratory testing. Ammonia release assays, on the other hand, are easy to perform and can be automated. To confirm the disorder, the F13A gene should be sequenced, and if there is no mutation in this gene, full sequencing of the F13B gene should be performed.

Keywords: Factor XIII deficiency, intracranial hemorrhage, rare bleeding disorders, morbidity and mortality

Parasitology Pannel

Name of Speaker: Dr. Mohammad Taghi Ahady

Position of Speaker:

Department of Biology, Ardabil Branch, Islamic Azad University, Ardabil, Iran

Title of Speaker:

Relationship Between Chronic Toxoplasmosis And Migraine

Introduction: More than 500 million people worldwide are infected with Toxoplasma gondii. This parasite is an obligatory intracellular protozoan that causes acute and chronic toxoplasmosis among intermediate hosts including human. The infection of this parasite could lead to death and stillbirth among immune-deficient hosts and pregnant women, respectively. On the other hand, migraine is known as the most common pain syndrome. It may occur with symptoms such as nausea, vomiting, or sensitivity to light and sound. The aim of this study was to detect anti-Toxoplasma gondii IgG in the serum of individuals with and without migraine.

Methods: Fifty person (7male & 43female, in the age range of 20-60 years) with history and symptoms of migraine (case group), and 50 individuals (7male & 43female, in the age range of 20-60 years) without migraine (control group) were selected randomly. Blood samples (5 ml) were collected from all the selected people, and the serum level of anti-Toxoplasma gondii IgG were determined using Enzyme-Linked Immunosorbent Assay (ELISA) technique. In this test, 10 IU/ml of anti-Toxoplasma gondii IgG was considered as the minimum titer.

Results: 38% of the individuals with migraine (case group) and 32% of the people without migraine (control group) had anti-Toxoplasma gondii IgG above 10 IU/ml. The mean amount of anti-T. gondii IgG in the serums of case group was 173.42 IU/m (table 1), while it was 68.25 IU/ml in control group (table 2), the mean amount of Toxo-IgG in migraine positive group was 2.5 time higher than the amount in the control group.

Conclusion: We concluded that the mean serum concentration of anti-Toxoplasma gondii IgG among the individuals with migraine was significantly higher than the individuals without migraine (sig= 0.026, $p<0.05$). Therefore, we recommend that the patients disordered with migraine be tested for toxoplasmosis.

Keywords: Antibody IgG, Toxoplasma gondii, Chronic toxoplasmosis, Migraine, ELISA

Code of ethics: IR.IAO.ARDABIL.REC.1396-12

Parasitology Pannel

Name of Speaker: Dr. Mehdi Mohebali

Position of Speaker:

Full professor of Medical Parasitology and Mycology Department , School of Public Health, Tehran University of Medical sciences, Tehran, Iran

Title of Speaker:

Diagnostic methods for human cutaneous and visceral leishmaniasis in Iran

Leishmaniasis is one of the most important neglected tropical disease (NTD) that is endemic in at least 92 countries of the World with more than one milliard people at risk. Ninteen provinces of Iran are endemic areas of cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL). Almost 15000- 20000 new cases of CL and 50-100 new cases of VL are reported in Iran annually.
Currently, For the diagnosis of human CL and VL, the following methods are used:

1. Parasitological methods:
Parasitological methods including microscopy and culture are gold standard for the diagnosis of CL and VL. Referring to our recent study, sensitivity rate of microscopic examination for the diagnosis of CL was calculated 89% and its specificity rate was 74%. The sensitivity rate of microscopic diagnosis of VL was calculated 72%.

2. Immunodiagnostic methods:
Immunodiagnostic methods are divided to Leishmanin skin test (LST) and serological tests.
- Leishmanin skin test (LST):
LST is a delayed type hypersensitivity (DTH) that is favorable test for the diagnosis of chronic forms of CL (i.e.Lupoid forms) as well as mucocutaneous leishmaniasis(MCL) but it is not appropriate test for the diagnosis CL and VL.
- Serological tests:
Serological tests are usually used for the diagnosis of VL and MCL that are included on:
Ags detection:
For Leishmania Ag detection, a commercial Ag detection test was introduced named KATex®. KAtext® is used for the diagnosis VL among immunocompromized individuals with favorable results.

Abs detection:
The serological tests which are currently used for the diagnosis of VL containing IF-A,ELISA,DAT and Dipstick rK39. Among these serological test, DAT with high sensitivity (96%) and specificity(95%), high reproducibility and simplicity and also Dipstick rK39 as a validated rapid test are the most predominant serological tests for the diagnosis human VL in Iran.
3. Molecular methods:
Since molecular methods are expensive and need to sophisticated equipments and materials thus, these tests usually applied for Leishmania species and strain identification, genetic resistance of Leishmania species against anti-Leishmania drugs and final diagnosis of chronic and complicated forms of CL and VL.
In this lecture, advantages and disadvantages of above diagnostic methods will be discussed.

Keywords: Cutaneous leishmaniasis,Visceral leishmaniasis,Diagnosis, Human,Iran

Parasitology Pannel

Name of Speaker: Dr. Soheila Nankali

Position of Speaker:

Obgyn, University of North Central at Sandiego CA, USA

Title of Speaker:

Toxoplasmosis and Effects on Abortion, And Fetal Abnormalities

The placenta is an immune-privileged organ that may tolerate antigen exposure without eliciting a strong inflammatory response that could result in an abortion. After that, the pregnancy can progress normally. Th1 answers, characterized by interferon-, are essential for suppressing intracellular infections. Therefore, the maternal immune system finds a catch-22 when intracellular parasites invade the placenta. The pro-inflammatory response required to eradicate the virus carries the danger of causing an abortion. Toxoplasma is a potent parasite that causes lifetime infections and is a leading cause of abortions in people and animals. This paper speculates that the pregnancy outcome may be affected by the Toxoplasma strain and the effectors of the parasite, both of which can modify the signaling pathways of the host cell.

Parasitology Pannel

Name of Speaker: Dr. Alireza Sazmand

Position of Speaker:

Department of Pathobiology, Faculty of Veterinary Sciences, Bu-Ali Sina University, Hamedan, Iran

Title of Speaker:

Atypical human infections by animal trypanosomes (a-HT) with focus on Trypanosoma evansi

Trypanosomes are protozoan parasites that infect mammals, including humans, birds, reptile, amphibians and fishes worldwide. They are most often transmitted by blood-sucking arthropods but also per oral, vertically and through coitus.

The typical pathogenic human trypanosomoses are sleeping sickness, or human African trypanosomosis (HAT), and the Latin American Chagas disease. HAT is mainly confined to tse-tse fly belt of sub-Saharan Africa, caused by two subspecies of trypanosomes: T. brucei gambiense (a primarily anthroponotic disease form that accounts for 98% of HAT case) and T. b. rhodesiense (an acute disease form representing 2% of HAT cases). Chagas disease, caused by T. cruzi, is transmitted via feces of triatomine bugs but also orally, congenitally, and iatrogenically especially via blood transfusion and organ transplantation. The disease is endemic in Latin America and in most cases is chronic and asymptomatic. In addition to these species, T. rangeli is also a human infective species, although considered nonpathogenic.

Climatic change, deforestation, globalization, trade agreements, close association and genetic selection in links with environmental, vector, reservoir and potential susceptible hosts' parameters have led to emergence of "atypical human infections by animal trypanosomes" (a-HT) all of which are animal pathogens. So far, human infections with T. vivax, T. congolense, T. b. brucei, T. evansi and T. lewisi or T. lewisi-like have been reported. Among these, a growing number of human cases with T. evansi infections are being reported particularly in Asia.

Trypanosoma evansi, the causative agent of 'surra' kills thousands of animals every year and causes significant animal morbidity and loss of productivity. T. evansi originated from Trypanosoma brucei through deletion of the maxicircle kinetoplast DNA which conferred the capacity for mechanical transmission by flies and allowed T. evansi to expand beyond the tsetse belt. Presently, it is the most widely distributed pathogenic trypanosome in Africa, Asia, and Latin America, but its potential for geographical extension is not limited, as shown by sporadic

cases in Spain and France. Human cases of T. evansi infection have been reported from India, Vietnam, Sri Lanka, Egypt and Thailand. For a decade it was hypothesized that human susceptibility to T. evansi could be linked to insufficient or missing levels of human trypanocide apolipoprotein L1 (APOL1), a trypanocidal component of normal human serum. However, a report of infection in a Vietnamese patient in 2016 with no previous immunological risk, 2 wild-type APOL1 alleles and a normal serum APOL1 concentration suggested that T. evansi is a true zoonosis with a risk of infection for the general population. Clinical presentation among humans is quite similar to the first stage of the chronic form of human sleeping sickness caused by T. brucei.
Diagnosis of T. evansi is typically made by detection of parasites in blood however, this method has low sensitivity when the parasites are few in number or absent in blood while present in the nervous system. Epidemiological surveys in Indian and Indonesian populations using the Card Agglutination Test for Trypanosomosis/Trypanosoma evansi (CATT/T. evansi), enzyme-linked immunosorbent assay (ELISA) and PCR targeting VSG (variant surface glycoprotein) gene demonstrated previous and/or active T. evansi infections in examined individuals.
In this presentation, reported a-HT cases with focus on Trypanosoma evansi infection are discussed.

Keywords: atypical human trypanosomosis, diagnosis, human African trypanosomosis, One Health, Trypanosoma evansi, surra, zoonosis

Parasitology Pannel

Name of Speaker: Dr. Bibi Razieh Hosseini Farash
Position of Speaker:
Department of Parasitology and Mycology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Title of Speaker:
Lophomonas blattarum: an emerging protozoan causing respiratory infection

Lophomonas blattarum is a flagellate protozoan parasite as a commensal in the gut of cockroach reservoirs. The primary reports have been started since 1990s from patients' republic of China about its probable role in bronchopulmonary disorders, and followed by many reports from some other countries as well. The gold standard of diagnosis of this protozoan is observation of the motile flagella in the direct smear. However, some scientists believe that bronchial ciliated epithelial cells have been misdiagnosed as L. blattarum. Molecular method is an aid in clearing the controversy. Although, it has recently been employed and more papers is needed for its validation. Biology, epidemiology, clinical manifestations, laboratory diagnosis, and the treatment aspects of the parasite are the subjects will be focused in this lecture.
Keywords: Lophomonas blattarum, emerging protozoan, respiratory infection

1. **Antimicrobial effect of fungi metabolites isolated from livestock diet on Gram-negative Escherichia coli (ATCC 25922) (Research Paper)**

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Introduction: Secondary metabolites are organic compounds produced by any lifeform, e.g. bacteria, fungi or plants, which are not directly involved in the normal growth, development, or reproduction of the organism. These compounds have been used because of its antimicrobial effects.

Methods: In this study secondary metabolites of Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Acreomonum spp. and penicillium spp. isolated from moldy Livestock ration and its antimicrobial properties against of Escherichia coli (ATCC 25922) was investigated.

Results: Results of this study showed that the Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Acreomonum spp MIC was 250 (Âµl/ml) and the MBC was 500 (Âµl/ml).

Conclusion: Based on the results; secondary metabolites of Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Acreomonum spp. had the antibacterial effects on Escherichia coli and can able be newest antimicrobial agent against this microorganism.

Keywords: Secondary metabolites, Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Acreomonum spp.

Antimicrobial effect of metabolites of fungi isolated from animal feed on Gram-positive bacteria Staphylococcus aureus (Research Paper)

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Introduction: Secondary metabolites, also called specialised metabolites, toxins, secondary products, or natural products, are organic compounds produced by any lifeform, e.g. bacteria, fungi or plants, which are not directly involved in the normal growth, development, or reproduction of the organism. These compounds, isolated and have been used in modern medicine because of its antimicrobial effects.

Methods: In this study secondary metabolites of Aspergillus flavus, Aspergillus fumigatus and penicillium spp. isolated from moldy Livestock ration and its antimicrobial properties against of Staphylococcus aureus was investigated.

Results: Results of this study showed that the MIC was 416.66 Â± 144.33, 333.33 Â± 144.33 and 500 Â± 0.00 (ml) respectively for Aspergillus flavus, Aspergillus fumigatus and penicillium spp. secondary metabolites isolated. The MBC was 500 Â± 0.00, 416.66 Â± 144.33 (ml) respectively for Aspergillus flavus and Aspergillus fumigatus; penicillium spp. had no any bactericidal effect on Staphylococcus aureus. Disk diffusion test shows no inhibitory zone in 100, 120 and 150 Âµl for secondary metabolites. Also There was no any inhibitory zone around secondary metabolites in well diffusion in 170, 200 and 220 Âµl.

Conclusion: Based on the results; secondary metabolites of Aspergillus flavus, Aspergillus fumigatus and penicillium spp. especially Aspergillus flavus and Aspergillus fumigatus have the antibacterial effects on Staphylococcus aureus.

Keywords: Secondary metabolites, Aspergillus flavus, Aspergillus fumigatus, penicillium spp.

Application of Machâ€“Zehnder Interferometer and statistical physics in Bence Jones proteins detection (Research Paper)

Ali Mohammadi Ruzbahani,[1,*] Abbas Javadian,[2]

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Introduction: Detection of Bence Jones protein may be suggestive of multiple myeloma or WaldenstrÃ¶m's macroglobulinemia. Quantitative approximation of Bence-Jones proteins is done through electrophoresis and densitometry. Bence-Jones protein can be detected at the threshold of 10 mg/liter by laboratory analysis of the patient's urine. In this research, we have developed a new method using a Mach-Zehnder interferometer with a detection limit of 10 Î¼g/L using computer simulation.

Methods: A single-mode waveguide allows the development of a Mach-Zehnder interferometer detection method with performance and reproducibility. We have used a single-mode waveguide with a core thickness of 30-50 nm at an operating wavelength of 1565 nm, which is achieved by a large difference between the refractive index of the core and the cladding. field intensity, the mode polarization and cross section dimensions of this rib waveguide are optimized through finite difference method simulation. Using statistical physics methods as well as artificial neural networks, we identified and quantitatively approximated the amount of Bence Jones proteins in the target solution, from the data obtained from the interference scheme.

Results: The use of optical methods along with detailed analysis based on probability equations in statistical mechanics can lead to accurate results in the identification and quantitative counting of proteins in urine or blood samples.

Conclusion: Quantitative detection of biomarker proteins that are directly related to various diseases, to diagnose and monitor diseases; It is needed and it allows us to accurately diagnose the disease by identifying the right protein. We have developed the Mach-Zehnder interferometer method with statistical physics to detect and estimate the number of Bence-Jones proteins. The results of this method were compared with the results of electrophoresis and were encouraging. Considering that we obtained the results based on simulation, we hope to achieve similar results in practice.

Keywords: statistical physics, Machâ€“Zehnder Interferometer, Bence Jones proteins, ANN

Application of pyroptosis in Acute myeloid leukemia and myelodysplastic syndromes: from current concept to future perspectives (Review)

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Introduction: Acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are hematopoietic cancers that develop in the bone marrow. Patients with higher-risk MDS and AML continue to have a dismal prognosis with short survival despite recent improvements in treating these illnesses. Although the pathophysiology of MDS and AML contains an immune component, it has been known for a while that immune treatments haven't been very effective in treating these conditions.

Methods: It is common knowledge that tumor cells tend to gradually evade cell death pathways, a trait known as apoptosis resistance, which dominates tumor drug resistance. Therefore, treatments that aim to prevent non-apoptotic cell death have received much attention lately. An essential physiological regulator of inflammatory reaction, cell growth, tissue homeostasis, and stress response is pyroptosis, a newly developed kind of cell death. The effects of various pyroptotic forms play a significant role in treating hematological malignancies. If given local or systemic therapy, pyroptosis might be produced and subsequently affect carcinogenesis, progression, and metastasis. Excessive or unchecked cell death, however, can result in tissue damage, acute inflammation, or even cytokine release syndrome, which promotes the growth or recurrence of tumors. In this article, we sought to describe the molecular mechanisms of pyroptosis and highlight and discuss the opportunities and problems associated with activating pyroptosis pathways through various oncologic therapies in hematological malignancies.

Results: We reviewed and summarized the current role of pyroptosis in the treatment and diagnosis of leukemia through a comparison made between traditional approaches applied in the treatment and diagnosis of leukemia via the existing investigations about the pyroptosis molecular mechanisms involved in various antitumor treatments, such as targeted therapy, chemotherapy, radiotherapy, and immunotherapy.

Conclusion: Finally, we discussed the challenges and future perspectives in clinical applications of pyroptosis. Applying pyroptosis and other novel forms

of cell death may provide a new direction in treating hematological malignancies.

Keywords: Acute myeloid leukemia; Myelodysplastic syndromes; Pyroptosis; Diagnosis; Molecular mechanisms.

Application of statistical physics and Nash equilibrium to Prenatal Screening for Down Syndrome (Research Paper)

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Introduction: Screening for a disorder may be carried out by assessing the risk that an individual is affected given the values of variables whose distributions alter when the disorder is present. Currently, our parameters for Down Syndrome (DS) risk prediction include maternal age as well as three biochemical markers and risk calculations for the biochemical markers use a quadratic discriminant function. Analogous problems have been studied for years by physicists extracting macroscopic states of various physical systems by examining microscopic elements and their interactions. In this article, we have checked the values of the evaluated parameters using the methods of statistical physics and the Nash equilibrium equation with the data of a screening program.

Methods: we start from a small set of initial findings and proceed by a sequence of hypothesis selection and testing. Due to the statistical nature of the Down syndrome screening results, we are facing a complex statistical system, because the results are checked according to the population ratio and the number of tests, etc., and finally the risk rate is determined according to the statistical classification. Here, by using the combination of Nash equilibrium and statistical physics relations, we were able to establish a relationship between the obtained parameters and previous rates and add error costs to the equation. Finally, using artificial neural networks and a small dataset we had available, we compared the results with current models.

Results: By using the models used in statistical physics and also using the Nash equilibrium to compare and categorize the data, we were able to reduce the range of useful predictions with a more accurate probabilistic model and also reduce the standard deviation.

Conclusion: In a general statement, it can be said that in addition to the parameters examined in prenatal screening for Down syndrome, other parameters such as defects in the statistical data set should also be considered. The main challenge is to balance the efficiency and predictability of the model against the available data, because even if we achieve a perfect model, due to its statistical nature and dependence on the parameters in the databases, we cannot comment on the success rate of the model.

Keywords: statistical physics, Down Syndrome ,Prenatal Screening, Nash equilibrium

Application of the CRISPR/Cas9 System in transgenic animals (Review)

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Introduction: In recent years, novel genome editing technologies based on the CRISPR-associated RNA-guided endonuclease Cas9 has provided the ability to rapidly and economically introduce sequence-specific modifications depends on the generation of double-strand break (DSB) and DNA repair process into the genomes of cell and organisms. Gene modification can be introduced into the animal genome through homologous recombination and embryonic stem cell technology. Genetically modified animals, especially gene knockout editing is one of great interest in the prevention and treatment of human diseases. In this review, we discuss the CRISPR/Cas9-based transgenic models to enhance engineering a wide spectrum of mutations found in human cancers.

Methods: CRISPR/Cas system is the most flexible and user-friendly platform to generate transgenic animals. Non-viral vectors, viral vectors, and physical delivery are the most widely used method for delivery of CRISPR/Cas9 for genome editing. The physical delivery, including microinjection, electroporation and somatic cell nuclear transfer (SCNT) procedure are widely used for target delivery of CRISPR/Cas system to generate transgenic animals.

Results: CRISPR/Cas9 technology has been used to generate target genome modifications. Gene modification can be introduced into the animal genome through homologous recombination and embryonic stem cell technology. The discovery of site-specific endonucleases has provided the ability to establish deletion (Knock Out) or insertion (Knock In) of specific genomic sequences on a single step, directly applied to zygotes. Genetically modified animals, especially gene knockout editing is one of great interest in the prevention and treatment of human diseases. Methodology delivery of crispr/cas system: Viral vectors are efficient in gene delivery, but they have some contraindication due to many drawbacks such as off-target effect, immunogenic and inflammatory responses, limited packaging capacity, and high cost in production. Non-viral vectors, including Nano carriers and nanoparticles such as Nano polymeric- and lipid-based structures, rigid nanoparticles, nanoparticles coupled to specific ligand systems including arginineâ€“glycineâ€“aspartate (RGD) peptide, porous silicon, mesoporous silica, metalâ€“organic, cell-penetrating peptides. This method is efficient but

expensive. The physical delivery, including microinjection, electroporation and hydrodynamic delivery show high efficiency for the application in vitro, but not satisfy for in vivo application especially in large animals.

Conclusion: The simplest and the most flexible and user-friendly platform to engineering nuclease system to generate transgenic animals is the CRISPR/Cas9 system. Genetically modified animals, especially gene knockout models, have been valuable for mimic human disease. This system provides multiplex genome engineering, based on site-specific recombinases, primarily the Cre-LoxP system, enables the creation of animal transgenic models, have the capacity to engineer a wide spectrum of mutations found in human cancers.

Keywords: Genome Editing tools, CRISPR/Cas9, Transgenic animals

Biochemical profiles and expression of some microRNAs in rheumatoid arthritis (Review)

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Introduction: While the reason for rheumatoid arthritis is unclear, it is assumed to affect genetic and environmental factors. Considerable investigators have recently thought about the potential that microRNAs are involved in the pathogenesis of RA, and they have lately become more critical in this subject. Considerable studies have revealed the altered expression of many microRNAs in both inflammatory and metabolic disorders.

Methods: The central objective of this review is to consider how miRNAs act by controlling cellular and molecular targets in rheumatoid arthritis. Two advanced searches were conducted in databases, one using "micro-RNA" and "rheumatoid arthritis" as keywords and another one with "micro-RNA," "Biochimical," and "metabolic."

Results: Because considerable amounts of miRNAs are found in the body fluids, especially in the bloodstream, they supply the unparalleled potential for novel biomarkers: they exhibit specific properties for certain disorders and are readily available and stable molecules. Therefore, examining miRNA patterns in liquid biopsies represents a promising way for the early detection of rheumatoid arthritis and other diseases.

Conclusion: This review explains that the unregulating of crucial miRNAs, such as miR-146a-5p and miR-155-5p, could result in RA and metabolic disease. These miRNAs handle critical molecular pathways involved in nociception, inflammation, and autoimmune responses; the NF-ÎºB, TNF-Î±, interleukins, and TLR4. Finally, microRNAs may play a vital function in RA as an epigenetic connection between RA inflammation and cardiometabolic diseases.

Keywords: microRNAs; miR-4270; miR-146b; Rheumatoid Arthritis; Biochemical profiles

Calprotectin as a serodiagnostic marker for bacterial sepsis (Research Paper)

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Introduction: This study aimed to assess the serum levels of calprotectin and a more widely used sepsis biomarker in patients with bacterial sepsis (BS).

Methods: Subjects were classified into the BS group with patients who met the sepsis criteria at the beginning of the study and the control group. We investigated concentrations of the biomarkers in 300 blood samples collected at admission from all patients hospitalized in the Fatemeh Al-Zahra Hospital, Najafabad, Isfahan in April 2019 and April 2020.

Results: The microbial etiology in the BS group was confirmed in 35 patients (100%). The most frequently cultivated pathogens were Escherichia coli (n=11). The serum concentrations of calprotectin and CRP were significantly higher in patients with BS (n= 35) than the healthy controls (n= 20).

Conclusion: Our results suggest that the serum level of calprotectin could have substantial added value in the management of BS and is a reliable biomarker of BS.

Keywords: Bacterial sepsis, Serum calprotectin, C-reactive protein

Cholera as a Problem in Laboratory Diagnosis; A Review on Diagnostic Methods and Its Molecular Mechanisms. (Review)

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Introduction: Cholera is an infectious disease that occurs in humans after drinking or eating liquids or foods contaminated with Vibrio cholera bacteria. This disease causes fatal symptoms such as severe diarrhea, which eventually kills a person due to excessive loss of body water. This disease becomes acute in two or three days and can lead to the death of the patient in five days. Therefore, on-time treatment and correct diagnosis of this disease in communities are very effective and useful for controlling and preventing upcoming epidemics.

Methods: Authors have done their best try to study different papers which have been published in English in recent decades. Due to this fact, different search engines (e.g., Google Scholar, PubMed, MEDLINE, Web of Sciences, and Scopus) read the abstracts and full articles and select effective papers.

Results: Although the diagnosis of this disease is usually based on the symptoms and the physicians make the diagnosis directly, in some people this disease can be asymptomatic and the person is the only carrier that has the potential to cause an epidemic. Therefore, to distinguish cholera from other diarrheal diseases, the laboratory diagnosis of this bacterium becomes important. The good potential of diagnostic methods in the laboratory to find this disease among people requires the investigation and creation of molecular, microbial, and serological methods. This bacterium is located in the digestive system and can be detected through the patient's stool, so most diagnostic tests are designed and produced based on stool samples; Furthermore, this disease can also be diagnosed by measuring the amount of immunoglobulins (Ig)/antigens (Ag) in the blood (e.g., IgM) and in the stool (e.g., IgA). To identify this bacterium, like other pathogenic microorganisms, rapid and time-consuming methods have been designed. Microbial diagnosis including culture and detection of bacteria with Kerry Blair as the transfer medium, and selective medium thiosulfate-citrate-bile salt (TCBS) agar. cholera rapid diagnostic tests (RDTs) including the CrystalÂ® VC dipstick rapid test based on the immunochromatographic assay, beacon-based real-time nucleic acid sequence-based amplification (NASBA), other molecular assays that investigate the genome sequence and DNA such as Enzyme-labelled oligonucleotide/DNA probe hybridization assay, genosensor, and Multiplex-polymerase chain reaction (MP-PCR) assay. Serological methods which measure the immunoglobulins (e.g., IgG) including Bandi's test, Radial

passive immune hemolysis test, Coagglutination test, Cholera-Direct fluorescent assay, GM1-ganglioside-enzyme-linked immunosorbent assay (GM1-ELISA), latex agglutination assay. Furthermore, Vibrio cholera is viable but nonculturable (VBNC) in aquatic environments, so taking environmental samples is mistakable; molecular tests cover this problem and make the diagnosis from environmental samples before people are infected.

Conclusion: More than 100 serogroups have been identified for Vibrio cholera bacteria, but only two serogroups O1 and O139 are cases of the pandemic. In the microbial method, the observation of yellow colonies in the selective culture medium indicates the presence of bacteria. To perform different methods from the samples prepared in molecular diagnosis, we use the expansion and amplification of the bacterial genome with ELISA and PCR assays. structural and non-structural proteins of lytic vibriophage that are antigenically unique in feces that cause monoclonal antibodies (MAbs) secretion; can be an effective factor in rapid molecular diagnostic methods. In this article, we investigate the cellular and molecular mechanism of various diagnostic methods for the diagnosis of Vibrio cholera.

Keywords: Cholera AND Vibrio cholera AND Infectous Disease AND Laboratory diagnosis

Comparison of AstraZeneca and Sinopharm in protection against COVID-19 infection (Research Paper)

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Introduction: Acute Respiratory Infections (ARIs) are the most prevalent diseases that affected individuals of all ages worldwide. Multiple viruses cause ARIs including coronaviruses. The global burden of the SARS-CoV-2 pandemic evaluated about 45 million confirmed cases including over 6 million deaths. Studies showed that two doses of vaccination play an important role in decreasing hospitalization and mortality rate among patients but the efficacy of a booster dose is also important. We aimed to show which type of vaccine causes better immunity and fewer symptoms manifestation against Omicron as a booster dose.

Methods: We conducted a cross-sectional study on individuals who were admitted to the hospital with respiratory symptoms. Possible SARS-CoV-2 infection by using Real-time PCR was conducted and after that, We have limited the study to infected people with a history of 3 doses of vaccination, injected 2 doses of BIBP (Sinopharm) and a similar or different booster dose, BIBP or AZD1222 (AstraZeneca), and inquired them about their age, gender, type of injected vaccine for the third dose, and all respiratory symptoms of these patients were investigated.

Results: Among 346 cases, 120 cases were positive for SARS-CoV-2 but vaccinated with two doses of Sinopharm and a different booster doses of AZD1222 or BIBP were 94 among these 120 cases. patients vaccinated with AZD1222 as a booster dose showed fewer symptoms compared to those vaccinated with three doses of BIBP.

Conclusion: As a result, the patients vaccinated with 2 doses of BIBP and AZD1222 as a booster dose(n=26) manifested mild symptoms to those who were vaccinated with 3 doses of BIBP(n=68). Therefore, our study showed injecting a booster dose will help in decreasing hospitalization and severity of the infection, and also it seems that the third dose of vaccination with AZD1222 is better than BIBP and it is suggested to make better immunity against SARS-CoV-2.

Keywords: ARIs, COVID-19, SARS-CoV-2, Sinopharm, AstraZeneca

Detection of Leptospira spp., from sheep and goats blood in West Azerbaijan province, Iran (Research Paper)

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Introduction: Leptospirosis, an infectious disease that affects both humans and animals, is recognized as one of the most widespread zoonosis worldwide. Annually, an estimated one-half million cases of severe leptospirosis are reported globally. However, this number is probably underestimated because of the lack of reported cases and the misdiagnosis of this disease in many countries. Leptospirosis is caused by the pathogenic strains of the bacterium Leptospira. Currently, there are nearly 300 known serovars, and most of them have their primary reservoirs in wild and domestic animals, of which rodents and rats are the most common source worldwide. Infected rats shed Leptospira spp., in their urine over an extended period of time. Humans and animals get infected through direct or indirect contact with urine, water, or soil contaminated by Leptospira spp. Approximately one-half of the pathogenic serovars belong to L. interrogans or L. borgpetersenii. Classically, the diagnosis of leptospirosis is based on serological tests, such as the microscopic agglutination test (MAT). In this test, reaction takes place between a leptospiral isolate and reference hyperimmune rabbit antisera. However, this method is laborious and time-consuming, and it requires extensive collection of reference strains and their corresponding rabbit antisera. Various molecular approaches have been developed, such as polymerase chain reaction (PCR)-based methods, to improve the diagnosis of leptospirosis. PCR has been successfully applied as a rapid, sensitive, and specific tool for the detection of several microorganisms, including Leptospira, in a variety of specimens from different hosts. The rapidity and reproducibility of pulsed-field gel electrophoresis (PFGE) makes it a very useful technique for typing Leptospira strains.

Methods: A number of 215 blood samples were randomly collected from sheep (n = 117) and goats (n = 98) belonged to 15 sheep and goats' flocks randomly selected in three different geographical regions of west Azerbaijan (north, center and south) during four seasons in 2022. A number of ten flocks from each region, including five flocks of sheep and goats were randomly selected and 25 animals were sampled from each flock. Sampling of apparently healthy animals was performed. Each blood sample was collected from the jugular vein of the sheep and goat into a sterile tube containing an anticoagulant (ethylene diamine tetra acetic acid, EDTA).The collected blood samples were placed on ice and immediately transferred to the microbiology laboratory at the Faculty of Veterinary Medicine. DNA extraction from re-

suspended pellet was performed using Blood Genomic DNA Extraction Mini Kit, (Favorgen-Taiwan) according to the kit's manufacturer instructions. The quality and quantity of the extracted DNA was evaluated by Nano Drop 2000c (Termo Scientific, USA). The extracted DNA from samples was kept at âˆ’20 Â°C for the later use in Nested PCR. During DNA extraction procedure, elution buffer from the extraction kit was used as Negative Control of Extraction. Primer for Nested PCR F- CATGCAAGTCAAGCGGAGTA FN- ACGCCCAATGATTCCGAACA R- AGTTGAGCCCGCAGTTTTC RN- TTCGGCCACAATGGAACTGAGA

Results: The percentage of positive blood samples for Leptospira spp., in sheep and goat was by using 16S rRNA gene 16.2% and 8.1% respectively. Prevalence of Leptospira spp., in the blood samples collected from sheep and goat dairy farms from West Azerbaijan Province. Animal Sheep (No.117) Goat (No.98) p-value Gene 16SrRNA 16SrRNA Genus female 13/77 (16.8%) 5/67 (7.4%) $P < 0.05$ male 6/40 (15%) 3/31 (9.6%) Total 19/117 (16.2%) 8/98 (8.1%) $P < 0.05$

Conclusion: It was concluded that sheep and goats can play an important role in the epidemiology of Leptospiral disease as the reservoir for Leptospira spp. The molecular detection of Leptospira spp., using Nested-PCR method in blood samples showed that PCR can be used an easy and reliable approach for detecting Leptospira spp. According to the reported results, the prevalence of Leptospira spp., was higher in sheep blood than goat blood.

Keywords: Leptospira spp., Nested-PCR, blood, sheep, goat

Detection of the pathoadaptibility gene in Escherichia coli facilitating genetic adaptation (Research Paper)

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Introduction: Escherichia coli is considered as a facultative anaerobe (that creates ATP through aerobic respiration when oxygen is accessible, but it can switch to anaerobic respiration or fermentation when oxygen is absent). The cells of this bacterium have characteristically rod form, (2.0 Î¼m long and 0.25â€“1.0 Î¼m diameter), having a cell volume of 0.6â€“0.7 Î¼m3. Escherichia coli is Gram-negative since its cell wall contains, in addition to the cytoplasmic membrane, a thin layer of peptidoglycan and an outer membrane. Strains that own flagella are motile. Escherichia coli own the capability to laterally transfer DNA through bacterial transformation, transduction, and conjugation, which allows the foreign DNA to spread over the bacterial population. The transduction process is mediated via bacteriophages. Escherichia coli strain IHE3034 is a neonatal meningitis-associated K1 pathovariant. The K1 capsule is very similar to the capsule formed by the Group B Neisseria meningitidis strains. The ycgG (pdeG) gene is found among most of the genomes of E. coli strains. It codes for an EAL phosphodiesterase that contains a membrane-binding domain. In the genome of IHE3034, the ycgG gene is evolved to a new allelic variant, i.e. ycgG2 (pdeG2) that only encodes the EAL domain of the protein. Escherichia coli K1 IHE3034 is a neonatal meningitis isolate that belongs to the group of extra-intestinal pathogenic strains. The focus of this study is to delete ycgG to comprehend the role of modified ycgG in E. coli IHE3034 in terms of biofilm formation, motility, and pathogenicity.

Methods: PCR-amplification of antibiotic resistance maker carried on a plasmid for one-step inactivation of chromosomal genes using PCR products. Recombination between H1 & H2 on the PCR fragment and H1 & H2 on the chromosome was done. PCR amplification for deletion fragment using pKD3 as a template was carried out. To Electro-competent cell preparation, the IHE3034 strain carrying pSIM6 plasmid was grown at 30ËšC, overnight. For activation of the red system in pSIM6 plasmid, bacterial culture with OD = 0.5 was incubated at 42ËšC for 30 min. Centrifugation was done at 2700 rmp. Pellet was washed with 20% glycerol 3x. To check if transductants are MG1655Î”ycgG::aph, we used blue-white screening Xgal-IPTG plate by knowing JW5174 chromosomal markers: Î”(araD-araB)567, Î”lacZ4787(::rmB-3), Î»-, Î”ycgG757::aph, rph-1, Î”(rhaDrhaB)568, hsdR514. Two mutant

candidates were selected on a Kanamycin-containing plate and verified by sequencing.

Results: YcgG2 regulated the IHE3034 virulence features. The ycgG2 deletion mutant displayed lower expression of the S-fimbriae, consistent with the immunoblotting against SfaA and the SEM of the cells, in comparison with the wild type. The agglutination test confirmed the agglutination of the K1-encapsulated mutant cells. The detection of YcgG2 expression was accomplished in a medium with high osmolarity, which also linked YcgG2 to adaptation to osmotic stress. IHE3034Î”ycgG2 (NMEC) is less fimbriated as compared to IHE3034. The ycgG2 mutant cells make more K1 capsules shown by anti-Grp. B meningococcal agglutination assay. Protein expression levels of YcgG2 and its effector factors. NMEC produces more K1 capsules indicated by agglutination assay.

Conclusion: we suggest phenotypic assays (e.g. acid stress), a comparison of growth rate between wild-type and mutants at 37, 42, and 16ËšC, and checking for YcgG protein levels in wild-type and mutants in different conditions for future plans.

Keywords: Escherichia coli, Neonatal Meningitis, Pathoadaptibility, C-di-GMP, Genetic Adaptation

Determination of spatial epitopes on human immunoglobulin light chain by computational immunology (Research Paper)

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Introduction: Immunoglobulins are a set of proteins which have a critical function in defense. Against microorganisms. Immunoglobulins include heavy and light chains. In human, Immunoglobulin light chain comprises of isotypes: Kappa (k) and lambda (Î») based totally on amino acid differences in carboxylic end in their consistent area. Marked modifications in the k to Î» ratio can occur in monoclonal expansion of neoblastic B cells or HIV infection in neonatal periods. Highly sensitive and particular anti-light chain MAbs have clinical importance inside the diagnosis and immunotherapy of patients with B-cell immunoproliferative diseases. Therefore, specific dedication of unique epitopes in mild chains could be very important. Computational immunology makes use of the computational data for more accurate diagnosis of diseases. This study describes determination of conformational epitopes in constant area of human immunoglobulin light chain via computational immunology.

Methods: The amino acid residue and third structure of reference human immunoglobulin G light chain become observed in PDB database. The second immunoglobulin G structure become described by Phyre 2 software. Conformational epitopes of the immunoglobulin light chain have been specified with the aid of using CEP software.

Results: In this study, the CEP software identified five conformational epitopes located in the constant domain of the human immunoglobulin light chain. These conformational epitopes were located in light chain sequences of 100-214 amino acids.

Conclusion: In this study, several conformational epitopes located in the constant domain of the human immunoglobulin light chain were identified. These epitopes are valuable tools for generating specific anti-immunoglobulin light chain monoclonal antibodies and could have a potential impact on the production of specific human immunoglobulin light chain diagnostic kits, the control of monoclonal light chain diseases and the treatment of related B-cell tumors have, immunoglobulin light chain epitope mapping and evolution studies.

Keywords: Human Immunoglobulins, Light chains, Conformational epitope, Computational immunology

Dose-dependent histopathological effects of hexaflumuron on the reproductive system of male albino rat (Research Paper)

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Introduction: Hexaflumuron (HFM) is an insect growth regulator which is widely used in agriculture. Despite its beneficial effects, it is a hazardous substance for human and animal health and has potential risks and harm for non-target organisms. Due to the lack of histopathological assessments of this insecticide on the reproductive system, the present study aims to investigate possible dose-dependent histopathological effects of hexaflumuron on the reproductive system of adult male albino rats.

Methods: 16 male rats were divided into five groups of 4 each and received daily treatment by gavage for 28 days as follows: Group (1) control, Group (2) 10% of LD50, (3) 15% of LD50, (4) 20% of LD50 of HFM.

Results: Our results reveal moderate to severe histopathological alternations such as a decrease in spermatozoa count, edema, vacuolar degeneration, vascular congestion and hyperemia in the testes, epididymis and prostate gland. These effects have been made mainly by middle and high doses.

Conclusion: It can be concluded that exposure to middle and high doses of hexaflumuron led to histopathological alternation in the male reproductive system and also raise concerns about this insecticide that possesses a potential hazard to human health and breeding animals.

Keywords: Hexaflumuron, Male reproductive system, Histopathology

Drug Repurposing approach in colorectal cancer (Review)

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Introduction: Colorectal cancer (CRC) is the third most common cancer in the world, accounting for 11% of cancer cases. Also, this cancer is the second-leading cause of cancer-related mortality worldwide. Currently, the treatment of CRC mainly includes surgery, radiotherapy, chemotherapy, target therapy, and immunotherapy. Among these treatments, surgery and chemotherapy (with 5-FU, oxaliplatin) are the main treatments for this malignancy. Considering the high cost, time-consuming and high risk of failure during the production process of new drugs, the use of repurposed drugs in the pharmaceutical industry for the treatment of cancers seems logical. Of course, this strategy is new for cancer treatment and these drugs cannot replace chemotherapy drugs, but they can be used together with chemotherapy drugs to increase the effectiveness of these drugs and to complete the cancer treatment process.

Methods: In the present study, by using the keywords drug repurposing and CRC and using PubMed and Google scholar databases, we reached a list of drugs, which usually have their therapeutic use, but it has been shown in studies that they can be used to treat CRC. Among these drugs, we can mention Metformin, Celecoxib, Aspirin, Diclofenac, Cimetidine, Disulfiram, Doxycycline, Niclosamide, Chloroquine, and Artesunate.

Results: For example, it has been shown that metformin, which is used as the main treatment for type 2 diabetes, prevents the growth of cancer cells and metastases in colorectal cancer. Diclofenac, aspirin, and celecoxib are also NSAIDs and are used to reduce inflammation and pain. These drugs are COX-2 inhibitors, and by inhibiting COX-2, they prevent the development of CRC.

Conclusion: By studying more of these drugs, instead of using drugs with high side effects, drugs that were usually prescribed to treat simpler diseases and had much fewer side effects can be used.

Keywords: Colorectal cancer, Chemotherapy, Drug repurposing

Efficient In Vitro Differentiation Of Hematopoietic Stem Cell Into Erythroid Progenitor Cells (Research Paper)

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Introduction: Pure red cell aplasia is defined by a normocytic normochromic anemia with severe reticulocytopenia and marked reduction or absence of erythroid from the bone marrow. Abnormalities from pure red cell aplasia is limited only to the red cell lineage. The main cells involved in pure red cell aplasia are erythroid progenitor cells (EPCs). To perform cellular and molecular researches on this disease, EPCs in culture is required. In this study, EPCs were differentiated from hematopoietic stem cells using a highly efficient method.

Methods: For the generation of EPCs, CD34+ cells were isolated from mononuclear cells derived from human umbilical cord blood. The isolated cells were cultured for 14 days in erythroid differentiation medium consisting IMDM containing 20% fetal bovine serum, 10% heat-inactivated fetal bovine serum, 1X ITS, 50nM Î²-mercaptoethanol, supplemented by 25 ng/mL IL-3, 100 ng/mL SCF, and 4 IU/mL EPO.

Results: The cultured cells were showed morphological changes at the end of the culture period. The cells were grown as suspended colonies. Microscopic findings, GATA-1 and EPOR gene expression and specific cell surface marker analysis proved differentiation into erythroid lineage. Based on flow cytometry results, 86% of the differentiated cells were EPCs.

Conclusion: As the results are illustrative, the current differentiation method is an efficient method for production of EPCs in culture. These cells can be used in a wide range of researches of the red blood cell lineage specially to investigate molecular pathogenesis of red cell aplasia.

Keywords: Pure red cell aplasia, Hematopoietic Stem Cell, erythroid progenitor cells (EPCs), GATA-1, EPOR

Evaluation of antibacterial effect of garlic extract on Escherichia coli isolated from patients with urinary tract infections (Research Paper)

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Introduction: Introduction: Urinary tract infection (UTI) is a bacterial infection that affects part of the urinary tract. The main cause of this infection is garlic, however rarely other bacteria, viruses or fungi may also cause it. Urinary tract infections are more common in women than men.

Methods: materials and methods: In this study,50 bacterially cultured urine samples were included in the study after determining the type of bacteria. Blood agar and EMB, Mollerhinton agar culture medium was also used for antibiogram test.Garlic extract was purchased commercially from Elixir Technological Test Company and antibiotic extract was prepared from the above disk.:

Results: Result:In this study,it was observed that 35 samples (70%) of the samples were sensitive to garlic extract (Sensitive).10 samples (20%) had moderate sensitivity (Intermediat) and 5 samples (10%) were resistant to the case substance. Our opinion was garlic extract.

Conclusion: Discussion and conclusion: Nowadays, due to the excessive use of antibiotics has caused bacterial drug resistance and one of the ways to solve this problem can be the use of drugs based on plant extracts, which we also found in this study that garlic extract can be combined with other drugs Be used therapeutically.

Keywords: UTI, garlic, Escherichia coli, antibiogram,

Evaluation of Antibiotic Resistance Pattern in Clinical Isolates of Staphylococcus aureus (Review)

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Introduction: Antimicrobial resistance (AMR) means when microorganisms develop the ability to defeat and adapted over time and no longer respond to antimicrobial medicines designed to kill them, and they continue to grow. Resistant makes infection difficult to cure and sometimes impossible, to treat. Antimicrobial resistance (AMR) is a global health threat, killing at least more than 1 million people worldwide and associated with approximately 5 million deaths in recent years. Antibiotic-resistant is a type of antimicrobial resistance that is described as resistance to antibiotics that are used to treat bacteria. Staphylococcus aureus is a Gram-positive spherically shaped bacterium, that causes serious problems such as bloodstream infections, pneumonia, bone, and joint, and several different infections. it has a unique ability to quickly respond and create resistance to every other antibiotic presented against it. The prevalence of antibiotic resistance in this bacterium is increasing significantly which limits the treatment conditions for this superbug.

Methods: In this study, the test is done to determine antimicrobial susceptibility to Staphylococcus aureus with a disc diffusion test by using the Kirby Bauer testing method. To assess antimicrobial resistance patterns, thirteen different antibiotics, including Oxacillin (Ox1), Ampicillin (Amp10), Vancomycin (VA30), Gentamycin (GN10), Kanamycin A (K30), Streptomycin (S10), Erythromycin (E15), Tetracycline (TE30), Ciprofloxacin (Cip5), Clindamycin (DA2), Fosfomycin (Fos50), Cefoxitin (Fox30), and Fusidic acid (FD10), were evaluated in non-duplicate isolates of MSSA and MRSA isolated from two hundred sixty-five different clinical samples (i.e. blood, urine, and tissue). Most cultures were identified as multi-drug resistant (MDR).

Results: Disc diffusion tests indicated that the resistance against ampicillin and erythromycin was 88% for each which was the highest resistance against antibiotics recorded. Oxacillin with 70% resistance and ciprofloxacin with 66% resistance also showed great resistance levels. The Cefoxitin resistance test identified 165 isolates 66% as MRSA and 85 isolates 34% as MSSA, out of 250 related Staphylococcus aureus isolates. As a result, resistance against oxacillin, Fosfomycin, cefoxitin, and ciprofloxacin were worrying. No strain was sensitive to all antibiotics. Resistance levels of MSSA against ampicillin, erythromycin, Fosfomycin and Fusidic acid were also highly significant. the average level of resistance also showed in cases of clindamycin, gentamicin, and tetracycline i.e., 54.5%, 45.5%, and 48% respectively. The resistance rate for kanamycin was approximated as 77% in MRSA, and 25 % in the case of MSSA. The Least level of resistance was for vancomycin Only 12% of isolates were resistant to vancomycin, among which 24 were MRSA and 6 were MSSA.

Conclusion: The current portion of antibiotic resistance in Staphylococcus aureus has been increasing in MRSA as well as in MSSA. In the meantime, the number of available antibiotics for the treatment of MRSA infections is limited, needs a new collection of antibiotics to control this destructive superbug. the public has an important role to prevent antibiotic resistance. It must be used carefully to avoid the further spread of antibiotic-resistant bacteria and diseases. A better understanding of how bacteria evolve resistance will allow us to improve how use current antibiotics, as well as the ones we will develop in the future.

Keywords: Antibiotic-resistance, Staphylococcus aureus, Disc diffusion

Evaluation of Antifungal Susceptibility Testing of 6 Antifungals Drugs against Resistance and Susceptible Aspergillus fumigatus by Microdilution Broth (Research Paper)

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Introduction: In recent years, Aspergillosis infections have increased dramatically and, unfortunately, this disease causes many deaths in hospitals. Invasive aspergillosis is a severe and fatal fungal infection that is observed in immunocompromised patients, neutropenia, chronic granulomatosis, hematologic malignancies, bone marrow transplant recipients, stem cells and other tissues and people using long-term antibiotics and Steroids. Aspergillus fumigatus is the most common cause of Aspergillosis infection and is of increasing importance in the medical field, but other species such as Aspergillus flavus, Aspergillus niger and Aspergillus terreus are also important in this regard. Most high-risk patients with susceptible background to invasive Aspergillosis infection and post-clinical infection can be identified after treatment of underlying disease during hospitalization. Although the number of drug agents with anti-aspergillus activity has increased in the past decade, mortality due to invasive Aspergillosis is unexpectedly increasing. Increasing resistance of Aspergillus species to antifungal drugs in the past 20 years has led to an increase in therapeutic failures. This study aimed, Determination of A. fumigatus species isolated from clinical and environmental samples using molecular methods (DNA sequencing) and evaluation of medicinal sensitivity of A. fumigatus species isolated from environmental and clinical samples against common drugs (Amphotericin B, Voriconazole, Itraconazole, Posaconazole , Caspofungin. and Micafungin)

Methods: The present study was conducted in 2021-2022 during a one-year period by examining environmental and clinical samples of A. fumigatus species that had been previously isolated and confirmed by amplification and sequencing of the B-tubulin gene region. Susceptibility patterns of antifungal drugs such as Amphotericin B, Itraconazole, Voriconazole, Posaconazole, Caspofungin and Micafungin were determined against isolates identified by CLSI method, M38-A2 protocol for stranded fungi.

Results: A total of 103 isolated Aspergillus fumigatos (30 clinical and 73 environmental samples) were identified. Based on morphological characteristics and confirmation of molecular method, they were identified. A. fumigatus was the most susceptible to antifungal drugs Posaconazole,

Voriconazole, Micafungin and Caspofungin. However, most species of A. fumigatus in MIC50 and MIC90 were resistance to drugs, Itraconazole, and Amphotericin B. However, in the case of Amphotericin B and Itraconazole, resistances have been observed that should be considered in the treatment of these drugs. Considering that successful treatment depends on rapid identification of the species and its susceptibility pattern to antifungal drugs, therefore, accurate identification of the cause of the disease and investigation of new and old drug sensitivities profiles on isolated strains from clinical samples can be used for rapid treatment of this type of drug. Aspergillosis is a severe and fatal fungal infection that is observed in immunocompromised patients, neutropenia, chronic granulomatosis, hematologic malignancies, bone marrow transplant recipients, stem cells and other tissues and people using long-term antibiotics and steroids, Aspergillus fumigatus is the most common cause of Aspergillosis infection, often under certain conditions in susceptible individuals. The risk to the deep tissues of this species is of increasing importance in the medical field, but other species such as Aspergillus flavus, Aspergillus niger, Aspergillus terreus are also important in this regard. Successful therapeutic management of invasive Aspergillosis depends on the early onset of treatment, the selection of an effective antifungal drug and the lack of resistance of the fungus to it. In these patients, treatment should be started quickly and after suspecting the disease and continue until full recovery. There are different methods for determining fungal species, among which molecular methods have special attention due to their high speed and accuracy. Infections and avoid spending extra money and unsuccessful treatments are very useful. To confirm the diagnosis of Aspergillus fumigatus isolates isolated from plates containing Saboro dextrose agar, DNA of the samples after extraction was amplified using primers of beta-tubulin gene region and sequenced by sequencing method. The results of sequencing for these products after matching the sequences in the gene bank using BLAST software, based on Coverage Query and Max identity, clearly identified Aspergillus species.

Conclusion: According to the results of this study, it can be concluded that Voriconazole, Caspofungin, Micafungin and Posaconazole have a good effect on A. fumigatus species and due to low concentrations of MIC in Caspofungin and Posaconazole, these two drugs are effective in the treatment of Aspergillosis and are used.

Keywords: A. fumigatus, Antifungal, Susceptibility, Microdilution Drug, Iran

Evaluation of mitochondrial DNA level among different blood products (Review)

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Introduction: DNA found in the extracellular environment, regardless of its structure, is called extracellular DNA (ecDNA). The ecDNA consists mainly of nuclear DNA (nucDNA) and mitochondrial DNA (mtDNA). EcDNA can be found in the extracellular milieu of blood products. MtDNA has a similar structure to bacterial DNA due to its proteobacterial origin. They are known as damage associated molecular patterns (DAMPs) that contribute to inflammation. The mtDNA modulates immune cells and may cause adverse transfusion reactions. It has been demonstrated that extracellular mtDNA can contribute to adverse transfusion reactions such as nonhemolytic transfusion reactions (NHTRs), transfusion-related acute lung injury (TRALI), and acute respiratory distress syndrome (ADSR) and febrile nonhemolytic transfusion reaction (FNHTR). Stored blood products can contain variable amounts of mtDNA pro-inflammatory fragments. Many questions about the amount of mtDNA in different blood products have been established. Based on this, our purpose in this review was to compare the amount of mtDNA in different blood products including types of RBC units (RBCU), fresh frozen plasma (FFP) and platelet concentration (PC).

Methods: The result of our review is based on the analysis of articles published between 2010 and 2022. In PubMed, Google Scholar, and Scopus databases, we found relevant articles by searching keywords such as mtDNA DAMPs, blood products, mitochondrial DNA, mtDNA AND adverse transfusion reactions.

Results: Results showed that mtDNA levels are different among blood products. A higher level of mtDNA in FFP and PCs than in RBCU has been showed. However, the result of comparison of mtDNA levels between FFP and PCs varied in different investigations regarding various measurement methods. A higher level of mtDNA was present in whole blood filtration units than in red cell filtration units. Moreover, among the different platelet products based on the preparation method, platelet-rich plasma (PRP) had a significantly higher mtDNA level than buffy coat (BC) and apheresis units.

Conclusion: Based on the obtained results, FFP and PCs had the highest amount of mtDNA compared to RBCU. The high levels of mtDNA in FFPs could be due to the occurrence of leukocyte rupture during the thawing process before transfusion. In addition, a high amount of mtDNA in PCs could be due to oxidative mtDNA damage and subsequent development of mtDNA

DAMPs. As these products contain a higher amount of mtDNA, they are more likely to cause adverse transfusion reactions associated with mtDNA. Given that, further research should focus on minimizing the level of mtDNA in blood products, specifically PCs and FFP.

Keywords: Mitochondrial DNA, DAMPs, Damage associated molecular pattern, mtDNA, Blood products

Evaluation of probiotic effect of Lactobacillus Casei and Bacillus Coagulans on AGS and DU145 cancer cell line (Research Paper)

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Introduction: Probiotics are live microbial supplements with a wide range beneficial in human life. Nowadays, probiotics are known as a factor for prevention of infectious diseases and cancer.

Methods: In this work the inhibitory effect of the supernatant of an autochthonous isolate of Lactobacillus Casei and Bacillus Coagulans on the AGS and DU145 cell Lines was investigated. Different concentration of 100,200, and 300 Âµl/ml of the supernatant of the probiotic bacteria harvested at 24,48 and 72 hours of these growth in MRS media were applied in to the 96 well microplates each containing 8000 cells of AGS and DU145 cell lines after neutralization of the pH with 1N NaOH.

Results: The percentage of cancer cells inhibition observed from 1000 Âµg/ml (72h)and 300 Âµl (72h) supernatants

Conclusion: The inhibitory effect of the probiotic bacteria on human cancer cells seems to be concentrated dependent and not affected by neutralization.

Keywords: Probiotic,Gastric Cancer,Prostat Cancer

Evaluation of the difference in melting temperature of different strains of corona virus (Research Paper)

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Introduction: The Covid-19 disease, which is caused by a viral pathogen called SARS-Cov-2, has caused one of the biggest recent pandemics in the world. Considering the creation of different strains of the SARS-Cov-2 virus from beta, gamma, delta and omicron in the world and the rapid spread of the corona virus, creating a fast and accurate diagnosis method with the aim of controlling possible sources of infection, in order to design effective measures for Preventing further transmission is considered vital. It is also important to know the physiological structure of each virus strain to deal with it. One of the most important factors in investigating the physiological structure of the virus is the detection of the melting point of each strain, which was investigated using the technique of determining the biological melting point.

Methods: In this research, beta, gamma, delta and omicron strains, which were prepared from Pasteur Institute of Iran, were used. To measure the biological melting point, a fully intelligent and automatic melting point device of Nasim tashkhis azma Company was used. Spectrophotometry technique was used to validate the test process and check the complete removal of the virus from the viral cell culture process and also to check the removal of the virus genome (RNA) structure.

Results: According to this research, the alpha strain of the coronavirus at a temperature of 94.444 degrees Celsius, the beta strain of the coronavirus at a temperature of 78.222 degrees Celsius, the gamma strain of the coronavirus at a temperature of 75.222 degrees Celsius, the delta strain of the coronavirus at a temperature of 96.666 degrees Celsius and the strain Omicrons of the coronavirus reached the melting point and complete removal of cells at a temperature of 76.666 degrees Celsius.

Conclusion: Considering the aggressive behavior of alpha and delta strains compared to the other three strains and on the other hand the high ratio of the melting point of these two strains to the other three strains, there is a significant relationship between the melting point of the virus and its aggressiveness.

Keywords: melting temperature / corona virus strain / evaluation

Free mitochondrial DNA DAMPs in blood products associated with adverse transfusion reactions (Review)

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Introduction: Mitochondria is mostly known as the center of energy production in the cells, as its main role is to produce ATP. Damage-associated molecular patterns (DAMPs) are endogenous danger molecules that are released from cells during cellular stress or tissue injury. Extracellular mitochondria and their various fragments, such as mitochondrial DNA (mtDNA), are considered DAMPs and can be released from blood products during blood collection, blood processing, and storage. MtDNA can stimulate the innate immune system and induce inflammation due to its similarities with bacterial double-stranded circular DNA. Several studies have demonstrated a potential role for extracellular mtDNA in adverse transfusion reactions. Therefore, mtDNA has become a critical issue in blood product transfusion. In this study, we aimed to investigate the relation between mtDNA presence in blood products and adverse transfusion reactions.

Methods: Electronic databases including: PUBMED and Google Scholar were searched with keywords such as free mitochondrial DNA AND transfusion, mitochondrial DAMPs, and mtDNA AND adverse transfusion reactions. Articles published between 2010 and 2023 were examined.

Results: Our review showed that the presence of mtDNA in platelet concentrates (PCs) is significantly associated with transfusion reactions such as febrile non-hemolytic transfusion reaction (FNHTR), and hypersensitivity transfusion reactions (HTRs). Fresh frozen plasma (FFP) and PCs's mtDNA levels are closely correlated to the occurrence of acute respiratory distress syndrome (ARDS) in recipients. In addition, extracellular mtDNA DAMPs present in transfusion products can act as a potential TRALI (transfusionâ€• related acute lung injury) agent. The transfer of blood products from the donor to the recipient and the presence of extracellular DNA including mtDNA in these products can lead to the transfer of genetic and epigenetic information from the donor to the recipient. Furthermore, the presence of DNA (including mtDNA) derived from the donor in recipient's body can be related to real or potential health implications in autoimmune diseases and graft-versus-host reactions (GVHR).

Conclusion: The presence of mtDNA in blood products is one of the principal challenges of blood transfusion, which is leading to complications in recipients. Hence, identifying the mechanisms of mtDNA release in blood products is a major step forward to reduce mtDNA, and further research is

needed to investigate these mechanisms. Several methods can be used to reduce mtDNA in blood products, including reducing the storage time, using leukoreduction filters and adding addictive solutions to blood products, which by reducing mtDNA, subsequently reduce adverse transfusion reactions.

Keywords: Mitochondrial DNA, DAMPs, Blood products, Adverse transfusion reactions.

Fusion of two stable gene confers plasmid instability to the vector containing the hybrid gene (Research Paper)

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Introduction: Cloning DNA fragments in a plasmid is usually uncomplicated, but bacterial cells attack the plasmid from time to time. Plasmid loss and elimination of a part of the plasmid during bacterial cell duplication threatens subsequent utilization of a plasmid. Plasmid instability may originate from expression of toxic gene products, metabolic burden of the plasmid, plasmid copy number, the genotype of the host strain, or recombinogenic potential of sequence present in the plasmid. For instance, repetition of a particular sequence and formation of secondary structures can confer instability to a plasmid. Overall, lengthy sequences and sequences that are from different genes increases the risk of plasmid instability. Sometimes it is hard to distinguish plasmid instability from common errors in cloning, and it is even called â€˜unclonabilityâ€™. While tackling plasmid instability can be challenging, there are some reports that claim lowering the cultivation temperature is advantageous. If this strategy fails, the alternative approach is to examine bacterial hosts that allow faithful maintenance of the plasmid. E.coli strain Stbl4 has been shown to be effective in cloning unstable DNA inserts. E.coli strain Stbl4 has endA1 mutation which enhances the plasmid stability. E.coli strain Stbl4 has the following genotype: mcrA, Î”(mcrBC-hsdRMS-mrr), recA1, endA1, gyrA96, gal-thi-1, supE44, Î»-relA1, Î”(lac-proAB)/F', proAB+lacIqZÎ”M15, and Tn10 (TetR).

Methods: In this study, We fused the sequence of a membrane protein with the sequence of a polymerase from two vectors. Both of these vectors showed no plasmid instability during propagation, and we were able to extract high yields of plasmid. We fused the two sequences with overlap-extension PCR. Then the PCR product was double-digested and purified. Consequently, the purified PCR products were ligated with double-digested pet21 vectors.

Results: After transformation of E.coli DH5-Alpha with ligated products, the colony-PCR showed that the transformed bacterial cells possessed a shorter gene than the expected size. Interestingly, these completely rearranged the hybrid gene after several rounds of duplication. Since lowering temperature during transformation was not effective, we employed E.coli strain Stbl4 strain as the host. Around 10 percent of screened transformed Stbl4 colonies showed correct size, which indicates the plasmid stability.

Conclusion: Therefore, we observed that fusion of two genes undermined the stability of the plasmid harboring the hybrid gene. Fortunately, this plasmid instability can be overcome by employing Stbl4 strain.

Keywords: Plasmid Instability- Colony PCR- Hybrid Gene- Transformation- Recombination

Gene therapy in cancer (Review)

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1.
2.

Introduction: Gene therapy is a medical approach, it is a method of correcting defective and disease-carrying genes, this treatment method is very new and it allows to treat a disorder by changing the genetic structure instead of using medicine or surgery. And for the treatment of a wide range of diseases other than rare hereditary and monogenic disorders, it has attracted a lot of attention. For this purpose, in this article, an overview of the process of gene therapy in cancer, as well as several examples of gene therapy in ovarian cancer. And we pay prostate and esophagus.

Methods: Before gene therapy becomes popular as an acceptable method for treating diseases, some intracellular and extracellular barriers need to be overcome.

Results: In this study, independent variable: gene therapy Dependent variable: Cancer The main goal: the attention of many researchers to the method of gene therapy in all types of cancer

Conclusion: Today, a wide range of carriers have been developed for gene transfer. Several safe viral and non-viral vectors have been developed and used to successfully treat some hereditary, immunodeficiency, eye, and cancer diseases. It seems that gene therapy is the final solution of the current century for the treatment of human diseases.

Keywords: gene therapy, cancer, viral and non-viral vector

Haploidentical Hematopoietic stem cell transplantation, when and how? (Research Paper)

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1. TUMS
2. TUMS

Introduction: hematologic and non-hematologic diseases. first of in HSCT, patients need HLA full-match donor for HLA-*A, *B, *C, *DRb1, *DQB1, *DPb1 loci as most polymorphic loci in humankind. Any patients have 30 percent chance to find full-match donor in family. In recent years, by development and progress of donor registry bank, patientsâ€™ chance increased by 70 percent by use of about 40 million unrelated donors. With all this, significant percentage patients canâ€™t find full-match donor and because of urgent HSCT and probability of relapse in malignant patients or severe infection, there is no any other choice except haploidentical HSCT that leukemia patients are more at risk. Any kind of HSCTs act as double-edged sword, rejection and GvHD might be happen and those probabilities are more likely in haploidentical HSCT. So choosing the right haploidentical donor will be avoid patientsâ€™ complication after HSCT.

Methods: Immunosuppression prophylaxis drugs prepare environmental condition to prevent severe acute GvHD in haploidentical HSCT patients. So immune reconstitution after HSCT must be determined. By now two protocols of haploidentical HSCT contain T Cell Replete (TCR) and T Cell Deplete (TCD) has been defined that both have own cost and benefit. In TCR protocol patients need younger, sex match, ABO match, NIMA mismatch donor and no donor specific antibody in patients. In TCR, the GvHD will be more likely to happen. In TCD protocol, KIR matching is needed. younger, sex match, ABO match, NIMA mismatch donor is preferred and donor specific antibody in patients must be ruled out. More rejection in TCD protocol is expected.

Results: Haplo identical HSCT compare to unrelated one locus mismatch shown lower transplanted related mortality and increased of overall survival.

Conclusion: batter matching in HLA and KIR can improve Haplo identical HSCT out come and it will be solution for patients with no HLA full-match donor.

Keywords: Haplo identical HSCT - HLA matching -

Histopathological effects of different doses of Hexaflumuron on the liver of Wistar rats (Research Paper)

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Introduction: Pesticide use has recently increased due to population expansion and increased food demand. Hexaflumuron is a systemic pesticide of the benzoyl urea group that kills insects by preventing the formation of chitin in their bodies. This insecticide is used to control a wide range of plant pests and is more effective on the immature stages of insects. The liver is part of the body's reticuloendothelial system and It can effectively eliminate the toxic effect of agents entering the body.Only a few data are available related to the effects of Hexaflumuron on animals; this study investigated Histopathological effects of different doses of Hexaflumuron on the liver of Wistar rats

Methods: sixteen rats were divided in four groups. Group A presented as standard control. Group B, C and D were administered hexaflumuron by gavage with different doses (22, 16.5, 11 mg/kg corresponding to 20% of LD50, 15% of LD50, 10% of LD50) for 28 days. Immediately after sampling, the liver tissues were washed with sterile normal saline, placed in 10% formalin buffer and then processed for routine paraffin embedding. Stained by H&E and examined under a light Olympus microscope to determine any pathological alterations.

Results: Liver tissue sections of the control rat showed normal histological structure. The high dose group (20% of LD50) demonstrated the most congestion and infiltration with inflammatory cells. The 10%of LD50 group showed the lowest amount of congestion, we didn't observe infiltration with inflammatory cells in this group.

Conclusion: These findings show that the liver of the Hexaflumuron receiving group showed moderate to severe histopathological alterations, so special attention should be addressed to the harmful effects of this insecticide on the liver.

Keywords: Hexaflumuron, histopathology, liver, Wistar Rats

Identification and diagnosis of pathogenic Clostridium species in medical microbiology (Review)

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Introduction: Clostridium genus is a phylogenetically heterogeneous group of prokaryotic bacteria which currently consists of 204 validly described species (http://www.bacterio.net). Clostridium species are Gram-positive (mostly), pleomorphic spore-forming rods with a considerable variety in their oxygen tolerance, from obligate to aerotolerant. They are widely distributed in the environment as well as the microbiota in humans and animals. They produce a variety of potent exotoxins/enzymes, which lead the clinical features of disease in their hosts. Tetanus, gas gangrene, botulism, pseudomembranous colitis, antibiotic-associated diarrhoea, food-borne illness, cholecystitis, pneumonia, bacteremia, empyema, abscesses, and etc. are the most important clostridial diseases in humans. So, the Clostridium spp. can be isolated from various clinical specimens and thus their reliable identification is important. This study summarizes the standard identification of Clostridium species involved in medical microbiology.

Methods: Primary isolation of Clostridium spp. can be performed by the culture of specimens on agar plates containing blood and incubation anaerobically at 35-37 Â°C for 40-48h or Egg Yolk agar incubated anaerobically at 35-37 Â°C for 16-24h. The selective culture media are also available for some species as tryptose sulfite cycloserine (TSC) agar for C. perfringens, and cycloserine cefoxitin fructose agar (CCFA), C. difficile moxalactam norfloxacin (CDMN), and cefoxitin cycloserine egg yolk agar (CCEY) for Clostridioides difficile. Colonial appearance on agar plates varies with each clostridia species. Gram and spore staining techniques are useful to determine the gram-positive rods and the shape and position of spores, respectively. The specific biochemical tests (Lecithinase, Lipase, Indole, Urease, â€¦) as described in Bergeyâ€™s manual can be carried out to differentiate the Clostridium species. The Nagler and reverse CAMP tests can be used for differentiation of C. perfringens from other Clostridium species, too. The specialized methods as enzyme immunoassay (EIA), ELISA, Matrix-assisted laser desorption ionizationâ€“time-of-flight mass spectrometry (MALDI-TOF MS), and molecular assays as PCR, real-time PCR, Pulsed-Field Gel Electrophoresis (PFGE), Fluorescent Amplified Fragment Length Polymorphism (AFLP),16S rDNA gene sequencing, PCR- restriction fragment length Polymorphism (PCR-RFLP), Microarray analysis, Multiple-Locus Variable-Number Tandem-Repeat Analysis (MVLA), and even whole-genome sequencing (WGS) were also can be carried out. To confirm the clostridia isolates, they can be referred to the anaerobe reference laboratory for further identification as the clostridia laboratory in Razi Vaccine and Serum Research Institute-Kerman branch, Iran.

Results: Different Clostridium species can be isolated as the commonly (C. perfringens, C. septicum, C. tertium, and C. difficile), rarely (C. novyii type A and C. sordellii), very rarely (C. tetani, C. histolyticum, and C. botulinum) and the commonly â€œnon-pathogenicâ€• clostridia (C. sporogenes, C. ramosum. C. innocuum, C. paraputrificum, C. cadaveris, C. bifermentans, C. fallax, and C. clostridioforme) from human clinical specimens. They can be differentiated by the identification methods that described above.

Conclusion: Despite the clinical significance of clostridia in medical microbiology, reliable, practical, and fast identification methods are few. Although simple tests can serve to identify most commonly isolated Clostridium species, the identification of other clostridia by conventional biochemical testing is still laborious, expensive, and time-consuming. Due to these evident drawbacks of conventional methods, there is a growing trend toward molecular diagnostics of clostridia that are difficult to identify by phenotypic characters.

Keywords: Identification; Diagnosis; Clostridium; medical microbiology

Identification of Staphylococcus aureus enterotoxin genes of seb and tsst toxin from the nose of sheep in Sistan region by PCR method (Research Paper)

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Introduction: Staphylococcus aureus is known to be a common cause of food poisoning and is also seen as a natural flora in humans and animals. Staphylococcus aureus produces several extracellular enterotoxins, which is regarded one of the key virulence factors of this bacterium and has extremely important effects on its host. It colonizes the anterior portion of the nasal passages and raises the risk of staphylococcal infections. Because each enterotoxin causes a distinct disease and shares numerous antigenic similarities with other enterotoxins, for instance, enterotoxins are responsible for food poisoning and the TSST-1 toxin is responsible for toxic shock syndrome. The toxin released by this bacterium can be identified using a variety of techniques. One of these methods is the PCR test, which is very sensitive and fast and very specific. This research was carried out with the aim of identifying the enterotoxin genes (SEB, TSST-1) of Staphylococcus aureus by multiplex PCR method.

Methods: In this work, sheep nasal swab samples were collected from livestock farms in the Sistan region in order to identify the enterotoxin genes of Staphylococcus aureus. 100 strains of Staphylococcus aureus were identified and verified by biochemical assays out of 300 strains found in sheep's samples. After that, bacterial DNA was extracted by boiling, and the DNA concentration was measured using a Nano drop device. The extracted samples were then kept at a low temperature until PCR tests were run, which were then used to identify the genes for Staphylococcal enterotoxin B (seb) and tsst-1 toxin (tsst), using multiplex PCR. The seA and seC genes' PCR products were examined using an Agarose gel at a concentration of 1.5%.

Results: 100 samples were verified after Staphylococcus aureus were cultured and isolated. To detect the enterotoxin gene and the Staphylococcus aureus toxin gene in sheep nasal samples collected from livestock farms in the Sistan region is the goal of this investigation. Out of 100 positive samples, 20% tested positive for the seb gene and 37% tested positive for the tsst gene. The results of this investigation demonstrated that the seC gene is more sensitive to detecting Staphylococcus aureus enterotoxin.

Conclusion: Staphylococcus aureus has been isolated from the nostrils of a sheep that appeared to be in good health; therefore PCR testing can be helpful for identifying bacteria that have the enterotoxin B genes and the sheep-specific TSST-1 toxin. In general, Staphylococcus aureus represents a

possible health danger, especially when it is present in enterotoxigenic strains.

Keywords: Enterotoxin, Staphylococcus aureus, Sistan

Immune thrombotic thrombocytopenia caused by Covid-19 vaccine (Review)

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Introduction: The common reported adverse effects of COVID-19 vaccination consist of the injection siteâ€™s local reaction followed by several non-specific flu-like symptoms. However, recent reports of thrombosis with thrombocytopenia syndrome (TTS) associated with adenovirus vector vaccines have raised concern. Objective: This is narrative review to investigate TTS after the Covid-19 vaccine.

Methods: Studies of TTP after ChAdOx1 nCoV-19 or Ad26.COV2 vaccine were searched in PubMed, Scopus, Embase and Web of Science databases until August 2022. Summary effects between studies were observed regarding incidence, presentation, site of thrombosis, diagnostic findings, and clinical outcomes.

Results: TTS, also known as vaccine-induced immune thrombotic thrombocytopenia, is a reaction associated with exposure to the ChAdOx1 nCoV-19 and Ad26.COV2 vaccine, which may result in thrombocytopenia and thrombotic events. There are several case series of patients diagnosed with TTS, but the overall incidence is rare. TTS is characterized by exposure to one of the aforementioned vaccines 4â€“30 days prior to presentation, followed by thrombosis, mild-to-severe thrombocytopenia, and a positive platelet factor-4 (PF4)-heparin enzyme-linked immunosorbent assay (ELISA). Thrombosis typically involves atypical locations, including cerebral venous thrombosis and splanchnic vein thrombosis. Evaluation should include complete blood count, peripheral smear, D-dimer, fibrinogen, coagulation panel, renal and liver function, and electrolytes, as well as PF4-heparin ELISA if available. Consultation with hematology is recommended if suspected or confirmed. Treatment may include intravenous immunoglobulin and anticoagulation, while avoiding heparin based agents and platelet transfusion.

Conclusion: Health care providers should be familiar with the clinical presentations, pathophysiology, diagnostic criteria, and management consideration of TTS. Early diagnosis and quick initiation of the treatment may help to provide patients with a more favorable outcome.

Keywords: ITP, Covid-19, Vaccine, Immune system, Thrombocytopenia

In vitro and ex vivo effects of Astragalus adscendens extract against hydatid cyst protoscoleces and its effect on induction of apoptosis (Research Paper)

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Introduction: This study aims to evaluate in vitro and ex vivo antiparasitic activity of Astragalus adscendens root chloroformic extract against hydatid cyst protoscoleces and its effect on induction of apoptosis.

Methods: Various concentrations of the A. adscendens root chloroformic extract (56.25, 112.5, 225, and 450 mg/mL) were treated with hydatid cyst protoscoleces collected from the liver of infected sheep for 5-60â€‰min in vitro and ex vivo. Eosin exclusion test was also utilized to measure the mortality of protoscoleces. Moreover, the extract effect was assessed on apoptosis induction in hydatid cyst protoscoleces by Caspase-3 activity measurement.

Results: The mortality rate of protoscoleces in in vitro was 100% after being exposed to 450 and 225 mg/ml of A. adscendens extract for 20 and 30 min and in ex vivo for 30 and 60 min, respectively. Following 48 h treatment of protoscoleces, A. adscendens chloroformic extract at the doses of 56.25, 112.5, 225, and 450 mg/ml, dose-dependently motivated the caspase-3 enzyme ranging from 8.8% to 29.6% .

Conclusion: A. adscendens root chloroformic extract had a significant protoscolicidal effect; however, extra surveys are required to assess its efficacy and safety as a promising protoscolicidal agent in clinical settings.

Keywords: Hydatid cyst, Echinococcus granulosus, Scolicidal activity, Caspase, Herbal medicine.

Interferon gamma as a biomarker of multiple sclerosis (Review)

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Introduction: Multiple sclerosis (MS) is one of the most common diseases related to central nervous system (CNS). It predominantly affects people between the ages of 20 and 50, and the prevalence of this disease is higher in women than men. This disease has increased significantly in recent decades in different countries. Even the countries with low prevalence of MS in the past, are now among the countries with high prevalence of MS. In order to control and reduce the prevalence of the disease, it is important to identify the patients in the early stages of the disease. Using different biomarkers for early identification of MS patients can be useful to control and reduce the prevalence of MS. Interferon gamma (IFN-Î³) is one of these biomarkers. IFN-Î³ is a pro-inflammatory cytokine that is produced by some immune cells such as T helper1. This cytokine is the only member of type II interferon family and plays an important role in the function of the immune system against various pathogens. But the abnormal expression of this cytokine can cause some autoimmune diseases.

Methods: We reviewed 250 articles about IFN-gamma, multiple sclerosis and their relationships from January 1, 2017, to September 30, 2022, and finally used information in 10 of them to write this article.

Results: During this disease, activated T cells pass through the Blood-brain barrier (BBB) and enter the CNS and produce IFN-Î³, which plays an important role in the pathogenesis of MS. In low doses, IFN-Î³ has a protective effect against microglia and oligodendrocytes, but in higher doses, it can have destructive effects. IFN-Î³ in high doses can aggravate damage to myelin and oligodendrocytes through inflammation, activation of macrophages or microglia, increase in the amount of inflammatory mediators and increasing MHC molecules. Therefore, IFN-Î³ is a key component in MS pathology, which has higher levels in serum and CSF of MS patients than healthy people.

Conclusion: Therefore, measuring the levels of IFN-Î³ as one of the biomarkers of MS can play an important role in the diagnosis of at-risk individuals and the diagnosis of patients in the early stages of the disease. The use of IFN-Î³ along with some other easy and low-cost tests such as other MS biomarkers can be used to accurately diagnose MS in less advantaged countries. Also, the measurement of IFN-Î³ along with several other MS biomarkers such as melatonin can be used as an easy and cost-effective screening test to check the at-risk people.

Keywords: MS, multiple sclerosis, IFN-Î³, interferon gamma

Investigating the antibacterial effect of fungal metabolites isolated from fish diet and its effect on E.coli bacteria (Research Paper)

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Introduction: In recent years, due to the resistance of pathogens against synthetic antibiotics, the study of natural plants such as essential oils and extracts of plants, animals and minerals has increased. To date, more than 200 secondary metabolites have been reported from endophytic fungi, and some of these secondary metabolites have antimicrobial properties. Therefore, the purpose of this study was to investigate the effect of antifungal metabolites isolated from fish diet and its effect on Escherichia coli bacteria.

Methods: For this purpose, samples and secondary metabolites were extracted from the molds in the diet using mycological methods, and the effect of these metabolites was evaluated using the MIC and minimal lethality tests (MBC). Then the obtained data have been subjected to statistical analysis.

Results: The results obtained in the present study indicated that the MIC of Aspergillus is 5.00 microliters/ml, the MIC of Aspergillus flavus is 5.0 microliters/ml, the MIC of Penicillium is 5.00 microliters/ml, and the MIC of Rhizopus is 11. 00 microliters per milliliter

Conclusion: According to the obtained results, it can be claimed that fungal metabolites can be used as useful antimicrobial chemical compounds to control the growth or even bacterial bacteria

Keywords: fungus, secondary metabolite, Escherichia coli, Aspergillus, Penicillium, Rhizopus

Investigating the anticancer effects of Saccharomyces bulari probiotic (Review)

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Introduction: Saccharomyces boulardii is a type of yeast that is actually a type of fungus. This yeast was once known as a specific type of yeast, but today it has been determined that it is actually a strain of Saccharomyces cerevisiae (or bread yeast). Saccharomyces boulardi is used as medicine.

Methods: The purpose of this study is to review the systematic review of past studies and current studies to investigate the anticancer effects of the probiotic Saccharomyces bularii. Articles related to the subject in EBSCOHost, Google Scholar, GetSite, ScienceDirect in English and research and review articles that To investigate the anticancer effects of Saccharomyces bularis, they were investigated and included in the study. In this review, we consider various preclinical and clinical aspects of biotherapy as basic drugs and biotherapeutic powers of their use in the treatment of some surgical enteropathies.

Results: Research results indicated that probiotics are live microbes that play an important role in protecting the host in many ways. Cancer is one of the most important causes of death worldwide. Although cancer treatment has received a lot of attention in recent years, probiotics alter the immune and cellular responses by strengthening the epithelial barrier and stimulating the production of anti-inflammatory, antioxidant and anti-carcinogenic compounds, thereby reducing the cancer burden and growth.

Conclusion: reduce The current review focuses on the different mechanisms of the role of probiotics in the prevention and treatment of cancer, so detailed human clinical studies are needed to be able to use the information for treatment.

Keywords: Saccharomyces boulardi, probiotic, anticancer, treatment, clinical

Investigating the infection of the Covid-19 virus and its effects on the lactate dehydrogenase (LDH)enzyme in the first quarter of 2019 in Tabriz. (Research Paper)

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Introduction: Corona virus is one of the group of viruses that play an important role in causing respiratory diseases. Covid-19 is one of the most important viral diseases in the current decade, which has caused a widespread pandemic in the world. This disease was first reported on December 17, 2018 from Wuhan, China, among patients with severe pneumonia symptoms.

Methods: The current study is a descriptive-cross-sectional type. In this study, the primary diagnosis of COVID-19 was made by the treating doctors. 250 blood samples were collected in clot tubes. The samples were tested for lactate dehydrogenase parameters using an autoanalyzer. .

Results: Based on the results obtained from the number of 250 samples examined, 138 cases (55.2%) of their lactate dehydrogenase levels were higher than the normal value. 50 cases (20%) had a decrease and also in 62 cases (24.8%) of the samples. No change in their value was observed.

Conclusion: In the current study, according to the measured parameter (lactate dehydrogenase) in people infected with the SARS-COVID-2 virus, it was found that this virus can have different physiological effects in different people and one of its side effects is related to the increase in the amount of lactate dehydrogenase. Therefore, it seems necessary to conduct additional studies.

Keywords: SARA, COVID, lactate dehydrogenase

Investigating the methods used in the PCR method in the laboratory diagnosis of HIV. Review (Review)

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Introduction: HIV (human immunodeficiency virus) is a virus that attacks the cells of the immune system and makes the infected person more vulnerable to other infections and diseases. Structurally, HIV consists of two strands of RNA, 15 viral proteins, and several proteins from the last host cell to be infected, all surrounded by a lipid bilayer membrane. It is estimated that 0.7% of people aged 15-49 worldwide live with HIV. AIDS is the last stage of a person's HIV infection and it is when the infection affects the entire immune system of a person. PCR (Polymerase Chain Reaction) is a laboratory method used to produce large amounts of specific DNA or RNA fragments with a particular length and sequence from small amounts of short oligonucleotide side sequences (primers). Our aim in this study is to investigate the genetic sequences in the PCR method in identifying HIV-positive people.

Methods: In this review study, using the keywords "PCR" and "HIV" and "laboratory diagnosis" as well as extracting the synonyms of the keywords from the MeSH database and searching in the articles, we searched in the PubMed and Google Scholar databases. In this study, original articles published in English between 2000 and 2021 were used. The exclusion criterion was lack of access to the full file of articles and not being aligned with the main purpose of this study.

Results: In total, according to the inclusion and exclusion criteria, 4 studies were extracted. The studied samples are divided into three groups: 1- HIV positive people who have symptoms in favor of this disease along with the final laboratory diagnoses 2- HIV negative people who are asymptomatic and their negativity was confirmed by western blot and serology methods. 3- Control panel. Age and gender did not affect the result. 2 studies investigated the gag gene, which was observed on 60 samples (28 negative samples, 19 standard panel samples, 13 pre-specified positive samples) in all positive cases, the desired band was observed on agarose gel, while in none of them No bands were observed from the negative samples. 2 studies investigated the sequence of Y181C, K103N on 161 samples. These two studies showed that both sequences are very sensitive and show excellent correlation in detecting mutations at low frequencies.

Conclusion: Conclusion: Certainly, the PCR method is the most accurate method for detecting viral infections such as HIV. The use of different genetic sequences can be useful in identifying the virus and its mutations.

Keywords: Keywords: HIV(human immunodeficiency virus), laboratory diagnosis, PCR(Polymerase Chain Reaction)

Investigating the pathway of resistance to Novobiocin in Campylobacter jejuni by using microarray analysis (Review)

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1. Department of Biology, Central Tehran Branch, Islamic Azad University, Tehran, Iran

Introduction: C. jejuni is one of the main and effective Gram-negative bacteria in food poisoning and causing gastrointestinal infections in the intestine. This bacterium is a hidden microbe in food, so-called foodborne, which is able to cause infection by penetrating the small intestine, and for this reason, it has become one of the main sources of digestive and internal infections. The main challenge in dealing with C. jejuni infections is the resistance of strains of this species to various antibiotics. Until now, various antibiotics, including Novobiocin, have failed against the infection of this bacterial strain, and today, a combination of various antibiotics such as vanomycin, polymixin-B, and acitidone is used as an antibiotic cocktail in the treatment of this disease. Investigating gene expression profiles in antibiotic resistant strains of this disease can clarify the process of resistance and pathogenicity of resistant strains and play a role in designing new drugs, prescribing antibiotics and finally eradicating C. jejuni infections be effective.

Methods: The GSE18415 dataset has been used to investigate resistance to the Novobiocin antibiotic. After downloading the data and performing the initial preprocessing and normalization, the analyzes previously reviewed on ciprofloxacin resistance and for these data are also run. Only because the microarray data is normal, the limma library is used this time.

Results: For this dataset, the design of the experiment consists of two control groups and treated with a concentration of 256 micrograms of Novobiocin antibiotic, each group having 4 samples with both Cy3 and Cy5 colors so that color bias does not occur. Also, PCA analysis and principal component analysis also show a proper separation of the samples of the control and antibiotic treatment groups, which indicates a significant change in the gene expression profile of this bacterium in response to Novobiocin and as a result, the occurrence of antibiotic resistance.

Conclusion: With the established resistance to the Novobiocin antibiotic, as it is known, generally genes related to translation pathways that generally involve ribosomes and translation factors, genes related to movement, tag synthesis and bacterial motility and response proteins are down-regulate and proteins involved in protein degradation pathways and have protease activity, genes involved in substance transfer and genes of the oxidation and reduction chain family and cytochromes are up-regulated.

Keywords: Antibiotic resistance , Campylobacter jejuni , Microarray

Investigation and identification of bacterial infectious agents isolated from patients admitted to Khorshid Medical Center in Isfahan, 2019 (Research Paper)

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Introduction: Bacterial infectious diseases can affect the quantity and quality of life. Escherichia coli are the most common bacteria that cause urinary tract infections. Due to the various mechanisms of antibiotic resistance, treatment of these infections is difficult. Therefore, choosing the right antibiotic has an effective role in controlling and improving the infection. Therefore, the aim of this study was to determine the frequency and pattern of antibiotic resistance in Escherichia coli and Klebsiella pneumoniae strains isolated from patients admitted to Khorshid Hospital in Isfahan.

Methods: This cross-sectional study was performed on 30 samples of patients admitted to Khorshid Hospital in the first 6 months of 1398. The strains were identified and identified using biochemical tests and differential culture media. The pattern of antibiotic resistance of the studied strains was investigated by disk diffusion (Kirby-Bauer). Chi-square test was used to analyze the data.

Results: Thirty samples were positive for Escherichia coli and Klebsiella pneumoniae. Of these, 50% of Escherichia coli strains and 50% of Klebsiella pneumoniae strains were isolated. The highest and lowest antibiotic resistance in Escherichia coli were Cotrimoxazole and Nitrofurantoin, respectively. Klebsiella pneumoniae strains had the highest resistance to Nitrofurantoin and the lowest resistance to Gentamicin.

Conclusion: Nitrofurantoin, Ciprofloxacin are recommended for the initial treatment of urinary tract infections.

Keywords: Escherichia coli, Klebsiella pneumoniae, Drug resistance, Isfahan

Investigation of covid 19 infection and its effect on angiotensin (Review)

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Introduction: Background: Corona viruses have positive sense single-stranded RNA and belong to the Coronaviridae family and the Nidovirades category. The disease of Covid-19 was first reported in December 2019 in the city of Wuhan, China. Being infected with the corona virus can have different physiological effects, affecting different cells, proteins and hormones, which in the present study examines the infection of Covid-19 and its effects. It is focused on angiotensin.

Methods: Materials and methods: The present study is a review study and in 2022 without time limit, Farsi and English articles were studied by searching in Civilica, Pubmed, NCBI and Google scholar databases.

Results: Discussion and conclusion: considering that angiotensin 2 is present in tissues such as lung, heart, liver, and kidney, and covid-19 virus with spike protein has a greater tendency to bind with angiotensin, the results of this study show that inhibition or control of angiotensin Reduce the possibility of damage to tissues or organs by the Covid19 virus.

Conclusion: Discussion and conclusion: considering that angiotensin 2 is present in tissues such as lung, heart, liver, and kidney, and covid-19 virus with spike protein has a greater tendency to bind with angiotensin, the results of this study show that inhibition or control of angiotensin Reduce the possibility of damage to tissues or organs by the Covid19 virus.

Keywords: Keyword: Covid19, renin, angiotensin, aldosterone, angiotensin II, 2ACE receptor

Investigation of Hematological and Coagulation Indices in Patients with Pulmonary Thromboembolism (Review)

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Introduction: Objective: Pulmonary thromboembolism (PTE) is the most common type of pulmonary embolism, which is mostly caused by venous thromboembolism (DVT), and it has increased significantly in recent years. DVT and PTE both have similar causes of disease. Inflammation is one of the causes of PTE and PTE itself leads to inflammation. The purpose of this review was to evaluate hematological and coagulation inflammatory indices in patients with pulmonary thromboembolism and compare them in two control and patient groups and the prognostic value of these indices.

Methods: Methods: Electronic databases including Scopus, PubMed and Google Scholar were searched and related articles were studied. Keywords such as Pulmonary Thromboembolism, Neutrophil to Lymphocyte Ratio, Plasma D-Dimer, and Laboratory Diagnosis were searched and related articles between 2010 and 2022 were studied.

Results: Results: Studies have shown that the neutrophil-to-lymphocyte ratio (NLR) is increased in PTE, an important indicator that can determine the state of inflammation and immune system function. In other words, in this disease, the neutrophil count increases and the lymphocyte count decreases. The importance of D-dimer in thrombotic diseases is widely known which is associated with PTE and according to the studies, its level increases. The sensitivity of NLR in the diagnosis of PTE was significantly higher than D-Dimer amount. This feature shows that the combined determination of NLR and D-Dimer has great importance for laboratory diagnosis of PTE. Other hematological inflammatory indices such as lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), C-reactive protein (CRP), albumin and white blood cell count (WBC), neutrophil (Neu) and monocyte (Mo) were all significantly higher in PTE patients; while the amount of lymphocyte (Lym) was lower compared to the control group. No change in PLT count is another hematological finding of people with PTE. Also, no significant change was observed in markers such as fibrinogen, D-dimer, and CRP in patients with corona and involved with PTE.

Conclusion: Conclusion: Although hematological and coagulation indices are critical and significantly altered in diagnosing inflammatory diseases such as PTE, only a few studies have aimed at these issues. Therefore, a greater understanding of the experiences associated with the diagnosis of this inflammatory disease is still needed.

Keywords: Keywords: Pulmonary Thromboembolism, D-dimer, platelets, C-reactive protein, neutrophil/lymphocyt

Investigation of important laboratory markers in breast cancer diagnosis (Review)

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Introduction: Cancer refers to a group of diseases that arise from the uncontrolled proliferation of some cells. Today, due to the change in lifestyle and some behaviors and patterns, this disease is considered as one of the three causes of death in the world. It is one of the most important diseases. The most common cancer among women is breast cancer. Therefore, in this review article, due to the importance of this issue, the important diagnostic markers in breast cancer disease have been investigated.

Methods: The present study is a review type, the information of which is collected from the valid databases of NCBI, PUPMED, CIVILICA and valid articles

Results: The results of the present study showed that physiological examinations, x-rays and mammography are considered as prognostic in 70% of cases. For the final diagnosis, sampling and histological and pathological examinations and diagnosis of the stage in 90% and also examination Serum markers CA15.3, CA27.29, CEA can be used in breast cancer diagnosis in 60%.

Conclusion: According to the favorable factors in breast cancer, it can be said that the methods and tests as well as the laboratory equipment are progressing rapidly, which doctors can use in order to diagnose this disease early. become me

Keywords: gene mutation, marker, breast cancer

Investigation of Long Non-coding RNA HOX A11-AS Expression in Iranian Patients with Glioblastoma (Research Paper)

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Introduction: Background and Objectives: Glioblastoma is one of the most malignant and common brain tumors, accounting for about half of all gliomas. Glioblastoma is a central nervous system tumor that originates from the glial tissue of the brain. The present study aimed to investigate changes in the expression of long non-coding RNA HOXA11-AS as a possible biomarker in glioma.

Methods: For the purposes of the present study, first, the medical records of the patients in Imam Hossein Hospital in Tehran, Iran were reviewed. The ethical considerations were respected as well; accordingly, written informed consent was obtained from the patients and the code of ethics was achieved as well. Finally, the paraffin blocks, including the biopsy of brain tumor tissue of the patients who referred to Imam Hossein Hospital during 2015-17 were collected and their degrees were confirmed by the pathologist. In total, 50 samples of grades 1 and 2 as well as 50 samples of grades 3 and 4 were examined in this research project. The RNA extraction and cDNA synthesis were performed for all the tissue samples donated by the patients. Subsequently, a specific primer and probe were designed and the expression of the HOXA11-AS gene was investigated using real-time polymerase chain reaction technique. The mean age of the subjects was 43.70Â±16.416 years. The collected data were analyzed in SPSS software (version 20) using descriptive and analytical statistics. Moreover, the expression levels of this gene in lower- and higher-grade tumor tissues were compared using the unpaired samples t-test.

Results: Based on the results, the tumor samples with grade three and four underwent a 2.76 fold increase in expression (fold change), compared to tumor samples with grade one and two. This difference was statistically significant.

Conclusion: Based on the findings, it can be concluded that the expression of the HOXA11-AS gene has a significant positive relationship with the degree of disease (P=0.0002).

Keywords: Glioblastoma; HOXA11 protein; Long non-coding; RNA; Xenopus.

Isolation of Clostridium perfringens toxinotype G from antibiotic-associated diarrhoeal (AAD) patients (Research Paper)

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Introduction: Different Clostridium perfringens (C. perfringens) toxinotypes can be caused gas gangrene, antibiotic-associated diarrhoea (AAD), food-borne disease and etc. in humans. Toxinotype F reported as the cause of 15% of AAD or sporadic diarrhoea (SD) cases, while the association of toxinotype G with this disease was not reported. Here, the isolation of C. perfringens toxinotype G from AAD patients was reported for the first time in the hospitalized patients in Kerman province of Iran.

Methods: A total of 151 stool specimens from AAD patients were investigated for C. perfringens and the suspected isolates were analyzed for the cpa, cpb, etx, iap, cpe, and netb toxin genes by the multiplex and simplex PCRs and toxinotyped by the existence of each gene.

Results: C. perfringens isolation ratio was 28.5% (43/151) and this ratio for toxinotype G was 1.3% (2/151). The cpa genes was detected in all C. perfringens isolates (n=116). The netB gene was detected in two isolates (1.7%), thus they belonged to toxinotype G. These were isolated from two female hospitalized patients (9 and 39 years old) with AAD in infectious pediatrics and infectious wards. They had a history of long-term use of cephalosporin and metronidazole antibiotics. The older patient had AAD signs included fever, abdominal pain, intestinal cramps, nausea, vomiting, colitis, and diarrhoea, whereas the younger patient showed only diarrhoea.

Conclusion: Necrotic enteritis B-like toxin (NetB) is a recently discovered toxin that is produced by C. perfringens toxinotype G strains. Toxinotype G is associated with avian necrotic enteritis and it is not known as a diarrhoeal agent in humans, routinely. Remarkably, the isolation of C. perfringens type G in this study suggesting the importance of this type in C. perfringens-associated AAD or SD cases, for the first time.

Keywords: Isolation, Clostridium perfringens; Toxinotype G; Antibiotic-associated diarrhoea (AAD); Sporadic di

Isothermal amplification of syrD gene as a tool for detection of pseudomonas syringae pv. Syringae (Research Paper)

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Introduction: Pseudomonas syringae pv. syringae is one of the most important bacterial pathogens infecting stone fruits throughout the world. It can lead to diseases in more than 180 plant species such as fruit trees, annual, and perennial plants. P. syringae damages are determined by the growing region of stone fruits and host plants. Biochemical assays such as LOPAT (Levan production, oxidase production, pectinolytic activity, arginine dihydrolase production, tobacco hypersensibility) and GATTa (Gelatin liquefaction, aesculin hydrolysis, tyrosinase activity, tartrate utilization) are common tools for detecting this pathogen. Serological tests and culturing on King B (KB) medium were also used to detect/isolate this bacterium. Nevertheless, mentioned methods are not enough accurate to differentiate the strains. On the other hand, PCR-based techniques are sensitive and efficient in detecting plant diseases. However, these techniques are not practicable for those researchers who do not have access to a thermal cycler. In the current study, we have used Loop-mediated isothermal amplification (LAMP) as a fast, highly specific tool to couple with a target.

Methods: 65 bacterial canker samples taken from stems, buds, twigs, and shoots were collected from gardens of apricot (Prunus armeniaca) fruits. A total of 65 bacteria were isolated from 65 infected parts of apricot trees. The 65 samples were divided into two groups; one cultured on a King B medium for detection of the strains. For this purpose, 65 samples were kept in nutrient broth containing 20% glycerol at â˜85â—¦C and cultured on KB at 25â—¦C for 48 h before usage. After 24-48 h of incubation, fluorescence on KB was observed under UV light. Another group was used for genomic DNA extraction. Genomic DNA was extracted and PCR was carried out for syrD (Syringomycin D). PCR amplification reactions were performed in a C1000 Touchâ„¢ Thermal Cycler. The amplified products were stained by SYBR Gold after running on the agarose gel. Equal dilutions were prepared for both LAMP and PCR products and run on the electrophoresis gel to perform the sensitivity assay of PCR and LAMP products. To remove the electrophoresis step optionally and direct visualization of PCR products by SYBR Gold, it was directly added to the PCR products in the microtube to be visualized by a UV transilluminator. To eliminate the electrophoresis step optionally and direct visualization of LAMP products by SYBR Gold, it was directly added to the

productâ€™s microtubes to be visualized by a UV transilluminator. The specificity of the LAMP with 60Â°C and PCR methods performed with an annealing temperature of 55Â°C. Similar dilutions were prepared for both LAMP and PCR products to compare the PCR and LAMP productsâ€™ sensitivity. To confirm whether Pseudomonas syringae pv. syringae was identified correctly, the suspected samples were cultured on KB medium at 28Â°C. After 48-72 h of incubation, Fluorescence on Kingâ€™s medium B was observed under Ultra Violet light.

Results: SyrD gene amplification using LAMP and PCR primers resulted in molecular detection. The results indicated that the direct add-on of SYBR Gold in microtubes was 100 times more sensitive than electrophoresis in direct visualization. The results revealed that the sensitivity of gel-free staining is 10 times greater than that of gel-based staining in direct visualization. The findings indicated that the bacterium has been identified correctly. 20 Pseudomonas syringae strains from 65 ones were fluorescent on the KB medium.

Conclusion: The results confirmed that molecular detection (LAMP, PCR, and electrophoresis) assays have more efficiency in comparison to direct culture (King B medium).

Keywords: Pseudomonas syringae pv. Syringae, syrD gene, King B medium, PCR, LAMP

Management and prevention of red cell alloimmunization in pregnancy (Review)

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Introduction: If the mother is RhD negative and the fetus RhD positive, the mother may react to fetal blood cells in her circulation by developing a template for producing anti-D antibodies. Rh Immune Globulin (RhIg) can be given to RhD-negative women to prevent sensitization and hence prevent HDN. The objective of this systematic review management and prevention of the red cell in all immunized pregnancy.

Methods: We searched four computerized databases for studies that described the treatment or prevention of alloimmunization in pregnancy (PUBMED, MEDLINE, EMBASE, Cochrane Database of Systematic Reviews) from 2017 to July 2021.

Results: Although the data suggested when women receive anti-D at 28- and 34-weeksâ€™ gestation, a reduced incidence of immunization during pregnancy (0R O.44, 95% CI 0.18-1.12), after the birth of a Rhesus-positive infant (OR 0.44, 95% CI 0.18-1.12), and within 12 months after the birth of a Rhesus positive infant (OR 0.22 95% CI 0.05-0.88), none of these differences were statistically significant. In the trial, which used the larger dose of anti-D (100ug; 500IU), there was a clear reduction in the incidence of immunization at 2-12 months following birth in women who had received Anti-D at 28 and 34 weeks (OR 0.22 95% CI 0.05-0.88). No differences were observed in the incidence of neonatal jaundice.

Conclusion: Anti-D, given within 72 hours after childbirth, reduces the risk of RhD alloimmunization in Rhesus-negative women who have given birth to a Rhesus-positive infant. However, the evidence on the optimal dose is limited.

Keywords: Rh Blood-Group System, Neonatal Alloimmune, pregnancy

Molecular Characterization of toxication agent Staphylococcus epidermidis strains in the clinical sample in Isfahan (Research Paper)

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Introduction: Coagulase-negative Staphylococci and especially Staphylococcus epidermidis are posed as an emerging cause for the occurrence of hospital infections. The present investigation was done to study the pattern of antibiotic resistance and the prevalence of virulence genes associated with toxication agent outbreaks in Isfahan

Methods: During six- months, 60 clinical specimens to isolated from strains of Staphylococcus epidermidis were screened. Following identification strains, MRSE isolates were isolated by PCR method and, then the antibiotic resistance pattern of them was determined by Kirby â€“ Bauer method. The presence of the sea, seb, sed and, sei genes was analyzed by PCR

Results: 45 isolates of Staphylococcus epidermidis were isolated from 60 samples, 30 isolates (66.6 percent) were MRSE. MRSE isolates exhibited the highest rates of resistance to penicillin (80 percent), and cefoxitin (56.6 percent), while they showed the lowest resistance to levofloxacin (13.3 percent), and rifampicin (6.6 percent). The prevalence rate of Moreover, the frequency of enterotoxin genes sea, seb, sed and, sei was 60 percent, 63.3 percent, 13.3 percent and, 76.6 percent respectively, in the isolate.

Conclusion: In this study, the level of gene expression and antibiotic resistance was high. Therefore, it is necessary to investigate these strains in order to control infection.

Keywords: toxication agent-Staphylococcus epidermidis-clinical sample

Molecular Detection of Borrelia Spp. from ticks in sheep and goats herd inWest Azerbaijan province, Iran (Research Paper)

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Introduction: Ticks are ecto-parasites that feed on humans as well as wild and domestic animals. Ticks are also vectors for distributing viruses, protozoa, and bacteria, e.g., Borrelia, Coxiella, or Rickettsiales. borreliosis is also a tick-borne zoonotic disease. The disease is caused by the spirochete and the tick bite considered as the most common mode of transmission. Borrelia spp., belong to the best studied tick-borne pathogens. These spirochetes are Gram-negative, motile, spiral-shaped prokaryotes with endo-flagellae. They can be divided into two major groups: 1) Lyme borreliosis (LB) and 2) the relapsing fever (RF), they are groups of spirochetes; named after the diseases occurred. LB group spirochetes form a bacterial genospecies complex named Borrelia burgdorferi sensu lato, and the RF group of spirochetes includes the emerging pathogen. Etiological agents of RF borreliae contain more than 20â€¯species, e.g., B. hermsii in North America and B. duttonii in Afica. The main vectors of RF borreliae are soft ticks of the genus Ornithodoros. However, some RF borreliae are transmitted by hard ticks, such as B. lonestari, B. miyamotoi (Ixodes) and B. theileri (Rhipicephalus).

Methods: Ticks were collected from all parts of the body surface of sheep and goats in west Azerbaijan providence during the spring and summer of 2022. Samples of ticks were collected one at a time in sterile glass bottles containing 95% ethanol, 4% methanol, and 1% pyridine. Then, These samples were transferred to the Parasitology Laboratory at Urmia University, Faculty of Veterinary Medicine for the identification of tick species. the molecular identification of bacteria were don in bacteriology laboratory by nested-PCR method for detection of 16S rRNA ,5S-23S and ospA genes. Adult ticks were identified using a loupe microscope and reliable diagnostic keys. In order to extract DNA in Borrelia, ticks were initially dehydrated on clean paper in the presence of airflow after being withdrawn from 70% ethanol. After that, we used a commercially available DNA extraction kit (DNA Extraction Kit, MBST, Iran) to extract DNA. The DNA samples were frozen at -20 â„ƒ until the molecular testing was finished.

Results: The positive samples for Borrelia spp by using 16S rRNA ,5S-23S and ospA gene was 15.60% ,10.63% and 2.83% respectively. Moreover, the results of the molecular prevalence of Borrelia spp DNA was presented 69 (n=141; 15.6%; 95%CI: 10.5%-22.4%) based on 16SrRNA 42 (n=141; 10.6%; 95%CI: 6.5%-16.8%) positive on 5S-23S genes and for ospA 9(n=141; 2.8%; 95%CI: 1.1%-7.0%) depending on genes respectively (Table 1). Table 1: Prevalence of Borrelia spp., in tick samples from West Azerbaijan in Iran assessed by the nested-PCR Number of ticks Ticks species No. Genus

16srRNA 5s-23s ospA p.v 141 Rhipicephalus sanguineus 98 Male 13/98 10/98 2/98 (13.26%) (10.20%) (2.0%) P<0.05 43 Female 9/43 5/43 2/43 (20.93%) (11.62%) (4.6%) Total 141 22/141 15/141 4/141 (15.60%) (10.63%) (2.83%)

Conclusion: This study provides the first study regarding the prevalence of Borrelia spp. within hard ticks collected from West Azerbaijan presence of Iran. Further application of this molecular tool to investigate the genetic variability among Borrelia spirochetes detected in different vector ticks and reservoir hosts may facilitate our understanding of the significance of genetic diversity in relation to the epidemiological features of Borrelia spirochetes in West Azerbaijan, Iran.

Keywords: PCR, Borrelia Spp., Sheep, Goat, West Azerbaijan

Molecular identification of Ehrlichia in the blood and urine of horses in northern Iran (Research Paper)

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Introduction: The Anaplasmataceae family is responsible for the newly discovered zoonotic disease ehrlichiosis. Equine ehrlichiosis is indeed a seasonal disease of horses that was initially detected in 1969 by Gribble in horses in northern California. Ehrlichia is a genus of tick-borne bacterial diseases that infect people, domestic and wild animals, and are mainly made up of Gram-negative, obligate intracellular bacteria. Ehrlichia is a genus in the Rickettsiales order with six identified species: Ehrlichia canis, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris, Ehrlichia ruminantium, and Ehrlichia minasensis. Ehrlichia equi is the main agent. The equine species, especially donkeys, are the natural hosts of E. equi. Any age of horse is vulnerable, however clinical symptoms are less severe in horses under the age of 2 to 3 years. Agents from the genera Neorickettsia (also known as N. risticii) and Anaplasma have mostly been linked to equine ehrlichiosis (i.e., A. phagocytophilum). Rhipicephalus microplus, Amblyomma hebraeum, Hyalomma marginatum, and Haemaphysalis have been found to parasitize horses among the tick species that potentially vector this bacterium, implying that infection by E. minasensis could further transfer to other hosts, such as equines. The most noticeable symptoms of acute granulocytic ehrlichiosis in both dogs and horses are high temperature and exhaustion, usually accompanied by inappetence. Furthermore, horses frequently suffer distal limb edema, ataxia, and are hesitant to move. particularly in comparison to serological approaches, the specialized identification of granulocytic Ehrlichia DNA in blood and urine utilizing PCR method is extremely sensitive and specific, and active infectious disease caused by this pathogen may be swiftly recognized and treated attributed to the ability to trace the parasite. The PCR test was performed four days after the illness began

Methods: In the summer of 2022, 400 horse samples (200 serum and 200 urine) were gathered at random in three distinct geographical districts of Mazandaran province. Six races were represented in the population examined. The Caspian horse was the most common, accompanied by Turkmen, Kurd and Dukhon, Karabagh, and Arabian horses. Mares (n=180) and stallions (n=220) were the gender distribution. The animals were categorized into three age groups: (less than 6) (170 individuals), (6-12) (140 people), and above 12 years old (80 people). Each horse had a 10 ml blood sample taken from the jugular vein and placed in dry tubes without EDTA. After centrifugation (10 minutes, 3000 g), the serum was recovered, and catheters were used to aseptically take urine samples from horses. The urine

sample was then transferred into 10 ml collection tubes (Tarsons). The gathered samples were transported to the microbiology lab in sterile tubes that had been kept on ice. The samples' genomic DNA was extracted using a commercial DNA extraction kit (Favogen, Taiwan), and following extraction, the samples were kept at -20 Â°C. Nano Drop analyzed the DNA that was extracted in terms of both quality and quantity (Termo Scientific, USA). Additionally, 16s rRNA gene primers were employed for the first identification of Ehrlichia. The primer was created using Amplifx software (version 1.7.0) for the 16s rRNA gene's nesting stage. Using the chi square test and SPSS software, the acquired data were statistically evaluated (SPSS Inc., Chicago, IL). P 0.05 was regarded as a significant value

Results: Forty samples (10%) of the 400 collected blood and urine samples were positive for Ehrlichia after PCR amplification of a 357 bp fragment of the 16s rRNA gene. A total of 12 (6%) and 28 (14%) urine and blood samples were positive for Ehrlichia, respectively. The presence of Ehrlichia in the blood and urine of the test subjects was statistically significant. A statistical analysis was performed in this study regarding animal age, gender, and breed. According to the data based on age, gender, and race, the Caspian horse race has the greatest amount of contamination. This disparity may be attributable to the small number of samples collected from the Caspian horse race

Conclusion: In the northern part of Iran, ehrlichiosis should be regarded as a serious health risk, and tick and cattle infections should be continuously monitored. The prevalence of ticks and stray dogs close to the horse shelter in the region is likely one of the primary causes of Ehrlichia in the horses.

Keywords: Ehrlichia, Caspian horse, Mazandaran, 16s rRNA

Mutations in Thalassemia Carrier Couples: The Importance of Prenatal Diagnostic Tests (Research Paper)

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Introduction: Thalassemia carrier couples play an important role in increasing thalassemia patients. The study of thalassemia genotypes in carrier couples is also effective in improving genetic counseling for them. The aim of this study was to investigate the prevalence of thalassemia mutations and genotypes in couples.

Methods: This cross-sectional study was performed on 241 couples who were suspected of thalassemia from April 2018 to March 2020 in Lorestan province. Statistical analysis of data was performed using SPSS software 16.0 (SPSS Inc., Chicago, IL, USA). Online tools such as www.ithanet.eu/db/ithagenes and http://globin.bx.psu.edu/ hbvar/menu.html were also used to match patients' mutations with known cases.

Results: IVSII-1 (G>A), CD36-37 (-T), IVSI-110 (G>A), --Med, and Î±3.7 were the most common mutations in the beta and alpha genes, respectively. IVSII-1 (G>A) Î²0/Î² (26.1%), CD36-37 (-T) Î²0/Î² (21.1%), and IVSI-110 (G>A) Î²0/Î² (10.3%) genotypes were the most common in women. The frequency of these genotypes in men were 24.8%, 28.6%, and 12.8%, respectively. Among alpha thalassemia carriers, the Î±3.7Î±/Î± Î± genotype had the highest frequency among women (3.7%) and men (5.3%). Alpha and beta-thalassemia were 15 and 13 times higher in related women and 18 and 9 times higher in related men than non-related ones, respectively. This difference was statistically significant ($p < 0.001$). In addition, 12.8% of fetuses were thalassemia major, 31.9% beta thalassemia minor, and 10.3% normal.

Conclusion: Thalassemia screening in related couples plays an important role in reducing thalassemia major infants.

Keywords: Cross-Sectional Studies, Diagnostic Tests, Mutation, Thalassemia, Genotype

NETosis activation of Factor VII-activating protease (FSAP): A predictive role in SARS-COV-2 infection thrombosis (Review)

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Introduction: Multiple factors such as inflammatory cytokines and neutrophil extracellular traps (NETs) formation, NETosis, are involved in coagulation activation(1, 2). During inflammation and viral infection NETs actively released from neutrophils into the extracellular space(3). NETs act as a part of innate immunity, and thought to be responsible for inflammation and host defense(4). Pathogens such as respiratory viruses, induce NETs formation that physically immobilize pathogens and kill the microbes(5, 6). The NETosis contributes in sepsis and acute respiratory distress syndrome(ARDS) pathogenesis and causing vascular tissue damage , thrombosis, multiorgan failure and death(7, 8). Increased NETs formation correlates with COVID-19 related ARDS and is a potential biomarker for the disease severity(5, 9). SARS-COV-2 may directly infect monocytes/ macrophages and tissue factor (TF) expression/release from these cells that may play a critical role in the development of COVID-19 coagulopathy (10). NETs particularly by histone component lead to platelets adhesion and activation and may bind to von Willebrand factor (VWF) and fibrinogen(11). Neutrophils and platelets release microparticles that contain TF and to be trapped by NETs, TF has been detected in NETs inside venous thrombi in vivo as a factor of induce thrombosis (12, 13). NETs used several pathways that support fibrin formation, and enhance platelets activation and thrombosis by involvement in fibrinolysis inhibition, activation of contact-pathway of coagulation, and triggering coagulation initiation(14). NETs induce tissue factor pathway inhibitor (TFPI) degradation and increase blood coagulation(15). Additionally, to activation of extrinsic pathway, NETs promote intrinsic coagulation cascade by activation of FXII by nucleic acids and phosphates and may inhibit fibrinolysis by tissue plasminogen activator(tPA) inhibition and increase fibrin formation(16). FSAP is a serine protease produced mainly by liver and is present in the circulation in the form of zymogen (pro-FSAP). Histones and nucleosomes released from NETs can activate circulating pro-FSAP. The released histones degraded by FSAP and histone cytotoxicity towards endothelial cells was neutralized by FSAP. This activation of FSAP may be important in diminishing the cytotoxic effect of histones, thus limiting the damaging effect of NETosis (17). The first initially known described roles of FSAP was involvement in activation of FVII, fibrinolysis as an activator of pro-urokinase (18).

Methods: To provide a better prospect representing the prognostic value of alteration in NETosis and coagulation pathway in COVID-19, we searched national library of medicine Medline/PubMed and google scholar by using the keywords â€œcoagulationâ€• OR â€œcoagulopathyâ€• AND â€œCOVID-19â€• OR â€œcoronavirus 2019â€• OR â€œ2019-nCoVâ€• OR â€œSARSCoV-2â€• AND 'NETosis" between December, 2019 and the time of our analysis (i.e., May 25, 2021), without any restriction.

Results: FSAP bounds to NETs, colocalization of FSAP-NETs was reported in coronary thrombi from patients with acute myocardial infarction (19). Additionally, FSAP can inhibit TFPI and increase the chance of thrombosis. Increased FSAP activity is demonstrated in pregnancy(20), the use of oral contraceptives(21), deep vein thrombosis (19) or coronary heart disease as compared with health controls (22). More recently reports have been shown FVII is a poor FSAP substrate and TFPI was identified as a novel substrate and impaired FSAP modulation of TFPI levels was suggested as an explanation for the thrombus formation observed in FSAP deficient mice (FSAPâˆ’/âˆ’) (23). RNA and DNA components of nucleosomes could promote FSAP auto-activation, and inhibition of TFPI may contribute to prothrombotic actions and support arterial thrombosis (22, 23). COVID-19 patients seem especially prone to lead excessive NETs release, disease severity and survival parallel increasing markers of NETs formation (6, 9). Raised protein levels of FSAP was reported in the lungs of patients with ARDS (24). This may represent a novel pathological mechanism which contributes to pulmonary extravascular fibrin deposition and may also modulate inflammation in the acutely injured lung via hemostasis independent cellular activities of FSAP(18).

Conclusion: Because of the similarity of ARDS in COVID-19 infection with other infectious respiratory syndromes that is related to dysregulated immune response, releasing of inflammatory cytokines, and development of pathogenic microvascular thrombi, NETs formation may induce thrombosis and activate FSAP as a thrombosis inducer that may have a predictive role in SARS-COV-2 thrombosis, using the NETs inhibitors may dampen the severity of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection.

Keywords: Thrombosis, SARS-CoV-2, COVID-19, Angiotensin converting enzyme, NETosis,

neuroinflammatory chemokines in COVID-19 neurologic complications (Review)

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Introduction: The neurologic complications in COVID-19 patients comprise symptoms including depression, anxiety, muscle pain, dizziness, headaches, fatigue, and anosmia/hyposmia that may continue for months. Recent studies have been demonstrated that chemokines have brain-specific attraction and effects such as chemotaxis, cell adhesion, modulation of neuroendocrine functions, and neuroinflammation. CCL11 is a member of the eotaxin family that is chemotactic agents for eosinophils and participate in innate immunity. Eotaxins may exert physiological and pathological functions in the central nerve system, and CCL11 may induce neuronal cytotoxicity effects by inducing the production of reactive oxygen species (ROS) in microglia cells.

Methods: To provide a better prospect representing in ccl11 chemokine and and neuroinflammation in COVID-19, we searched national library of medicine Medline/PubMed and google scholar using the keywords "CCL11 "AND â€œCOVID-19â€• OR â€œcoronavirus 2019â€• OR â€œ2019-nCoVâ€• OR â€œSARSCoV-2â€• between December, 2019 and the time of our analysis (i.e., Agust, 2021), without any restriction.

Results: Plasma levels of CCL11 elevated in neuroinflammation and neurodegenerative disorders. COVID-19 patients display elevations in CCL11 levels.

Conclusion: As CCL11 plays roles in physiosomatic and neuroinflammation, analyzing the level of this chemokine in COVID-19 patients during hospitalization and to predicting post-COVID-19-related neurologic complications may be worthwhile. Moreover, using chemokine modulators may be helpful in lessening the neurologic complications in such patients.

Keywords: CCL11;Neuroinflammation; COVID-19; Eotaxin-1; SARS-CoV-2.

Neutrophil to lymphocyte ratio in COVID-19 prognosis (Review)

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Introduction: Coronavirus disease 2019 (COVID-19) is a global public crisis. Clinical presentation can range from the absence of symptoms to multiple organ failure and death. Several management guidelines were introduced, however, their effectiveness is still debated. Therefore, the presence of prognostic factors is necessary to predict which patients require more aggressive treatments.

Methods: Considering the wide spectrum of possible clinical manifestations and the potential variation during the evolution of the disease, the diagnosis of hyper-inflammatory state is the first step in identifying patients so that we can treat them in the most appropriate way according to the stage of the disease. Circulating biomarkers of inflammation play a predominant role in this regard. A simple blood test would be required to assess the inflammatory status and to help predict the outcome of patients. Apart from the well-known biomarkers of inflammation, such as C-reactive protein (CRP), serum amyloid A, interleukin (IL)-6, procalcitonin (PCT), the parameter of neutrophil to lymphocyte ratio (NLR) have been recently suggested to predict the disease severity or prognosis of COVID-19 patients. Specifically, NLR is a simple ratio obtained by dividing the absolute count of neutrophils from lymphocytes. Notably, neutrophils and lymphocytes are closely related to the pathophysiology of COVID-19. A number of recently studies have reported that neutrophilia, lymphopenia, and NLR increase are strongly associated with disease severity and mortality from COVID-19 and can be useful in distinguishing severe from non-severe cases of COVID-19 patients. In 2020, Qin C et al. reported that peripheral blood T-lymphocyte levels were significantly reduced, while neutrophil levels were augmented in severe cases of COVID-19 compared to mild cases of COVID-19. Another report done in 2020 showed that the severity rate in patients with elevated NLR was higher, but the recovery rate was lower than the cases with lower NLRs.

Results: All these data show that NLR is a reliable indicator to determine disease severity in COVID-19.

Conclusion: These findings provide evidence that NLR is a cheap and useful prognostic marker in distinguishing severe from non-severe patients with COVID-19.

Keywords: Coronavirus disease 2019 (COVID-19), Prognostic, Neutrophil to lymphocyte ratio (NLR)

New Endocrine Therapy Methods for Breast Cancer Patients with Low Positive ER (Review)

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Introduction: Cancer is a genetic and epigenetic disease so epigenetic mechanisms regulate its many aspects. As a heterogeneous clinical and biological disease, breast cancer is the most common malignancy in women worldwide, which includes various conditions. Since 2/3 of breast cancers have hormone receptors. The test of hormone receptors (HRs) is mainly the goal of treatment choices for patients with this type of cancer. Patients show better performance with treatment methods such as endocrine therapy (ET), compared to methods such as chemotherapy and immunotherapy. The estrogen receptor ER and progesterone receptor PR test was published for the first time in 2010 in America to improve analytical performance and diagnostic accuracy in the early symptoms of breast cancer and its diagnosis. The status of estrogen receptors plays a key role in clinical decisions. Clinical implications and prediction of outcomes for patients with invasive breast cancer IBCs and, ER-mediated signaling play a significant role in tumorigenesis, tumor progression, and treatment resistance. IHC immunohistochemical test is an accurate diagnostic method for ER. Tumors that are more than 10% positive by nuclear staining with IHC are called ER-positive, which comprise 79-84% of patients eligible for endocrine therapy. Patients with ER staining < 1% are called ER-negative, and patients with such tumors have to use chemotherapy, which leads to worse results. However, tumors of 3 to 9% of patients with ER staining are in the 1 and 10% range, which are called ER Low Positive. This category of patients usually has larger cancerous tissues than the carcinomas of ER-positive patients.

Methods: Relevant articles and updated information were extracted from the World Health Organization (WHO) and reliable scientific databases such as PubMed and Google Scholar search engines.

Results: In the guidelines of 2020, there is limited data on improvement in endocrine therapy for ER-positive people between 1 and 10%. This group of patients is a significant portion of the whole population. Studies have shown that there is a tendency to resistance to ET in this group of patients. Although low ER expression has a lower prognosis in patients with breast cancer, still, endocrine therapy is recommended. However, ET alone cannot have any effect on this group of patients. Patients with low-positive ER who received ET

for more than three years had a higher residual disease-free DFS than those who received ET. New studies have shown that drugs including aromatase inhibitor or tamoxifen sequentially followed by another aromatase inhibitor (AI/T+AI) along with ET can be an effective therapeutic alternative in patients with low positive ER. Patients treated with AI/T+AI can also benefit from adjuvant radiotherapy and trastuzumab. Other results have shown that patients with low ER-positive breast cancer who received sequential tamoxifen monotherapy followed by an AI had more favorable breast cancer-specific BCSS residuals than those who received ET alone. However, patients treated by AI/T+AI had no survival advantage. Other results have shown that the behavior and response to treatments for ER-low breast cancer are similar to treatments for triple-negative TNBC breast cancer, which accounts for 1/5 of breast cancers.

Conclusion: There has been no specific standardization for the treatment methods of breast cancer patients with low positive. In addition, in the proposed new treatments such as AI/T+AI, the side effects of tamoxifen and AI such as endometrial hyperplasia, and embolism in the coagulation system should be considered in the long term. Considering the similarity of the treatment of these patients along with other different types of cancer, our hypothesis is that the previously investigated methods along with the new methods with a larger sample size and higher accuracy tests on ER as well as on PR can lead to more consistent results in terms of the treatment of these patients.

Keywords: ER Low Positive / Breast Cancer / Estrogen Receptor / Progesterone Receptor/ Endocrine Therapy

No Human Respiratory Syncytial Virus but SARS-CoV-2 in children under 5 years old referred to Children Medical Center in 2021, Tehran, Iran (Research Paper)

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Introduction: Acute respiratory infections (ARIs) are one of the leading causes of illness and death among community members worldwide. Viral infections are the most common agents estimated to be involved in these patients. This study aimed to investigate the prevalence of human Respiratory Syncytial Virus (hRSV) and Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) among children with ARIs.

Methods: This study evaluated the presence of SARS-CoV-2 and hRSV infection in 168 throat and nasopharyngeal swab samples using Real-time PCR. All samples were collected from children under five years old with ARIs who attended in childrenâ€™s Medical Center, Tehran, Iran and sent to the Iranian National Influenza Center with appropriate conditions in 2021. Chi-square and Fisherâ€™s exact tests were used for comparison of the data of the prevalence of hRSV and SARS-CoV-2 infections among children.

Results: Of the 168 patients examined, 95(56.5%) were male and 73 (43.5%) female Out of the 47 (28%) were younger than one years and 121 (72%) cases were 1 to 5 years old. The most common clinical manifestation of patients was cough (78%), nausea (31%), diarrhea (27%) and fever (18%). Among 168 patients, no hRSV was detected, while the SARS-CoV-2 genome was identified in 16 (9/5%) patients. Among 16 positive cases of SARS-CoV-2, 8 (50%), 2 (12%) and 6 (38%) were under 1 years old,1 to 3 years old and 3 to 5 years old respectively.

Conclusion: This study was performed at cold months of the year but due to COVID-19 pandemic and adherence to health protocols, school closures and virtual classes, no cases of hRSV infection were identified.

Keywords: Respiratory Tract Infection, SARS-CoV-2, hRSV, Prevalence

Novel frameshift variant in the PCNT gene associated with Seckel/ Microcephalic Osteodysplastic Primordial Dwarfism Type II (SCKL/MOPDII) (Research Paper)

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Introduction: MOPD II (MIM 210720), as a rare autosomal recessive disorder, characterized by severe prenatal and postnatal growth retardation, microcephaly, skeletal dysplasia, severe teeth deformities, and typical facial features. The phenotype is caused by recessive loss of function mutations in the centrosomal pericentrin (PCNT; NM_006031.5) gene on chromosome 21q22.3, predominantly owning to frameshift, splice site and stop mutations. Additionally, biallelic mutations in the PCNT gene were shown to underlie some SCKL syndrome (MIM 210600) cases, while the majority of SCKL cases were occurred by mutations in ATR gene.

Methods: We evaluated the clinical features of a 5- year old Iranian boy with MOPDII. Subsequently, next- generation whole exome sequencing (WES) was performed to investigate genetic profile, which is followed by sanger sequencing to confirm the WES results.

Results: The patient presented with severe failure to thrive, short stature, microcephaly, typical craniofacial features, teeth deformity, and other suggestive characteristics of MOPD II. MOPD type II was confirmed based on a novel pathogenic true homozygous frameshift variant in the PCNT gene c.3836_3837ins17 | p. Arg1279Serfs*44, which was inherited from his healthy related- heterozygous parents.

Conclusion: Our investigation pinpointed a novel PCNT mutation associated with MOPD II, which is extended the mutation spectrum of the PCNT gene and improved our understanding of the molecular basis of MOPD II, especially to better perceiving the variable expressivisity. Moreover, establishing the correct diagnosis in an individual with MOPD II is therefore essential for adequate preventive disease management and determining high risk indices for cerebral vessel insults, cardiomyopathy and early onset type 2 diabetes.

Keywords: MOPD II, PCNT gene, growth retardation, microcephaly, novel frameshift mutation

oxidative stress during Virus infection (Review)

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Introduction: Some viruses are responsible the proliferation and death of host cells by affecting mitochondria and production of reactive oxygen species (ROS). Dysfunction of mitochondria especially in the pathway of Adenosine 5â€²-triphosphate (ATP) production leads to the production of free radical oxygen. In addition, the endoplasmic reticulum (ER) can also trigger oxidative stress. Oxidative stress is created by viruses that damage the body through regulating the activity of the immune system, increasing integration rate due to chromosomal instability and etc. This can result in a variety of cancers and problems such as encephalitis and organ dysfunction. A review study was carried out on the effects of oxidative stress on cells damage on 10 viruses, including HPV, EBV, SARS-CoV-2, Influenza(A), Rabies, Zika, Dengue, HSV-1, HIV-1 and Mumps.

Methods: Animal and human studies related to brain-damaging viruses and oxidative stress from 1990 to 2022 were extracted and analyzed from reliable scientific databases such as Pubmed and Google Scholar.

Results: The results showed that the damage caused by the decrease of antioxidants in the body, especially superoxide dismutase (SOD) and glutathione peroxidase (GPO) are very critical for brain damage. Viruses such as Zika, SARS-CoV-2, HIV-1, influenza-A, EBV, mumps, rabies, dengue, herpes simplex-1 and HPV play a critical role in the imbalance in the antioxidant system due to increasing Oxidants in cell which can lead to oxidative stress and because of that, damage to different cells leads to organ dysfunction such as brain.

Conclusion: Considering the various body injuries caused by the oxidative stress which is induced by viruses, we can obtain antioxidants through diet to decrease oxidative stress which is responsible for many damages caused by viruses and new approaches must go under investigation to pave the path of the exact mechanism of oxidative stress in virus pathogenesis.

Keywords: Cancer, oxidative stress, HPV

Phenotypic and Genotypic Diagnosis of Carbapenem-Resistant Enterobacteriaceae (Review)

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Introduction: The resistance to carbapenem among carbapenem-resistant enterobacteriaceae (CRE) is the key factor in the lack of definitive and effective treatment for widespread infections with enterobacteriaceae. Moreover, the high prevalence rate of CRE in contaminated environments indicates the necessity of timely screening of infected patients. Hence, identification of enterobacteriaceae based on molecular and biochemical methods is an appropriate therapeutic-epidemiological priority.

Methods: In the analysis of the results of selected research articles of the last decade in the databases of PubMed and Google Scholar, the efficiency of phenotypic tests used include disk diffusion, multi or combined disks, chromogenic media, immunochromatography, mass spectrometry, modified hodge test, carba NP , inactivation of carbapenem (CIM) and its modified forms and genotypic techniques especially polymerase chain reaction, whole genome sequencing and biochips such as microarrays were evaluated.

Results: Over time, under the supervision of clinical and laboratory standard institute, phenotypic methods with high sensitivity and accuracy namely msupercarba chromogenic medium, mCIM/eCIM assay, K-SeT rapid tests (Commercial Kits), ionization technique and specific enzyme inhibitor discs to identify carbapenemase hydrolyzing carbapenems or verification of the results of preliminary tests based on the change in pH, color and growth zone of the medium have been confirmed. However, genotyping methods based on bacterial DNA sequences have the validity and speed with remarkable accuracy compared to visual methods and in epidemiological emergencies, they are an important diagnostic option. The need for cost, special equipment and specialized personnel are obstacles to the use of genotyping methods for extensive clinical requires.

Conclusion: The current limitations guide CRE detection methods toward potential phenotypic tests for daily clinical situations. Benefiting from genetic detection mechanisms in research to control CRE infections, such as how to inhibit active vertical transfer of carbapenemase coding genes along with other drug resistance genes between bacteria, development of economic techniques and synergistic effect of two or more phenotypic or genotypic methods are the diagnostic challenges in the protocol of CRE-related infectious diseases.

Keywords: Enterobacterial infections; carbapenem; drug resistance genes; beta-lactamase; phenotypic detection

Phytochemical compounds and antifungal activity of aqueous and alcoholic extracts of artichoke herb (Cirsium vulgare) on Aspergillus flavus (Research Paper)

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Introduction: Given that one of the main problems today with pathogenic microorganisms is their increased resistance to antibiotics, many efforts are being made to obtain more information about the active ingredients in plants and their use in the treatment of diseases. This study the effect of aqueous and alcoholic extracts of Cirsium vulgare on Aspergillus flavus. In this study, the aqueous, ethanolic and methanolic extracts of Cirsium vulgare were studied on Aspergillus flavus with disc, wells, minimum inhibitory concentration (MIC) and minimum fungal concentration (MFC) concentrations.

Methods: It was collected from the stem and leaves of the artichoke plant in the plains of Babol city in the summer of 1401 and aqueous and alcoholic extracts were obtained by the Soxola method. Also, the essential oils of Cirsium vulgare were measured by gas chromatography. The average of growth inhibitory diameter for the aqueous, ethanol and methanol extracts in the disc method was 4.92, 12.50 and 11.25 mm, respectively. Also, in volumes of 60 and 70 microliters, a significant increase was observed in the average of growth inhibitory diameter between alcoholic and aqueous extracts.

Results: Based on the results of the present study, the average of growth inhibitory diameter in volumes of 90, 100 and 110 Î¼l in the well method showed a significant difference between 3 different types of extracts; In a way, the aqueous extract showed a larger growth inhibitory diameter compared to the methanolic and ethanolic extracts. The mean amount of aqueous, ethanolic and methanolic extracts in MIC method was 1041.67 Î¼g/ml and in MFC method was 25000.00, 29166.67 and 583333.33 Î¼g/ml, respectively; There was no significant difference in MIC and MFC values.

Conclusion: According to the present study, artichoke plant extract can be used to eliminate Aspergillus mold due to the presence of chlorogenic acid, cynarin, lutein 7-O-rotinoside and cynarozoid.

Keywords: medicinal plants, Cirsium vulgare, Aspergillus flavus, antifungal activity

Prevalence of C. burnetii DNA in sheep milk in the Eilam province of Iran (Research Paper)

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Introduction: Coxiella burnetii a member of family Rickettsiaceae is the causative agent of Q fever. C. burnetii is generally considered as a small micro- organism (0.2â€“0.4 Î¼m wide by 0.4â€“1.0 Î¼m long). With a cell wall si- milar to that of a Gram-negative bacterium. This bacterium has been detected in many animals including domestic and wild animals, pets, reptiles, and birds. Domestic ruminants are the main reservoirs for C. burnetii, playing an important role in Q fever infections in humans. The duration of C. burnetii excretion in milk is different in domestic animals, so that cows, goats, and ewes excrete the bacterium in milk for 13 months, 52 days, and eight days respectively. Shedding of C. burnetii in milk was sporadic and concentrated in the first month after parturition, whereas excretion in vaginal dis- charges and feces continued for longer. Similar results were reported by, although in the current study the shedding period was longer and for up to 150 days after parturition in fecal samples and up to 90 days in vaginal discharges. At 2 and 6 weeks later, treated animals continued shedding the bacteria and there were no significant differences in the number of shedders between treated and control groups. Moreover, the bacteria were excreted in feces for 5 months after parturition, for 3 months in vaginal discharges and for 4 months in milk.

Methods: A number of 315 milk samples were randomly collected from sheep sheep farms randomly selected in three different geographical regions of west Eilam in 2022. Sampling of apparently healthy animals was performed. Lambing and kidding usually occur in February and March. The collected milk samples were placed on ice and immediately transferred to the microbiology laboratory at the Faculty of Veterinary Medicine. DNA extraction from re-suspended pellet was performed using Blood Genomic DNA Extraction Mini Kit, (Favorgen, Taiwan) according to the kit's manufacturer instructions. The quality and quantity of the ex- tracted DNA was evaluated by Nano Drop 2000c (Termo Scientific, USA). The extracted DNA from samples was kept at â˜’20 Â°C for the later use in PCR. During DNA extraction procedure, elution buffer from the extraction kit was used as Negative Control of Extraction. Molecular detection of C. burnetii For the molecular detection of C. burnetii, nested-PCR targeting the transposon IS1111 gene was employed. The PCR products for both stages were electrophoresed on a 2% agarose gel containing safe stain (Labnet, ENDUROTM, USA) and then visualized using in genius Gel Documentation (Syngene Bio-Imaging, UK). Trans-PCR F:

TATGTATCCACCGTAGCCAGTC R: GAGCGAACCATTGGTATCG nested-PCR FN: CCCAACAACACCTCCTTATTC RN: CTTTAACAGCGCTTGAACGT

Results: Nested-PCR amplification of IS1111 gene C. burnetii DNA 13 out of 315 milk samples were positive for the presence of C. burnetii DNA (4.1%; 95% CI: 2.4% â€“ 6.9%). milk samples from sheep, were positive for C. burnetii.

Conclusion: It was concluded that sheep can play an important role in the epidemiology of Q fever as the reservoir for C. burnetii. The mole- cular detection of C. burnetii using Nested-PCR method in milk samples showed that PCR can be used an easy and reliable approach for de- tecting Q fever. Therefore, the consumption of sheep milk expose human at the higher risk of Q fever.

Keywords: Coxiella burnetii, Nested-PCR, Sheep milk, Eilam province

Prevalence of SARS-CoV-2 in sport clubs in 2021, Tehran, Iran (Research Paper)

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Introduction: Acute respiratory infections (ARIs) are a major cause of infection and sometimes lead to death. These infections may have a viral or bacterial source. In December 2019, a new type of coronavirus was identified. The first people to catch the virus were reported from Wuhan, China. The virus disease is called COVID-19. The spread of the virus was so rapid that it was declared a pandemic disease. Following the widespread outbreak of COVID-19, Sports clubs were one of the first places to be closed for decreasing morbidity rates. In this research, we examine the prevalence of SARS-CoV-2 among athletes with mild respiratory symptoms.

Methods: This study evaluated the possible existence of SARS-CoV-2 infection in 124 throat and nasal swab samples using Real-time PCR. All samples were collected from patients with respiratory symptoms in sport clubs, Tehran, Iran.

Results: From 124 people selected as the study sample, 11 samples (8.87%) tested positive using Real-time PCR. The results of the sample testify to the positive effect of sports clubs on the prevalence of SARS-CoV-2.

Conclusion: This study was performed to Investigate the risk of transmission in society among symptomatic athletes. Our study showed that SARS-CoV-2 can spread easily in society by this group of patients and all sport clubs should measure PCR negative results mandatory for entry into these sports clubs.

Keywords: Respiratory Tract Infection, SARS-CoV-2, ARIs, Prevalence, COVID-19

Regulatory effects of the novel synthesized Indole-3-carbaldehyde on expression of cell cycle genes: A study on Cyclin D and P21 expression by acute promylocytic leukemia cell line (NB4) (Research Paper)

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Introduction: A large variety of heterocycles are known to date and among these, indole and pyran rings are of particular interest. The present investigation was aimed to investigate the effects of novel Indole-3-carbaldehyde derivative (NI-3-CD) analogue on growth inhibition of cells and its regulatory effects on expression of cell cycle genes in acute promylocytic leukemia (APL) cell line.

Methods: NB4 cells were cultured in presence of RPMI1640 medium contained various concentrations of NI-3-CD and basal compound of indole (I3C) (15.12-1000 Î¼g/mL) for 24, 48 and 72 hours. The inhibitory effects of compound on cellular proliferation were assessed by both trypan blue staining and MTT assay techniques. when was confirmed apoptosis the changes in expression of Cyclin D and P21 were determined by quantitative Real-Time PCR. Western blotting analysis was also applied for evaluating the expression of P21 at protein level. Differences were considered significant if p values less than 0.05.

Results: Our results showed a significant difference between various concentrations of NI-3-CD and I3C when cells were treated for 24, 48 and 72 h. Real Time- PCR analysis indicated that the expression of Cyclin D was down regulated while P21 upregulated in compare to untreated control cells and I3C treated cells($P < 0.01$). In concert with RT-PCR, western blot analysis also showed that the P21 expression in NI-3-CD treated cells was significantly increased in compare to both untreated control cells and I3C treated cells.

Conclusion: According to these findings, the novel synthesized NI-3-CD analogue effects on the cell cycle arrest in APL cell line is possibly facilitated via modulating Cyclin D and P21 pathway mediators. NI-3-CD may introduce this compound as a promising therapeutic compound against APL.

Keywords: C19H15F3N2O; Gene; Cancer; Flow cytometry; Real-time PCR; Western blot.

Renalase as a novel biomarker for heart failure diagnosis (Review)

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Introduction: Heart failure (HF) is a response to a previous cardiovascular injury presented that leads to increased intra-cardiac pressures or decreased cardiac output. Many biomarkers have been proposed for the timely diagnosis and prognostication of patients with heart failure. Renalase is an amine oxidase, which contains a flavin adenine dinucleotideâ€“binding region that predominantly originates from the kidneys, as well as the heart, it is known to effectively degrade circulating catecholamines and to play a crucial role in human ischemia-related diseases.

Methods: Methods: PubMed databases were screened using the following search terms: ("renalase") AND (â€œheart failure.")

Results: Recent studies have shown that renalase exerts a more prominent cytoprotective role, independent of its catalytic activity, functioning as a cytokine with anti-inflammatory and anti-apoptotic properties, thus promoting cell survival. It was also reported that renalase prevented cardiac hypertrophy and interstitial fibrosis, as well as the adverse remodeling of the heart, by inhibiting profibrotic gene expression. Stojanovic et al. collected data from 75 H F participants and 35 community-based healthy volunteers. A comparison among patients with HF, including HF with a mid-range LV ejection fraction (LVEF, HFmrEF, 40â€“49 %) and HF with a preserved LVEF (HFpEF, LVEF â‰¥ 50 %), showed that the HF patients presented a higher plasma renalase concentration than patients in the control group and that this concentration was the highest in patients with a reduced LVEF (LVEF < 40 %). These findings suggested that the plasma renalase level could be measured to differentiate patients with an LVEF below 40 % and may serve as a potent biomarker for identifying HF patients with a reduced LVEF. Moreover, they also demonstrated that in patients with a reduced LVEF, high plasma renalase concentrations were positively correlated with LV hypertrophy and closely related to an increased LV mass index. A study demonstrated that elevated plasma renalase concentration (above 113 ng/mL), regardless of the LVEF, presents an independent risk factor for an increase in plasma concentrations of all evaluated cardiac remodeling biomarkers. Moreover, patients who presented with both, reduced EF (EFâ‰¤45) and elevated renalase levels were identified as the set with the greatest likelihood of having the highest plasma cardiac remodeling biomarker concentrations. Also demonstrated that HFrEF patients presented with higher renalase concentrations than HFpEF. Moreover, when both, elevated plasma renalase and heart failure, regardless of the EF being reduced or preserved, are present, that "partnership" represents a significant risk factor for an increase in the cardiac remodeling biomarkers` plasma concentration. However,

regarding biomarkers from different pathophysiological domains, BNP and cystatin C, only the combination of elevated renalase and reduced EF demonstrates significance as a risk factor for their plasma elevation.

Conclusion: Plasma renalase concentration provided significant discrimination for the prediction of ischemia in patients with CHF and appeared to have similar discriminatory potential to that of BNP. Although further confirmatory studies are warranted, renalase seems to be a relevant biomarker for ischemia prediction, implying its potential contribution to ischemia-risk stratification.

Keywords: Renalase, Heart failure, Cardiac remodeling biomarkers

Selumetinib, a promising small-molecule therapeutic: regulates apoptosis, autophagy, and reactive oxygen species pathways to the impairment of T-acute lymphoblastic leukemia cells (Research Paper)

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Introduction: T-Acute Lymphoblastic Leukemia (T-ALL) is a hematological malignancy that has faced many challenges in treatment. The first line of therapy in T-ALL is glucocorticoids (GC). Unfortunately, after a while, some patients show resistance to GC therapy. This can be with early relapse and low survival rates. Furthermore, they have suffered many side effects. Recently, a novel treatment called targeted therapy has been developed. It includes a wide range of new treatments from immunotherapy to intracellular signaling pathway inhibitors, which act specifically and with high efficiency. In this study, we investigated the effects of Selumetinib as a MEK inhibitor on three major cellular pathways (i.e., apoptosis, autophagy, ROS) in T-ALL cells.

Methods: Jurkat cells were treated with different concentrations of Selumetinib. Then cell viability and IC50 value were measured by Alamar blue assay. Next, gene expression profiles (BCL-2, BAX, P53, BECN1, and NFE2L2) were assessed with Real-Time PCR and analyzes with REST 2009 (version 2.0.13). All data analysis was evaluated by Graphpad prism (version 9.4.0.673) software statically.

Results: The results revealed that Selumetinib increased BAX gene expression ($p<0.05$) and BAX/BCL-2 ratio in a time- and dose-dependent manner. Interestingly, BECN-1 expression was increased via BAX stimulation ($p<0.001$). In addition, an increase in the level of NFE2L2 (due to ROS accumulation) was observed in the treated group ($p<0.001$).

Conclusion: Our data showed expression levels of BAX, BECN1, and NFE2L2 genes were significantly increased in Jurkat cells. This suggests that Selumetinib causes apoptosis through the induction of autophagy and ROS pathways. This study highlights that Selumetinib has the potential to be a promising prospect in the treatment protocol of T-ALL patients as a combined therapy with GCs. However, more in vivo and in vitro investigations are still needed.

Keywords: Acute Lymphoblastic Leukemia, apoptosis, autophagy, reactive oxygen species, Selumetinib

Seroepidemiological study of brucellosis disease in Varzeghan city in 2021 (Research Paper)

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Introduction: Brucella abortus bacteria and Malt fever disease is one of the common diseases of humans and animals. This disease has different effects on different people. One of the groups at risk is pregnant women. In this study, the prevalence and incidence of Brucella abortus among pregnant women in Varzeghan city was investigated by measuring IgG and IgM antibodies.

Methods: This study is a cross-sectional descriptive study that took place in the first 3 months of 1400 in Varzeghan city. In this study, blood samples were taken from 100 pregnant women. In the present study, all consumables and ELISA kits used commercially were purchased from Pishtaz Teb Company.

Results: The results of the study after conducting the ELISA test on the samples showed that 60 cases (60%) of IgG antibodies were negative and 5 cases (5%) of IgM antibodies were positive.

Conclusion: According to the results of the study, it can be said that the prevalence of Brucella abortus among pregnant women in Varzeghan city is high compared to other cities in the country. Considering the importance of this disease in pregnant women, further investigations in this city are necessary. It seems

Keywords: Brucella abortus, pregnant women, Varzeghan city, antibody

Serological investigation of paratuberculosis in goat milk (Research Paper)

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Introduction: Johnâ€™s disease (JD) is a chronic enteric granulomatous disease caused by Mycobacterium avium subspecies paratuberculosis (MAP). JD causes to massive economic losses to the infected animal production and also identified the potential risk to the human population, since infected animals could be excreted MAP in their milk, feces and colostrum. Live MAP bacilli were detected in food items such as chease, milk and milk powder. This study describes attempts to screen milk samples from flocks suspected of being infected with JD using an enzyme-linked immunosorbent assay (ELISA) method to detect MAP antibodies.

Methods: A total of 42 milk samples were collected from goats belonging to herds of farmers from different areas of northern India. All samples were analyzed for seroprevalence of JD in goats by a commercial ELISA kit.

Results: After transforming the OD values into S/P ratio, of a total of 42 milk samples taken from goats, 52.4% tested positive. The milk ELISA test detected zero, 52.4, 9.5, 2.4 and 35.7 % of goats as superpositive, positive, low positive, suspected and negative, respectively.

Conclusion: In short, the ELISA method can readily identify MAP-specific antibodies in milk samples from infected goats, while reducing costs and time compared to the standard mycobacterial culture, makes it very convenient method for screening animals suspected to be infected with paratuberculosis in small ruminant.

Keywords: Johnâ€™s disease, Mycobacterium avium subspecies paratuberculosis, ELISA, Goat, Milk sample.

Study of infection with SARS-CoV-2 virus and its effects on platelet coagulation factor in Tabriz city (Research Paper)

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Introduction: Corona virus is one of the group of viruses that play an important role in causing respiratory diseases. Covid-19 is one of the most important viral diseases in the current decade, which has caused a widespread pandemic in the world.

Methods: The present study is descriptive-cross-sectional. In this study, the initial diagnosis of COVID-19 was made by treating doctors. 100 blood samples containing anticoagulants were collected in CBC tubes. The samples were collected using the machine. Cell counters were tested for blood parameters.

Results: Based on the results obtained from the number of 100 examined samples, 45 cases (45%) of their platelet counts were lower than the normal value. 25 cases (25%) were faced with a decrease in the number of platelets up to 145000 and also in 30 cases (30%) of the samples, no change in their platelet count was observed.

Conclusion: In the current study, according to the measured parameter (platelet) in people infected with SARS-CoV-2 virus, it was found that this virus can have different physiological effects in different people, and one of its complications is related to the reduction of the number of platelets. be platelets. Therefore, it seems necessary to carry out additional studies.

Keywords: SARA, COVID, CBC, platelets

Studying the antibacterial effect of garlic extract on Escherichia coli isolated from patients hospitalized in private hospitals in Tabriz city (Research Paper)

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Introduction: Urinary tract infection (UTI) is a bacterial infection that affects part of the urinary tract. The main cause of this infection is Escherichia coli, however rarely other bacteria, viruses or fungi may also cause it. Urinary tract infections are more common in women than men.

Methods: In this study,50 bacterially cultured urine samples were included in the study after determining the type of bacteria. Blood agar and EMB, Mollerhinton agar culture medium was also used for antibiogram test.Garlic extract was purchased commercially from Elixir Technological Test Company and antibiotic extract was prepared from the above disk.:

Results: In this study,it was observed that 35 samples (70%) of the samples were sensitive to garlic extract (Sensitive).10 samples (20%) had moderate sensitivity (Intermediat) and 5 samples (10%) were resistant to the case substance. Our opinion was garlic extract.

Conclusion: Nowadays, due to the excessive use of antibiotics has caused bacterial drug resistance and one of the ways to solve this problem can be the use of drugs based on plant extracts, which we also found in this study that garlic extract can be combined with other drugs Be used therapeutically.

Keywords: antibacterial, garlic extract, Escherichia coli, urinary tract infections

The Effect of Beneficial Bacteriophage as a Supplement along with Antibiotics (Review)

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Introduction: Bacterial resistance can be considered as one of the most serious threats facing the earth's inhabitants, so that according to the 4.95 million deaths associated with bacterial resistance, lower respiratory tract infections alone account for approximately 33 percent of all deaths. A person who had contracted Klebsiella pneumoniae infection and showed resistance to antibiotics was saved by combination therapy of phage and antibiotics and the phage used in it showed no side effects for the patient. Another person was also used to treat drug-resistant Pseudomonas aeruginosa spinal cord infection, which was treated well and side effects were not reported and only the person suffered from diarrhea, in addition, in treatment with bacteriophage for prosthetic joint infection, the use of bacteriophage can be considered as an alternative treatment for limited surgery. Currently, antibiotics are recommended for most bacterial diseases, but because antibiotics harm beneficial bacteria in addition to the desired bacteria, it is also recommended to use phage therapy, which is contaminated due to the specificity of the only bacteria and does not enter into the beneficial bacteria of the patient's body. The use of bacteriophages is low cost and requires less time than antibiotic production. The aim of this study was to determine the beneficial use of bacteriophage as a supplement along with antibiotics.

Methods: This interventional research method was conducted with narrative review approach in 2022 by searching for keywords such as Bacteriophage, Pseudomonas aeruginosa, Antibiotics, Respiratory System infection in valid databases such as Scopus, PubMed, Direct Science and Web of Science. Finally, 15 articles were studied, of which 10 were included in the study.

Results: Based on studies from other researchers' papers, the results of this study are that phage therapy is an emerging option for complex BJI and especially in the worldwide age of resistance dissemination. Currently no phage is commercially available, and some companies have recently conducted clinical trials regulating burn patients or in patients with bacteremia, with no immune signal published little data on phage therapy in BJI patients especially in patients with spinal infection due to multidrug-resistant P. aeruginosa. We believe that personalized phage therapy is a potentially complex BJI adjunct therapy, especially because of the pandrug-resistant P. aeruginosa. In fact, without antibiotics that have anti-biofilm activity (meaning rifampin in infections associated with Staphylococcal implants, or fluoroquinolones in gram-negative infections), the cumulative probability of failure in patients with implant-related infections is considered very high. In the

case presented here, fluoroquinolone could not be used due to the multidrug resistance profile of the strain, and the potential anti-biofilm activity of phages used to treat the patient is likely to help with treatment. And it can also be very important for future treatments of such severe bacterial infections. In fact, as demonstrated here, Europe's unique academic collaboration in the field of life-saving treatment will facilitate the provision of important data that creates and conducts clinical trials at the most important relevant indication.

Conclusion: In the present case, a time limiting agent of screen, production, and purification of bacteriophages (total of 3 months) before a pre-assembled, personalized and targeted phage can be prescribed to the patient as a contributor to surgery and antibiotics. As a result, access to a set of refined phages can be used in a short delay.

Keywords: Bacteriophage, Pseudomonas aeruginosa, Antibiotics, Respiratory System infection

The effect of green synthesized zinc oxide nanoparticles on the cell death of acute lymphoblastic leukemia cell line (Research Paper)

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Introduction: Leukemia therapy via nanomedicine strategies, specifically via nanoparticle-based compounds used to deliver drugs, diagnose, and induce cell death, are prospective methods in the near future. Owing to the exceptional properties of green alkalinized agents, such as minor toxicity, higher biodegradability, high active surface, and environmental compatibility, in the present work, the green alkalinized agent (Satureja mutica) used to prepare zinc oxide nanoparticles (ZnNPs). In addition, the toxicity of synthesized NPs on the cell death of acute lymphoblastic leukemia cell line was also evaluated.

Methods: ZnNPs synthesized by the precipitation method in the presence of Satureja mutica plant extract as a green precursor acted as a reducing and capping agent. XRD, TEM, SEM, FT-IR, and DLS techniques used to characterize NPs. The Nalm-6 cell line (ALL) and PBMCs (Normal cells) treated with different concentrations of zinc oxide NPs for 24, 48, and 72 hours. Afterward, the cell viability and metabolic activity evaluated via trypan blue and MTT assays. In addition, Gene's expression was assessed using qRT-PCR.

Results: Our findings revealed that ZnNPs applied growth inhibitory effects in a dose- and time-dependent manner. In comparison, they had no significant impact on the viability of PBMCs. Moreover, Gene's expression analysis for apoptotic genes displayed a remarkable elevation in the Bax and a reduction in Bcl-2 genes compared to the control group.

Conclusion: Given the apoptotic effects of the zinc oxide NPs on leukemic cells, our study suggests a promising therapeutic strategy for ALL treatments.

Keywords: ALL; Zinc oxide; Hydrothermal; Herbal extracts; Apoptosis.

The Effect of Oxidative Stress and Lipids on Breast Cancer (Review)

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Introduction: Breast cancer is the most common type of cancer in women and is the main cause of death among women's cancers. The improper balance between the production of reactive oxygen metabolites (ROM) as oxidative stress and antioxidant defense system, changes in cholesterol metabolism, lipoproteins, and antioxidant vitamins are associated with breast cancer risk.

Methods: relevant articles and updated information were extracted from the reliable scientific databases such as PubMed and Google Scholar search engines.

Results: The role of high-density lipoproteins (HDL) is very prominent. In fact, in addition to the role of reverse cholesterol transport (RCT), HDL has antioxidant and anti-inflammatory properties, modulating intracellular cholesterol homeostasis, signal transduction, and proliferation. This means that low levels of HDL cholesterol (HDL-C) have been observed in breast cancer patients, which indicates the role of HDL-C in this cancer. In recent studies, higher levels of lipid peroxidation markers have been observed in the plasma of patients and indicate the inefficiency of HDL in breast cancer patients. Also, reactive oxygen species (ROS) are produced by enzymatic and non-enzymatic systems in eukaryotic cells and play an important role in cellular physiology and pathophysiology. Although physiological concentrations are crucial to ensure cell survival, excessive production of ROS is harmful to cells and is considered a key factor in the development of several diseases such as neurodegenerative diseases, cardiovascular disorders, and cancer. Cancer cells are usually exposed to higher levels of ROS, which further induce a malignant phenotype through stimulation for sustained proliferation, death evasion, angiogenesis, invasiveness, and metastasis.

Conclusion: The role of ROS in the cause and progression of breast cancer is gradually being clarified. However, less attention has been paid to the development of targeted strategies of the redox system for the treatment of breast cancer.

Keywords: Breast cancer / Oxidative stress / Reactive oxygen species / Cholesterol / High-density lipoprotein

The effect of plasma membrane xcâˆ’ cystine transporter inhibition on the cell death of acute lymphoblastic leukemia cell line (Research Paper)

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Introduction: Oxidative stress has a crucial causative and contributing role in the development and progression of leukemia. Sulfasalazine (SSZ) is an anti-inflammatory drug for ulcerative colitis or rheumatoid arthritis with potent xcâˆ’ inhibitory properties. Thus, in this study, the effects of Sulfasalazine on cell death of the acute lymphoblastic leukemia cell line were investigated.

Methods: The Nalm-6 cell line (ALL) and PBMCs (Normal cells) were cultured with various Sulfasalazine concentrations for 24, 48, and 72 hours. Afterward, the cell viability and metabolic activity were evaluated via trypan blue and MTT assays. In addition, the apoptosis, ROS, and Gene's expression were assessed using Flow cytometry and qRT-PCR, respectively.

Results: Our findings revealed that Sulfasalazine applied apoptotic and growth-inhibitory effects in a dose- and time-dependent manner with elevation in ROS levels in Nalm-6 cells, whereas it had no significant impact on the viability of PBMCs. Moreover, Gene's expression analysis showed a remarkable elevation in the Bax and a reduction in Bcl-2 genes compared with the control group.

Conclusion: Given the apoptotic effects of Sulfasalazine on leukemic cells, our study suggests a promising therapeutic strategy for ALL treatments.

Keywords: ALL; Sulfasalazine; Oxidative stress; Apoptosis.

The Functional Effect of Herpes Simplex Virus (HSV) on Alzheimer's Disease Approach: A Review Study (Review)

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Introduction: Alzheimer's disease is a neurodegenerative disorder in which progressive decline in cognitive function leads to memory loss and Dementia. In this disease, the limbic system and the structures of the cerebral cortex, especially the temporal lobe, are destroyed. In recent years, it was estimated that 35.5 million people worldwide have Dementia, and this number is projected to reach 65.7 million in 2030 and 115.4 million in 2050. The 2010 Alzheimer's World Report estimated dementia costs 604 billion U.S. dollars in 2010. Most cases of Alzheimer's disease are sporadic, and a small proportion of them are hereditary, called familial Alzheimer's disease. The main risk factor for Alzheimer's disease is aging. Different factors can cause Alzheimer's disease. Among the genetic factors of type 4 allele, Apolipoprotein E gene is very well known among environmental factors chronic brain infections have an effective role in the pathogenesis of Alzheimer's disease. Among the various factors associated with the pathogenesis of Alzheimer's disease (AD), more attention should be paid to the role of pathogens. Epidemiological and experimental evidence suggests that recurrent infections with herpes simplex virus type 1 can be a risk factor for Alzheimerâ€™s disease, but its functional and molecular mechanisms have not yet been fully identified. Multifactorial counties such as Alzheimer's are important to determine the role of different factors causing the disease and its related mechanisms.

Methods: This study is an interventional study with narrative review approach that was conducted in 2022 by searching keywords such as HSV, Dementia, Alzheimer and Apolipoproteins in valid databases such as Science Direct, PubMed, Scopus. Finally, 15 articles were reviewed, of which 10 were included in the study.

Results: According to studies from the papers, the results are that the risk of Alzheimer's disease with HSV1 in the brain increases by 3.1 times and this risk increases 7.2 times in simultaneous HSV1/APOE4 carriers compared to the control group. Herpes simplex virus type 1 is a pandemic that infects more than 80 percent of people over the age of 65 worldwide. HSV1 is a neurotropic virus with distant DNA that initially infects the epithelial cells of the nasal mucosa and mouth. New viral components that develop can enter sensory neurons and transmit their exons to trigeminal ganglions, causing a latent infection. The virus is periodically activated and causes herpes blisters. However, trigeminal ganglion bipolar neurons are also drawn to the trigeminal nuclei located in the brainstem. Neurons are drawn from these nuclei to the

thalamus and finally the sensory cortex. This is the pathway through which the activated virus can reach the central nervous system (CNS) and cause acute neuronal disorders such as HSE (Herpes Simplex Encephalitis) or a minor asymptomatic infection or a lifelong latent infection, aging with weakening of the immune system can exacerbate the occurrence of this condition, in addition to the neuronal pathway, HSV-1 can also enter the central nervous system through the bloodstream, chronic infection HSV_1 It causes continuous activation of microglia, which is caused by antiviral induction of neurotoxic agents at the same time, then ATP and MMP3 released from damaged neurons further activate the microglia, with chronic activation of microglia caused by HSV1 infection, creating a faulty cycle and paving the way for the creation of a stronger Alzheimer's. Activation of HSV_1 lytic cycles in the brain is commonly associated with stress and suppression of the immune system and inflammation

Conclusion: Dioxin responsive elements (DRE) are potentially numerous active in the regulatory regions of viral genes. In the five HSV1 genes these DREs are found in the observed monitoring areas of dioxin, a key member of the HSV1 activator complex, in brain tissue and may be associated with glial cells instead of neurons.

Keywords: HSV, Dementia, Alzheimer, Apolipoproteins

The impression of ABO blood group on complications caused by covid-19 infection (Review)

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Introduction: The 2019 coronavirus disease (COVID-19) has become a global pandemic. According to the World Health Organization (WHO), about 200 million cases of Covid-19 infection have been reported. Recently, several studies have investigated the association between ABO blood groups and the complications of COVID-19 infection. Therefore, the aim of this systematic review was to evaluate the available evidence regarding the susceptibility of ABO blood group to COVID-19 infection.

Methods: Studies of The relationship between ABO's blood group and Covid-19 infection were searched in PubMed, Google Scholar, Scopus, and EMBASE until October 2022. also A search was carried out in Medline and in MedRxive and BioRxive.

Results: This systematic review demonstrates the ABO blood groupâ€™s vulnerability to COVID-19 infection was significant. blood groups A and B may be risk factors for COVID-19 infection, whereas the blood group O appears to be protective. we also found higher risk of infection in A group compared to non-A, but not with each group independently and a lower risk of infection in O group compared to non-O groups and to each individual group. higher risk of infection in patients without anti-A or anti-B antibodies observed. O group showed a lower risk of infection compared to non-O groups but also with A, B, and AB. Group A, however, only showed a higher risk when comparing with non-A. The reason for the lower sensitivity of people with blood type O to be infected by viruses can be the natural anti-A and anti-B antibodies produced in people with blood type O, which potentially block the adhesion of the virus to cells.

Conclusion: We found that the COVID-19 infection rate in persons with blood group A > O > B > AB. Accordingly, this evidence-based systematic review study further indicates blood group A individualsâ€™ vulnerability to COVID-19 infection. Blood type AB is linked to a lower risk of COVID-19 infection.

Keywords: Blood Group, COVID-19 infection, infection, Vulnerability.

The Relationship between Alcohol Consumption by the Mother in the First Trimester of Pregnancy and the Likelihood of Having a Child with Non-Syndromic Oral Cleft (Review)

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Introduction: Oral clefts are one of the most common congenital abnormalities that have a significant physical and financial burden for patients and their families. It is also the most common congenital cranial-pink defect in humans that occurs in about 1-2 in 1000 births. Based on the fetal cause, they can be classified as cleft lip (CL/P) without cleft palate (CLO) or cleft palate (CPO). Maternal behavioral factors have been suggested to be potentially associated with oral cleft incision, including smoking, folate deficiency, antiepileptic drugs and alcohol consumption during pregnancy, which are important and effective factors in this disease. In addition to this, in the United States about 10 percent of pregnant women drink alcohol and about 2 percent frequently drink too much alcohol babies had fetal alcohol syndrome (FAS), and about 9 to 18 percent of them have oral clefts. In early 1978, he had a quantitative study focusing on the incidence of fetal oral cleft and consumption of alcohol by the mother. This study aimed, determine the relationship between alcohol consumption by mother in the first trimester of pregnancy and the probability of having a child with non-syndromic oral cleft.

Methods: This review of a study was conducted based on analytical research methodology with Narrative Review approach in 2022 by searching for keywords such as Maternal exposure, Binge drinking, Alcohol, Craniofacial lands, Cleft lip and Palate in valid databases such as Springer, PubMed, Direct Science and Scopus. Finally, 10 articles were studied, of which 8 were included in the study.

Results: Based on the findings of different articles, the results show that there are extensive debates and studies to discuss the role and etiology of folate in oral cleft (OFC) and have studied many studies to measure and calculate the nutritional status of folate to prevent oral incision. Only one knowledge and study can discuss the analysis of this effort to achieve evidence of the types of the disease. Approximately 20 genes are involved in the etiology of the disease, such as interferon-regulating factor 6 (IRF6), MSX1, Tgf-beta, Mthfr

and Foxe1, all of which are important and effective factors. Among these genes IRF6 on chromosome 1q32.3-q41 is the most valid gene. Subsequently, these authors further demonstrated that IRF6 plays an important role in the formation and maintenance of oral peridermafrost, spatial and temporal adjustment is necessary to ensure proper palatal adhesion. In this study, due to the difficulty of nutritional assessments, the relationship between OFC and various indicators of folate exposure such as dietary intake, supplementation, folic acid enrichment, blood folate concentration and known genetic variants on blood folate concentration may be considered. The effect of moderate alcohol consumption by the mother on the outcome of pregnancy has long been debated since moderate drinking alcohol is unlikely to be more dangerous than drinking too much alcohol, another confounding factor in studies is the definition of heavy drinking. Unlike smoking or drug use, it is difficult to assess exact alcohol consumption, as alcohol concentrations vary widely between drinks (such as Wine, Beer and Distilled Alcoholic Beverages), and the drink, commonly used as a scale for consumption, is fairly vague describing a pattern of heavy drinking should include the frequency and intensity of drinking.

Conclusion: Among mothers who did not use supplements, the chance of having a child with cl/p was 60% lower for women who had the highest quartile of folate intake in the diet compared to women who had a dietary folate percentile of 25-74 percentile.

Keywords: Maternal exposure, Binge drinking, Alcohol, Craniofacial lands, Cleft lip and Palate

The Relationship between Lack of Y Chromosome in Rats with Regard to Bio-Information Knowledge of Human Genetic Future (Review)

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Introduction: For any mammal, the loss of the Y chromosome should mean the loss of males and the destruction of the species. Thus, the issue of how Amami prickly mice managed to live without the Y chromosome has puzzled biologists for decades. Now Asato Koroviva of Hokkaido University in Japan and colleagues have shown that one of the natural chromosomes of this rat has become practically a new male sex chromosome. Korovia says Y chromosomes have been shrinking in many mammals, including humans, over tens of millions of years and may eventually disappear. He says this prickly rat shows how this might happen. There are several sex determination systems in the animal series, but in almost all mammals the gender depends on the X and Y chromosomes. If the royani inherits two X chromosomes, it will become female, and if it inherits an X chromosome and a Y chromosome, it becomes male. This is because the Y chromosome contains a gene called SRY that activates male genes on other chromosomes. The most important of these genes is sox9 gene which causes testicular growth. Tokudaia osimensis, found on japan's Amami Oshima Island, is one of the few mammals that lacks the Y chromosome. In addition, females as well as males have only one X chromosome. As the presence of female mammalâ€™s shows, the shrinking Y chromosome does not contain an important gene, so cells and individuals can live without it, the aim of this study was to determine the relationship between the absences of Y chromosome in rats, including receiving bio-information awareness of human genetic future.

Methods: This interventional research method was conducted with narrative review approach in 2022 by searching for keywords such Lack of Y Chromosome, Rats, Bio-Information and Human Genetic in valid databases such as Scopus, PubMed, Direct Science and Web of Science. Finally, 15 articles were studied, of which 10 were included in the study.

Results: In fact, recent studies have shown that the Y chromosome often disappears in cells when men grow old. But the loss of the Y chromosome from the entire population should lead to extinction, as there will no longer be males. Korovia and her colleagues first sequenced the genomes of several males and females to understand how prickly male mice still existed, but did not find a unique gene variant in males. They then examined more carefully and found that in male rats one of the two versions of chromosome 3 had a duplicate region right next to the SOX9 gene. The researchers conducted various experiments, including adding a repetitive area to laboratory mice, to show that this doubly increased SOX9 activity and thus practically replaced

SRY. This means that chromosome 3 has become a Y pre-chromosome with this repetitive sequence, while this version is a pre-chromosome X without a duplicate sequence. To definitively illustrate this, researchers need to show that no males are created by removing repetitive sequences, says Robin Lovell-Bej of the Francis Crick Institute in London, one of the researchers who discovered the SRY gene. Of course, such experiments cannot be done, because the prickly mouse is a endangered species. However, their evidence is quite convincing, and it is difficult to discern iterations of this type, known as variations in copy numbers, explaining why past attempts to uncover how prickly mice become males have been fruitless. The identified iteration must have arisen at some point in time after two million years ago, because that's when prickly mice were separated from related species that still have the Y chromosome.

Conclusion: Since both sexes in Amami prickly mice now have only one X chromosome, this chromosome may also disappear over time. Koravieva says: Since this chromosome is unstable and mutations are accumulating, I think that the X chromosome will eventually disappear, however, if the descendants of the Prickly Amami mouse survive long enough, the pre-chromosome X and pre-chromosome Y may move along the same evolutionary lines of the X and Y chromosomes, and the small, pre-chromosome Y chromosome X is distinguished.

Keywords: Lack of Y Chromosome, Rats, Bio-Information and Human Genetic

The role of Entosis in cancer prognosis (Review)

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Introduction: Recently, a novel type of programmed cell death occurring in cancer called entosis has been described, in which cancer cells engulf and kill their neighbors through a non-apoptotic mechanism involving autophagy and lysosome-mediated cell digestion, and benefit from their death, which is a mechanism whereby cells survive under stress and become more tumorigenic.

Methods: Cancerous tissues with increased number of entotic structures show a more malignant phenotype than the same variant without such structures. Therefore, entosis has the ability to promote tumor progression, as this process induces aneuploidy and polyploidy, and increases the intracellular nutrient pools to support the survival and proliferation of cancer cells and protect them from environmental factors such as chemotherapy or other adverse conditions caused by anticancer drugs. Such process can potentially facilitate the proliferation and metastasis of tumor cells and lead to chemotherapy failure or even cancer recurrence. Recently, it has been shown that resistance during tyrosine kinase inhibitor (TKI) nintedanib treatment in prostate cancer cells is induced through the activation of entosis.

Results: Entosis has been frequently identified in human malignancies, including lung, breast, stomach, liver, colon, and cervical cancers and melanoma, which are associated with poor prognosis. Several molecules and pathways are involved in the entosis process and induces entosis in human cancers, including cadherin proteins, E-cadherin or P-cadherin, and the Rho/Rho-associated kinase (ROCK) signaling pathway. On the other hand, TP53 and KRAS mutations increase the probability of cancer cells undergoing entosis. Interestingly, entosis has tumor suppressor activity and is able to induce cell death. There was only one case in which entotic structures were associated with reduced metastasis in pancreatic cancer, which is the opposite to other tumour types. Of course, it should be noted that the fate of entosis can be influenced by the interactions of cancer cell, tumor microenvironment and genetic factors.

Conclusion: All these findings open new perspectives to investigate entosis as a potential target for cancer therapy.

Keywords: Entosis, Cancer, Cancer prognosis

The Role of Microbiome in Pancreatic Cancer (Review)

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Introduction: Pancreatic cancer (PC) is one of the most lethal malignancies among diseases that is not directly caused by microbial agents. However, considering the diverse biological functions of the microbiome in known disorders, in this review, we aim to investigate the relationship between microbiome and pancreatic carcinogenesis.

Methods: Results of clinical trials were searched in the Google Scholar and PubMed databases between 2012 and 2022. In selected articles, novel genetic techniques have demonstrated that each of the healthy and cancerous tissues of the pancreas have distinct and unique microbial profiles.

Results: Most studies about microbial causes associated with PC in humans and laboratory animals have confirmed changes in the abundance and diversity of pancreatic, oral and gut microbiota (dysbiosis) compared to the healthy situation. The involvement of some infections in increasing the occurrence risk of PC, and eliminating drug resistance in cancer therapy are other microbial issues. Accordingly, the mechanisms of microbial migration pathways in the gastrointestinal system and blood circulation are currently options under study.

Conclusion: Dysbiosis can be closely related to the risk of progression and development of PC. The evidence of the last few years claims that the microbiome associated with PC has a potential role in the tracking, regulation of the host's immune responses during oncogenesis, and the emergence of new effective therapeutic paradigms.

Keywords: Pancreatic cancer, Microbiome, Dysbiosis, Gut microbiota, Oral microbiota

The Role of Procalcitonin in the Diagnosis of Bacterial Pneumonia in Heart Failure Patients (Review)

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Introduction: Introduction: Bacterial pneumonia is a common infectious disease mostly caused by Streptococcus pneumoniae, Mycoplasma pneumoniae, Haemophilus influenzae, Legionella pneumophila. It has higher risk by comorbidities such as, chronic obstructive pulmonary (COPD), asthma, and heart failure. Some of its symptoms includes cough, dyspnea, pleuritic pain, abnormal vital signs (e.g., fever, tachycardia). Since the role of biomarkers in the diagnosis of bacterial pneumonia is controversial, it is often difficult to distinguish pneumonia from other diseases that cause shortness of breath. Inflammatory markers, such as procalcitonin (PCT), can help make the diagnosis easier.

Methods: Methods: In this review article, the studies conducted using the keywords of procalcitonin, pneumonia, pneumonia biomarkers and Heart failure in the databases PubMed, Science direct, Scopus and Google Scholar.

Results: Results: Procalcitonin is one of the most widely used biomarkers for pneumonia. During a bacterial infection, the CALC-1 gene is upregulated, leading to increased production of procalcitonin by innate immune cells such as macrophages. Increased production of procalcitonin usually occurs in the liver, lungs, and intestines. Procalcitonin can be detected within 2-3 hours and its maximum is in 6 hours. Procalcitonin can reduce the use of antibiotics by reducing the duration of the antibiotic course. It is important to note that persistently elevated procalcitonin levels may indicate a complicated course, but there is also the possibility that they may be falsely elevated. In contrast, persistently low levels of procalcitonin can be seen in localized infections (e.g., empyema, abscess).

Conclusion: Conclusion: Using procalcitonin as a biomarker, its diagnostic accuracy is high in pneumonia and it can be used as a biomarker. In acute heart failure, PCT showed superior to CRP and WBC to diagnose. In conclusion PCT provide strong and additional information to clinical variables and to the established biomarkers CRP and WBC, for diagnosing pneumonia in patients with acute dyspnea. PCT seems particularly helpful to diagnose pneumonia among patients with concomitant acute HF.

Keywords: procalcitonin, pneumonia, pneumonia biomarkers, Heart failure

Using Berberine as an anticancer agent (Review)

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Introduction: Globally, cancer remains one of the leading causes of mortality and morbidity. Many efforts have been made to develop effective therapeutic strategies for cancer in recent years. Berberine is a phytochemical compound derived from various plant groups. BBR is a well-known nutraceutical because of its wide range of pharmacological activities including anti-inflammatory, antidiabetic, antibacterial, antiparasitic, antidiarrheal, antihypertensive, hypolipidemic, and fungicide. In addition, it exhibits inhibitory effects on multiple types of cancers. In this review, we have elaborated on the anticancer effects of BBR through the regulation of different molecular pathways.

Methods: This is a Review Article.

Results: As reported by many investigations, BBR is effective against hypertension, hyperlipidemia, gastroenteritis, fatty liver, and Coronary Artery Diseases (CADs), polycystic ovary, diarrhea, obesity, diabetes, metabolic syndrome, and Alzheimer's disease. Moreover, recent in vitro findings have shown BBR to possess significant anticancer effects on various cancer cell lines by inhibiting cancer cell migration and proliferation via inducing apoptosis pathways and arresting cell cycle. According to another study BBR suppressed the Signal Transducer and Activator of Transcription 1 (STAT1) phosphorylation inhibits IFN-Î³-induced IDO1 expression.45 Also, based on other several studies it has numerous effects on different types of cancer. Throughout this review, we tried to illustrate BBR antitumor activity occurring through different molecular pathways and mechanisms such as inducing apoptosis and autophagy, inhibiting the progression of the cell cycle, and suppressing metastasis and invasion in different types of cancer Considering these reports, we can conclude that BBR, as a natural product in cancer therapy, has a significant potentiality in stimulating both intrinsic and extrinsic apoptosis pathways both by increasing the expression of pro-apoptotic molecules such as BAX, BAD, and Bcl-2-like protein 11 (BIM), and also by inhibiting the expression of anti-apoptotic molecules such as BCL-2, tumor cell death occurs. BBR plays as a potential autophagy modulator and may trigger or inhibit autophagy, depending on the circumstances,113 however, it mainly induces autophagy in cancer cells. BBR can inhibit metastasis and migration in different types of cancer by affecting primarily p38 MAPK, JNK, ERK1/2, P13Kâ€“Akt and NF-kB signaling pathways to suppress the action of u-PA and MMPs.

Conclusion: Berberine (BBR), a natural isoquinoline alkaloid, is known as an outstanding biologically active natural product. It has efficient properties

against different types of cancer. BBR controls molecular mechanisms by a variety of signaling pathways which affect tumor cells, suggesting the possible therapeutic properties to fight different tumor cells. Reports have emphasized the great potential of BBR in inducing cancer cell death by stimulating both apoptosis and autophagy. Different studies reported that BBR could prevent the proliferation of cancer cells by inhibiting the molecules involved in cell cycle regulation and therefore, trigger cell cycle arrest in cancerous cells. In addition, many studies have examined the effect of BBR on the inhibition of metastasis and invasion of malignant cancer cells and reported this natural product to be efficient in the treatment of malignant and invasive cancers by inhibiting the expression of proteins involved in metastasis. Although the exact mechanism of action of BBR as an anticancer drug has not yet been completely explained and further research is needed, recent studies have indicated that it can be used in combination with chemotherapy agents.

Keywords: Berberine; cancer therapy; phytochemicals

Western Blotting: a tool for measurement of macromolecules (Review)

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Introduction: Blotting techniques are effective for detecting macromolecules such as proteins, DNA and RNAs. Blotting refers to a membrane on which biological molecules, such as proteins and nucleic acids, are immobilized. Western blotting isolates a specific protein from a complex sample or mixture of proteins. It can obtain protein quantity, molecular weight, and post-translational modifications. It is a very sensitive method because of the high affinity of antibodies to their epitope.

Methods: Applications of Western Blot 1. Detecting anti-HIV antibodies to diagnose HIV. 2. Quantification of proteins and other gene products in gene expression studies. 3. Evaluating the protein expressions in cells and analysis of protein fractions during protein purification. 4. Analyzing biomarkers like growth factors, cytokines, and hormones. The steps of Western blotting: 1. Preparation of WB buffers: Apart from the lysis buffer needed in sample preparation, other reagents such as loading buffer, running buffer, Coomassie brilliant blue staining solution, and Coomassie decolorization solution are also used to prepare SDS-PAGE. 2. Sample preparation: Western blot sample preparation is performed before SDS-PAGE. Sample extracts can be prepared from cell cultures or tissues by mechanical crushing, such as homogenization and sonication or high-pressure disruption, and then lysing them with an amount of cell lysis buffer to ensure maximum protein extraction. Extraction is performed on ice or at four Â°C to avoid protein degradation. Appropriate lysis buffers Can be selected based on the desired protein expression site. Protease and phosphatase inhibitors are also added at this stage to protect proteins from digestion by proteases that leak out during sample preparation. 3. Gel electrophoresis: Western blotting involves polyacrylamide gel electrophoresis (PAGE) followed by electrophoretic transfer to a membrane (usually PVDF or nitrocellulose) and an immunostaining method to visualize a specific protein on the blotting membrane. SDS-PAGE is a standard means of separating proteins based on their molecular weight. This technique includes one-dimensional electrophoresis and two-dimensional electrophoresis. PAGE Gel Preparation for One-di Western Blotting SDS-PAGE: A reducing agent is added to denature the protein for most Western blotting routines. 4. Primary antibody incubation for western blotting: After blocking, the membrane is incubated with a primary antibody. The choice of the primary antibody depends on the antigen and its antibodies. Primary antibodies for western blotting include monoclonal antibodies (MAbs) and polyclonal antibodies (PAbs). 5. Blocking the membrane and membrane processes: This crucial step prevents the non-specific binding of antibodies to the membrane and is often performed with BSA or nonfat dry milk diluted in TBST/PBST buffer. Regarding these buffers,

it is essential to note that TBST with AP (alkaline phosphatase) labeled antibodies are preferred because PBS interferes with it.

Results: Methods of western blot detection Direct detection: This method is not widely used. The primary antibody used to detect the antigen on the blot is labeled with a fluorescent dye or an enzyme. Indirect detection: This method is used more often because of its many advantages over the direct detection method. This method adds a primary antibody to bind to the antigen, followed by a secondary antibody labeled against the primary antibody. Labels include biotin, fluorescent probes, such as fluorescein or rhodamine, and enzymatic compounds, such as alkaline phosphatase (AP) or horseradish peroxidase (HRP).

Conclusion: Although Western blotting is accepted as a routine method for protein analysis, it has limitations as well as advantages. Advantage: Detection of a very small protein amount (picograms) in a sample. High sensitivity and specificity Most suitable and effective among other techniques for HIV detection. Limitations of western blot: It requires high skill In some cases, antibodies bind to unwanted proteins If no primary antibody is available for the target protein, it cannot be detected. Primary antibodies are expensive The membrane may not retain small proteins.

Keywords: Western Blotting-HIV-buffers