

# Laboratory &



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### **CONGRESS ABSTRACTS**

















### **Laboratory & Diagnosis**

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### Message of Congress Chairman



Dr. Sh. Hemmati DCLS

#### In the Name of God

With the grace of God and with the unceasing efforts of the colleagues of the administrative department and the members of the board of directors and the wisdom of the scientific and executive secretaries of the Congress, Prof.Amir Hasan Zarnani , Dr.Gholamreza Hamzeloo, and the tireless efforts of Dr.Fariba Shayegan in international affairs, Dr.Ali Shirin in the management of the Educational Workshops and Dr.Aireza Lotfi Kian in the education department, it will be possible to hold the 15th international congress and the 21st national congress on the Quality Improvment in Clinical Laboratories on 30April - 3May, 2024 in the conference hall of Milad Tower.25 main topics and 40 educational workshops will be held in the scientific department. It has always been tried to choose topics that are effective in improving the knowledge of the participants. Any congress or conference that can increase the productivity and quality of the country's laboratories will definitely have a positive effect on improving the health level of the society and this shows the central role of laboratories in the health system. The selection of. Educational workshops is also designed and planned based on the needs of participants at different scientific levels to meet the needs of all colleagues. In this congress, prominent domestic speakers and about 11 speakers from foreign countries will be present. Also, a number of foreign guests from reputable companies around the world will participate in this congress. We anticipate that we will have about 10,000 visitors in this congress and about 3,000 people will register in the scientific sections of the congress. In the exhibition section of the congress, there are about 200 knowledge-based companies, manufacturers and importers who are selling their products.Iranian Association of Clinical Laboratory Doctors and the Congress of the Quality Improvment of Clinical Laboratories are always honored to have the support of international scientific societies such as IFCC, CLSI, ILAC, APFCB, TBS and EFLM.We hope that we can take a small step in the development and improvement of the country's laboratory services. In the end, we would like to express our thanks and appreciation for the participation of all the respected scientists, thinkers and professors of the country's universities who helped us in holding the 21st national and 15 th international congress on improving the quality Improvment in Clinical Laboratories.



### **Message of Congress Secretaries**



Dr. A. H. Zarnani DCLS, PhD

#### In the Name of God

The 21st National Congress and the 15th International Congress of QICL will be held between 30April - 3May, 2024. The theme of the 21st Congress entitled "The Medical Laboratories of the Future: Smart, Evidence-based and Accountable" is a collection of approaches from past congresses. In this congress, the central role of the Medical Laboratories in the country's health system and the role of big data in the establishment of new generation smart laboratories will be discussed. The Covid-19 pandemic showed how medical diagnostic laboratories adapted to the Diagnostic needs in a short period of time by changing their infrastructure and management and played a unique role in controlling the pandemic. This valuable experience showed the central role of medical laboratories in the public health of society. Despite this, medical diagnostic laboratories have not been treated as they deserve and they have not been given the necessary value. Therefore, considering the central role of medical diagnostic laboratories in medical diagnoses, in this congress we intend to represent this unique position of medical diagnostic laboratories in public health by holding various meetings and workshops. On the other hand, maintaining the intrinsic and central values of medical diagnostic laboratories is a function of the forward movement through their adaptation to the scientific advances of the world. Meanwhile, artificial intelligence is one of the components that will change the position and role of medical diagnosis laboratories in the near future. Therefore, artificial intelligence and smart medical diagnosis laboratories will be the main pillars of the QICL 2024. Providing effective health-oriented services for laboratory workers depends on increasing knowledge and awareness. Scientific stagnation is the most important problem that threatens the provision of up-to-date services. Laboratory science is one of the fields of science that is evolving with very fast changes, so that every few years the previous knowledge is replaced by new findings. These rapid changes make it necessary to update information and present the latest scientific achievements. In this regard, the 21st congress will present the recent advances in laboratory science in the form of various educational panels and workshops. Another unique feature of this congress is the intersection of clinical sciences and laboratory sciences. In this congress, the presence of clinical experts in the panels is more prominent than in the previous congresses. This will provide an exceptional opportunity that will provide the possibility of a close exchange of opinions between clinical and laboratory experts and will cause the mutual scientific promotion of both fields. This congress is held in cooperation with national and international universities, organizations, associations, institutions and authorities, including IFCC, APFCB, EFLM, CLSI, ilac-MRA and TBS. And this provides an exceptional opportunity for colleagues and experts in different fields of laboratory science to meet international colleagues in an academic environment. We are sure that all the executive and scientific members of the Congress have tried their best so that the result of their one-year effort is a suitable and worthy scientific fund for all the participants. I hope that the 21st Congress will leave a memorable scientific memory in the minds of all participants. We are waiting for all of you colleagues, and scientists in laboratory and clinical fields in this prestigious congress.

Co-Scientific Chair: Dr. F. Shayeghan, Dr. A. Shirin, Dr. A. R. Lotfi Kian



### Message of Congress Executive Secretary



Dr. Gh. R. Hamzehloo DCLS

#### In the Name of God

Today, laboratory medicine is an inseparable part of public health and patient-centered healthcare, based on numerous analytical techniques and providing timely and objective data to healthcare professionals. It plays a decisive role in guiding, preventing, diagnosing, treating, and monitoring diseases. Undoubtedly, after twenty-one sessions, the Congress on Quality Improvement in Laboratory Services has played a significant role in defining the position of laboratories in the healthcare system, marking it as one of the largest and most important scientific events in the field of medical laboratory in the country Recent technological advancements have transformed modern laboratory medicine, adding significant value to its role in healthcare and clinical decision-making. The 21st Congress on Quality Improvement, featuring 25 scientific sessions and over 40 workshops, aims to address crucial clinical and practical issues, including top emerging technologies in medical laboratories—such as innovations in laboratory automation, genomics, Nuclear Magnetic Resonance (NMR) spectroscopy, Mass Spectrometry, microfluidics, Point-of-Care Testing (POCT), and the use of new tools like artificial intelligence and data mining to utilize large medical data obtained from these new techniques. At the 21st congress in 1403 (according to the Iranian calendar), over 200 manufacturing and research companies, mostly knowledge-based, as well as several representing reputable global brands, will showcase the latest world technologies including MALDI-TOF MS, significantly impacting microbiology in medical laboratories. The congress also features the largest annual exhibition of diagnostic kits and laboratory equipment. This year has seen unprecedented and widespread participation from producers and suppliers of kits and laboratory necessities. The exhibition will introduce new and advanced models of laboratory automation equipment and rapid POCT devices, which have found extensive use in medical laboratories. This year, special incentives are provided for companies at the exhibition to encourage them to offer more facilities to laboratories at more favorable prices. Efforts are made to ensure the satisfaction of colleagues by handling registrations, card issuance, meal arrangements, and surveys electronically. My advice, as the executive secretary of the congress, is to pre-select panels and workshops due to the diverse and appealing scientific programs available, as it may not be possible to attend all. Also, familiarization with the ELABMARKET system used for notifications during the congress is recommended for easy access to information on scientific sessions, workshops, and exhibition stands. Despite recent economic crises, sanctions, and foreign exchange restrictions impacting all players in the medical laboratory field, we have strived to meet the scientific, practical, and educational expectations of the laboratory community by leveraging previous experiences in organizing the congress. We also honor outstanding contributions in the Hakim Jorjani festival in a friendly atmosphere, remembering all colleagues and martyrs of health who have been with us over the years and are no longer present. We hope for the active participation of all laboratory community members in the congress to facilitate an even more magnificent event.



Prof. M. Ghasemzadeh, DCLS, PhD

Dr. F. Aziz Mohseni, DCLS

### **Congress Main Topics**

A Laboratory Guide to Diagnosis of Rash-inducing Viruses Dr. V. Salimi, PhD Accreditation in Medical Laboratories Dr. H. Bayat, DCLS, PhD Application of NMR and LC/MS in Clinical Laboratories Prof. M. Amini, PhD Challenges in Laboratory Diagnosing and Reporting HPV Infection Dr. S. Jalilvand, PhD Dynamic change in laboratory diagnosis and follow-up of patients with myelodysplasia neoplasms Dr. M. H. Mohammadi, PhD Harmonization in Medical Laboratories: Challenges and Solutions Dr. R. Mohammadi, DCLS, PhD Dr. N. Vazifeh-Shiran, PhD Hematomorphology in Anemias Immunohematology and Transfusion Medicine Dr. S. Mohammadi, PhD Infertility Due to Male Factor: Causes and Laboratory Diagnosis Dr. M. R. Sadeghi, PhD Dr. A. R. Lotfi-Kian, DCLS Interpretative Commenting in Clinical Laboratory: an Academic Approach Laboratory Diagnosis of Common Parasitic Diseases in Iran Prof. M. Mohebali, PhD **Laboratory Diagnosis of Inborn Errors of Immunity** Dr. M. Mesdaghi, MD Novel Laboratory Diagnostic Methods of Cardio-metabolic Disorders Dr. S. H. Samadanifard, MD Dr. M. R. Khalajzadeh, MD Patients' Rights in Medical Laboratories **POCT: Innovations, Challenges and Opportunities** Dr. M. Rahnemaye Farzami, MD Prenatal Screening and Diagnosis of fetal Abnormalities Prof. D. Farhud, MD, PhD Prerequisites for the Establishment of Smart Medical Laboratory: from Big data to Human Resources Dr. S. M. Tara, MD, PhD Role of resource management in effectiveness & quality improvement of medical labs Dr. M. Vanaki, DCLS Smart Medical Laboratory: the Role of New Generation Artificial Intelligence in Improving the Quality and Prof. H. Rabiei, PhD Management of the Medical Laboratories Sustainable Development of Laboratory Information Management System: Prospects, Challenges and Dr. S. Mirab Samiee, DCLS, PhD The Challenges of Training and Providing Technical and Managerial Human Resources for Medical Prof. A. Gharehbaghian, DCLS, PhD Laboratories The Position of Medical Laboratories in Health Policy Prof. A. H. Takian, PhD The Role of the Microbiology Laboratory in an Era of Increasing Antibiotic Resistance Dr. S. M. Bootorabi, DCLS, PhD

Platelets in Thrombosis and Hemostasis

**Young Scientists** 



## Coordinators of Congress Main Topics (in Alphabetic Order)



Prof. M. Amini PhD



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Dr. H. Bayat DCLS



Dr. S. M. Bootorabi DCLS, PhD



Prof. D. Farhoud MD, PhD



Dr. A. Gharehbaghian DCLS, Phd



Prof. M. Ghasemzadeh DCLS, PhD



Dr. S. Jalilvand PhD



Dr. M. R. Khalajzadeh MD



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Dr. R. Mohammadi DCLS, PhD



Dr. M. H. Mohammadi PhD



Dr. S. Mohammadi PhD



Prof. M. Mohebali PhD



Prof. H. Rabiei PhD



Dr. M. Rahnemaye Farzami MD



Dr. M. R. Sadeghi PhD



Dr. V. Salimi PhD



## Coordinators of Congress Main Topics (in Alphabetic Order)



Dr. S. H. Samadanifard MD



Prof. A. H. Takian PhD



Dr. S. M. Tara MD, PhD



Dr. M. Vanaki DCLS



Dr. N. Vazifeh-Shiran PhD



# **Keynote Speakers**



Prof. D. Farhoud



Prof. Kh. Adeli



Prof. F. Azizi



Prof. A.H. Zarnani



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# **ABSTRACTS**

The 15th International & 21st National Congress on Quality Improvement in Clinical Laboratory



# **Oral Presentation**



## A Laboratory Guide to Diagnosis of Rash-**Inducing Viruses**

01-04



### The Diagnosis Methods for Viral Vaccine-Preventable Diseases (Measles, Mumps and Rubella)

Nazanin Zahra Shafiei Jandaghi 1\*, Azadeh Shadab, Ghazal Fateminasab, Vahid Salimi, Talat Mokhtari **Azad** 

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Measles, mumps and rubella are three airborne viral diseases that can be prevented by combined Measles-Mumps-Rubella (MMR) vaccine. However, they have been considered as important health concerns as they are still circulating in different countries. Measles and rubella cause diseases with rash and fever. Measles can lead to severe complications and death especially in developing countries. Rubella primary maternal infection during the first forth months of pregnancy can cause Congenital Rubella Syndrome (CRS) which results in fetal death or abnormality. Mumps causes fever and swollen salivary glands. Probable serious complications include encephalitis, myocarditis and infertility. As these diseases have safe and cost-effective vaccines, measles and rubella elimination and eradication are programmed by World Health Organization. To reach this goal, strong routine immunization strategy and supplemental immunization activities should be followed by all countries. Robust surveillance through laboratory confirmation of disease and the serological and molecular surveillance are necessary, as well. For the precise screening and surveillance of these diseases, due to the limited time of virus existence in the clinical samples, detection of specific IgM in serum sample is recommended. Then in positive cases, the genome detection in throat swab or urine sediment is performed by Real time RT-PCR assay. Finally, virus type identification is done by conventional RT-PCR test followed by nucleotide sequencing. During current years through this strategy some countries have achieved the elimination approval, however recent COVID-19 pandemic had negative influence on this process that hopefully will be resolved by more efforts and catch up vaccination.

**Keywords:** Laboratory Diagnosis, Measles, Mumps, Rubella



# The Role of the Laboratory in the Measles and Rubella Elimination Program in Iran Seyed Mohsen Zahraei 1 \*

1- Infectious Diseases Specialist, Center for Communicable Disease Control, Ministry of Health and Medical Education zahraeicde@gmail.com

The most important indicators needed to prove the elimination of the indigenous measles/rubella virus in a country, along with vaccination coverage above 95% and proving the absence of a significant immunity gap in society, establishing a care system with precise and standard indicators of the World Health Organization and molecular testing Measles virus genotypes are circulating. According to the definition of the care system, every case of fever and maculopapular skin rash should be reported as a suspected case of measles and investigated to confirm or rule out measles and rubella. The standard method of diagnosis is the serology test for measles and rubella. At the same time, the serum samples were sent to the National Measles and Rubella Laboratory, which is located in the Faculty of Health, Tehran University of Medical Sciences, and the samples were checked for measles and rubella IgM, and if they were positive, virus isolation will be performed on pharyngeal or urine samples. By isolating measles viruses in a national reference laboratory and conducting their molecular analysis with the help of the World Health Organization, it is possible to determine the source and origin of the virus from which country it was imported. In addition, due to the diversity of measles virus genotypes, 3 or 4 virus genotypes may have entered the country at the same time, which is very significant in terms of epidemiology. Iran, along with Bahrain and Oman, were the first countries in the Eastern Mediterranean region to receive approval for the elimination of measles and rubella in 2019 from the World Health Organization. This confirmation was meant to prove that the local measles and rubella viruses have stopped circulating in the country since 2016. Fortunately, this approval has been extended twice in 2022 and 2023. Proving that the native virus has stopped circulating and that circulating viruses have entered requires a capable laboratory in the care system, and without it, it would not have been possible to access this valuable achievement.



**O3** 

### Laboratory Diagnosis Approach of Skin Rashes Caused by Herpes Viruses

Ramin Yaghobi 1 \*

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Skin rashes may occur due to infection of the wide variety of viruses. While many viral infections affect people of all ages, some are more common in children and babies, and others primarily occur in adults. One of the important families of viruses that play a determinative role in causing skin rashes is the Herpesviridae, which have linear, double strand DNA genome. Herpes viruses that cause skin rashes more are including: Varicella zoster virus (VZV), Herpes simplex virus (HSV), Herpesvirus 6 and 7(HHV-6,7), Cytomegalovirus (CMV), Epstein-Barr Virus (EBV). Among laboratory diagnostic methods for detection and monitoring of these viruses, can mention molecular methods, antigen detection, serology testing, microscopic evaluation and virus culture. The main challenge of detecting these viruses is the type of diagnostic method, clinically time-dependent laboratory analysis, and the source of sample supply. The choice of diagnostic method may also depend on the stage of the infection, the availability of resources, and the specific requirements of the healthcare provider. Combination of viral culture, molecular analysis, and serological testing to provide a comprehensive and accurate assessment of the viral infection is recommended.

**Keywords:** Rash, Herpesviridae, Varicella Zoster Virus (VZV), Herpes Simplex Virus (HSV), Herpesvirus 6 and 7 (HHV-6, 7), Cytomegalovirus (CMV), Epstein-Barr Virus (EBV)



### Differential Diagnosis of Dengue and Chikungunya: Challenges and Solutions

#### Mohammad Hassan Pouriayevali 1 \*

1- Department of Arboviruses and Viral Hemorrhagic Fevers (National Ref Lab), Pasteur Institute of Iran, Tehran, Iran m.h.pouria@gmail.com

Dengue and chikungunya are two mosquito-borne viral infections that are common in tropical and subtropical regions around the world. These two viral agents are major public health concerns and cause significant morbidity and mortality in many parts of the world. Their overlapping clinical presentations often confound clinicians, making differential diagnosis a complex task. Accurate and timely diagnosis is very important for effective patient management and disease control. Laboratory testing serves as a guiding light in this diagnostic maze. Rapid diagnostic tests (RDTs) serve as the frontline warriors of diagnosis. Serological assays, including the detection of IgM and IgG antibodies, play an important role. These tests detect antibodies produced by the immune system in response to infection. NS1 antigen testing facilitates early diagnosis of dengue infection, while IgM antibody tests are critical for the diagnosis of dengue and chikungunya. On the other hand, molecular techniques, especially RT-PCR, play an important role with their exceptional characteristics and the ability to detect all types of viruses, especially in the acute period of the disease, and even identify the virus in vector mosquitoes. However, limitations such as cross-reactivity in serological tests and the potential for misinterpretation highlight the importance of combining different diagnostic methods. Effective diagnosis depends on the seamless integration of clinical manifestations with laboratory findings. Finally, a comprehensive assessment, taking into account epidemiological factors, travel history and clinical symptoms, guides the selection and interpretation of diagnostic tests.

Keywords: Dengue Virus, Chikungunya Virus, Diagnostic Tests, Serology, RT-PCR, NS1 Antigen, IgM Antibody



## **Accreditation in Medical Laboratories**

**O5-O8** 



### The 2022 Revision of the ISO 15189: Changes and Challenges

#### Adrian Kruit 1 \*

1- Netherlands Standardization Institute and a Member of the ISO Technical Committee 212, Working Group a.kruit@nijsmellinghe.nl

Approximately four years ago, the decision was made to embark on a revision of the ISO 15189 standard, specifically the 2012 version. Through collaborative efforts involving input from various countries, a consensus was successfully reached to delineate the requirements for the updated standard. This culmination of efforts led to the official release of the ISO 15189:2022 standard. This revised standard represents a significant enhancement, offering heightened clarity regarding the prerequisites for medical laboratories to establish and uphold a robust quality management system. Noteworthy changes include a heightened emphasis on prioritizing the well-being of patients, a shift towards risk-based decision-making and process design, and a move away from stringent prescriptions. Consequently, this revised standard affords greater flexibility in how medical laboratories choose to implement their management systems. However, this newfound flexibility also brings about an increased level of responsibility, particularly in terms of leadership, necessitating a deeper understanding of the interconnectedness of various sections. The focus of this presentation is to delve into the evolution of the revised ISO 15189:2022 standard, shedding light on the challenges that may arise during its implementation and exploring the implications of the notable changes introduced.



**O**6

### Accreditation of Medical Laboratories – Transition from ISO15189 2012 to 2022

#### Pradeep Kumar 1 \*

1- Associated Maulana Azad Medical College, GNCTD, Delhi, India pradeep dabla@yahoo.com

Laboratory results play a central role in patientcare whether it is diagnosing diseases, managing effective treatments. Clinical Lab precise and fit for purpose results are desirable. International standard ISO 15189 provides an opportunity, offers to guide laboratories in achieving consistent and high-quality results while emphasizing a structured framework, including governance processes, document control, equipment maintenance, staff training, and competence requirements. Thus, accreditation serves as a valuable tool to demonstrate laboratory competence globally, stimulating regular audits that encourage the maintenance and improvement of quality standards and acceptability of results through international consortium. The implementation of internal (IQA) and external quality control (EQA) practices, stands as the initial step in establishing a Quality Management System. ISO 15189 is based on ISO 9001 (quality management requirements) and 17025 standards (requirements for testing and calibration laboratories). It is specifically designed for medical laboratories, outlining the examination processes and equipment requirements to ensure the production of reliable and high-quality results. The revised ISO 15189:2022 introduces significant changes, focusing on impartiality, confidentiality, ethical conduct, implementation of POCT requirements and emphasis on competency assessment. It addresses to promotes better communication with healthcare providers, and aligns with ISO 9001:2015 principles for effective management systems. The standard underscores risk management and the evaluation of process effectiveness, aligning safety requirements with ISO 15190. Accreditation, increasingly mandatory in certain countries, enhances laboratory processes, reducing errors and expediting diagnostics. It functions as a tool for continuous improvement, fostering efficiency in treatment, personalized medicine development, and overall service quality for patients and healthcare providers. The accreditation journey signifies an ongoing commitment to maintaining standardized procedures, ensuring laboratories not only uphold the highest quality but also adopt a systematic approach to continual enhancement with team work.



Ο7

# QMS in the Medical Laboratory - RILIBAEK or Accreditation by DIN EN ISO 15189 Matthias Orth 1 \*

1- Germany and Heidelberg University, Medical Faculty of Mannheim, Mannheim, Germany matthias.orth@vinzenz.de

Medical laboratories are complex institutions and belong to the critical infrastructure of a country. Laboratory results must be reliable and therefore, medical laboratories are at the forefront of quality management systems in medicine. Using an established framework for the QMS allows comparable levels of high quality among laboratories and garantee patients' safety and wellbeing. This quality can be surveyed by inspection (such as by federal offices), by accreditation, or by certification. DIN EN ISO 15189 is widely used as a standard, however, the development of an international norm is different to establishing a national or international guideline such as used in essentially all other areas of medicine. RILIBAEK was developed in Germany by the National Chamber of Physicians to serve as a framework for QMS which was developed and propagated similar to medical guidelines. Compliance to the rules and QMS of Rilibaek are mandatory for all healthcare professionals in Germany performing laboratory testing.



### CLSI's Global Imperative: Enabling Diagnostic Integrity and Innovation

#### Barb Jones 1 \*

1- Clinical and Laboratory Standards Institute (CLSI), Berwyn, PA, USA bjones@clsi.org

For more than 56 years, the Clinical and Laboratory Standards Institute (CLSI) has been focused on bringing together the worldwide medical laboratory community to advance laboratory excellence and diagnostic integrity. Our standards and guidelines are in use in more than 140 countries around the world. Clinicians, laboratorians, IVD manufacturers, and regulators in these countries rely on CLSI standards to guide them on practices and procedures that are critical for ensuring public health and safety. These standards are developed in cooperation with subject matter experts from all over the world who generously devote their time and expertise to contribute to the development of CLSI, standards. More than 300 documents, in 10 major areas of concentration, represent the Gold Standard in laboratory and diagnostic practices. An overview of the rigorous CLSI process, as well as recently published standards will be shared. Additionally, information on CLSI, s global CountryBased Pricing policy, an initiative that will allow for substantially greater access to CLSI standards around the world, will be presented. Through this effort, users from low and low-middle income countries will receive a 90% discount on all CLSI products, those from middle-income countries will receive a 50% discount. The tiered pricing structure, based on World Bank GNI tiers, adds transparency and fairness to the pricing model and will benefit organizations and individuals in 136 countries.



### Application of NMR and LC/MS in Clinical Laboratories

**O9-O12** 



### Application of LC-MS-MS for Quantitative Assay of Small Molecules and Proteins

Masood Amanlou \*

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Analysis of different samples with LC-MS-MS - Analysis of small molecules, Drugs, and Toxic agents with LC-MS-MS - Analyzing metabolites in the metabolomics with LC-MS-MS - Analysis of proteins in the proteomics with LC-MS-MS - Analysis of nucleuic acids in the genomix with LC-MS-MS.



**O10** 

### LC-MS-MS, High Sensitivity and Selectivity for Analysis of Biological Samples

Mohsen Amini \*

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Introducing of LC-MS-MS - Description of the device and the function of different parts- Expressing the relationship between the performance of the device components and the sensitivity and selectivity of the analysis method - How to maintain and care for the device.



### Application of NMR Spectroscopy for Biological Study

Mehdi Khoobi \*

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- Introducing of NMR spectroscopy - Description of the device and the function of different parts - Application of NMR in different field of sciences - NMR-based metabolomics in biomarkers identification and disease diagnosis.



## The Utilization of Omics Biology, Specifically Emphasizing Metabolomics, Represents a Pioneering Frontier in the Realm of Disease Diagnosis and Treatment

Ali Mohebi 1 \*

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The use of Omics biology, particularly metabolomics, as an innovative approach, holds great importance in the diagnosis and treatment of diseases. Metabolomics involves the comprehensive analysis of metabolites in biological samples and provides valuable insights into biochemical pathways and metabolic changes associated with diseases. Integrating metabolomics data with other Omics data enables a comprehensive approach to studying the molecular mechanisms of diseases. This integration aids in identifying disease biomarkers, monitoring disease progression, evaluating treatment effectiveness, and discovering new therapeutic targets. The personalized medicine approach in metabolomics, based on an individual's metabolic profile, leads to personalized and more effective treatments. This approach not only helps in more accurate disease diagnosis but also plays a significant role in assessing treatment efficacy and discovering new molecular targets. Overall, improved metabolomics plays a crucial role in the development of diagnostic and therapeutic methods for diseases, providing a deeper understanding of disease-related metabolic changes and the potential for enhancing public health.

Keywords: Omics Biology, Metabolomics, Novel Diagnosis and Treatment, Personalized Medicine



### **Challenges in Laboratory Diagnosing and Reporting HPV Infection**

013-015



O13

### Virology, Pathogenesis and Epidemiology of Papillomavirus

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Background: Papillomaviruses are a large group of DNA viruses that tend to squamous epithelial cells. These viruses can cause benign hyperplasia such as skin warts and genital warts or types of cancer in the epithelial cells of the genital tract or the head and neck area, the most important of which is cervical cancer. This cancer is considered the fourth most common cancer of women in the world, and it is usually caused by infection with high-risk types of papillomavirus. Methods: Searching for epidemiological studies on papillomavirus Results: Global studies revealed that HPV 16 and 18 are responsible for 70% and 12 types including 31, 33, 35, 45, 39, 51, 52, 56, 58, 59, 66, and 68 were found in the remaining of this cancer. Compatible with this finding, HPV 16 and 18 were found in 68% of cervical cancer, followed by five HPV types 31, 45, 33, 39, and 58 in Iran. In other cancers related to papillomavirus including vaginal, vulva, anal, penile, and head and neck cancer, HPV 16 are the most common type in the world. Conclusion: The distribution of high-risk papillomavirus types in the world and Iran indicates that HPV 16 and 18 are the dominant types. Therefore, the administration of Cervarix and 4-potency Gardasil vaccines can prevent up to 70% and 9-potency Gardasil vaccine up to 90% of cervical cancer.

Keywords: Papillomavirus, Genotypes, and Cervical Cancer



**O14** 

## Reciprocal Laboratory-Clinical Challenges in Diagnosis and Genotyping of Human Papilloma Virus (HPV) in Screening Program of Cervical Cancer

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Human Papilloma Virus (HPV) has more than 200 genotypes, about 50 genotypes could infect ano-genital mucosa which may result in genital warts. HPV infection in most people does not result in malignancy and the immune system of the majority could clear the virus during 6 to 24 months. Nevertheless, infection in some individuals result in cervical cancer, head and neck cancer, skin, or other types of malignancies. Not all genotypes of mucosal HPVs are related to cancers and most genotypes are considered as Low-risk genotypes, including HPV-6 and HPV-11, which are the most prevalent types causing warts. On the other hand, there are 14 High risk genotypes, among them HPV-16 and HPV-18 are responsible for about 70% of cervical cancers and a majority of other HPV-related malignancies. The prevalence of HPV infection is increasing at present and since virus detection tests are considered as the main laboratory method in screening program of cervical cancer, one of the most crucial necessities is precise diagnosis and genotyping of the virus in different clinical specimens. This presentation deals with different methods in diagnosis and genotyping of HPV and compare some advantages and disadvantages of them. Finally, some of most important reciprocal challenges between laboratory and clinics will be discussed.

Keywords: HPV, Human Papilloma Virus, Genotyping



### Cervical Cancer Screening Program-Establishment of Laboratory Requirements

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Background: Cervical cancer is a preventable disease, and if diagnosed early and managed properly, it is also treatable. Today, the use of cytology methods along with molecular technologies and the determination of different combined or reflex algorithms corresponding to various age groups at specified intervals have significantly altered the epidemiological pattern of this disease in countries that have integrated early detection and prevention of cervical cancer into their health surveillance systems. Methods: The prerequisite for any planning to manage this disease and implement effective interventions in various stages of prevention and treatment is the availability of reliable laboratory test results, conducted by qualified professionals using validated screening methods. Results: Given the multi-step screening process of cervical cancer screening and the involvement of different laboratory disciplines in various stages of screening and diagnosis, commitment to establishing and implementing quality assurance standards in all processes, as well as effective and continuous communication between relevant departments, holds paramount importance. Conclusion: In this presentation, we will review the requirements determined for laboratories performing cervical cancer screening tests in different countries and discuss the process required for the widespread implementation of this program in our country.

Keywords: Human Papilloma Virus, Quality Assurance, Cervical Cancer Screening



## Dynamic Change in Laboratory diagnosis and Follow-Up of Patients with Myelodysplasia Neoplasms

**O16-O19** 



**O16** 

### Flowcytometry of Bone Marrow Aspirate with MDS Diagnosis Approach

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Multi-parameter flow cytometry (MCF) is one of the widely used methods in the medical diagnosis laboratory and allows the evaluation of hematopoietic cells at a cellular level. Hematopoiesis in MDS patients as assessed by MFC can different from normal with altered antigen expression, abundance of cell subsets, and scattering properties. Currently, many abnormalities of progenitor cells, myelomonocytic lineage and erythroid lineage are well described. Altered immunophenotypic profiles have been shown to be useful in the diagnosis, risk stratification and treatment guidance of MDS patients. Next generation flow cytometry (NGS) can be used clinically for diagnosis, risk stratification and treatment monitoring. MFC scores are generally based on how flow cytometric abnormalities encountered in MDS are scored and combined to create a diagnosis or risk profile. Typically, a high number of abnormalities indicates a higher diagnostic accuracy and a higher risk for leukemic transformation. Significant differences in MFC scores are observed in the combination of indicators, the number of parameters (from single to several) and the weight assigned to each parameter. Multiparameter flow cytometry is useful in diagnosis, risk stratification and treatment guidance. More research is needed to compile optimal and simple panels that can be easily implemented in a medical laboratory. Furthermore, the adoption of new techniques such as automated analysis and high-dimensional single-cell analysis will potentially increase the clinical impact of MFC.



### Myelodysplastic syndromes: Updates in Classification and Diagnosis

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Myelodysplastic neoplasms (MDS, previously known as myelodysplastic syndromes) are clonal bone marrow diseases that usually affect the elderly. MDS is defined by the proliferation and apoptosis of hematopoietic progenitor cells. The WHO 2022 classification and the International Consensus Classification (ICC) reorganize MDS categories, emphasizing histological and genetic covariates. The new subgrouping aims to provide a more precise classification, which will serve as the foundation for personalized therapy. The revised classification system now differentiates between two categories: "MDS with defining genetic abnormalities" and "MDS, morphologically defined." A new subtype called MDS with biallelic TP53 inactivation (MDS-biTP53) is introduced, which is characterized by the presence of multiple TP53 mutations and takes precedence over other MDS subtypes. According to the WHO-5, the distinction between single and multilineage dysplasia is no longer required. Additionally, the grouping of "MDS, unclassifiable" has also been removed. The WHO 2022 classification maintains the distinction between MDS with low blasts (MDS-LB) and MDS with increased blasts (MDS-IB). Individuals without increased blasts are categorized as either hypoplastic MDS (MDS-h) or MDS-LB. Those with increased blasts are further divided into MDSIB1, MDS-IB2, and MDS with fibrosis (MDS-f). In conclusion, the most reliable method for diagnosing MDS is through the combination of cytomorphological bone marrow diagnostics, cytogenetics, and molecular genetics. This review aims to present the latest update of MDS as a hematologic neoplasm and to emphasize the similarities and differences between the WHO-5 and ICC classifications of MDS.

Keywords: Myelodysplastic Syndrome, Myelodysplastic Neoplasms, WHO, Update, ICC



### Classification of Myelodysplastic Syndromes (MDS) with Focus on New Entities

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The latest World Health Organization (WHO) classification (fifth edition) uses myelodysplastic neoplasm (MDN) to replace myelodysplastic syndrome (MDS) with the purpose to emphasize their neoplastic nature and being terminologically consistent with myeloproliferative neoplasms (MPN). The accurate diagnosis of MDS, that are are a heterogeneous group of clonal stem-cell disorders characterized by ineffective hematopoiesis, peripheral blood cytopenias, and a risk of progression to acute myeloid leukemia, poses significant challenges. Therefore, it is imperative to adopt a comprehensive approach that combines clinical symptoms, examination of bone marrow and peripheral blood morphology, immunophenotyping, and genetic testing in order to establish a definitive diagnosis. t is worth noting that, in addition to assessing bone marrow and blood blast percentage, degree of dysplasia, presence of ring sideroblasts, bone marrow fibrosis, and bone marrow hypocellularity, the 5th WHO Classification, published in 2022, introduces new entities that share molecular pathogenesis. This classification identifies three entities based on genetic abnormalities: i) isolated del (5q) cytogenetic abnormality, ii) SF3B1 mutation, and iii) TP53 mutation. As our understanding of the genetic abnormalities underlying the development of MDS improves with advancements in next-generation sequencing (NGS) technology, it is reasonable to expect notable changes in the latest MDS classification as new entities are integrated. Nevertheless, it is crucial to acknowledge that, morphological findings still will continue to play a vital role in the diagnosis of MDS despite all the expected advancements.

**Keywords:** Myelodysplastic Syndromes, Next-Generation Sequencing, Cytopenia, Dysplasia, Genetic Testing



019

### Clinical and Laboratory Interplay, Key Points in the Interpretation of Results

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Myelodysplasia syndrome is a clonal stem cell disorder of the bone marrow (BM) and the average age of onset is in the seventh decade of life. It is characterized by abnormal hematopoietic maturation and differentiation leading to cytopenia, mainly symptomatic anemia and potential for leukemic transformation. The current gold standard for diagnosis is BM aspiration and biopsy. In addition to modern molecular and flow cytometric methods, such an investigation depends on the interpretation of morphology. Many patients and their doctors prefer to avoid bone marrow sampling. Failure to diagnose or delay in diagnosis may lead to disease progression and may prevent the patient from accessing effective treatment. In some countries, this may also prevent the patient from receiving MDS-related benefits. There is a complex interaction between bone marrow, dysplasia, genetic lesions, and the immunological microenvironment. In particular, the presence of autoantibodies may identify a subgroup of MDS patients who, along with hypoplastic cases, may benefit from an immunosuppressive approach. However, transfusion dependence and resistance to r-EPO regroups patients with poor outcomes representing a true unmet need. Several pathogenic factors in MDS may be targeted by different therapeutic agents, including IST, TPO-RA, and novel biologics. Only by considering this biological diversity, the clinical management of MDS patients may be optimized in the near future.



### **Harmonization in Medical Laboratories: Challenges** and Solutions

**O20-O24** 



### **Evaluation of Commutability of Hematology QC Materials for Measuring Procedure Harmonization**

#### Elham Razani 1 \*

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Background: Harmonizing measurement procedures is crucial for medical labs, and one way to do this is by taking part in external quality assessment programs (EQAP). These programs require the use of quality control materials that can produce consistent results across different measurement procedures for a specific analyte. Therefore, evaluation of the compatibility of these materials is essential for ensuring that they can effectively harmonize the measuring procedures for a given measurand. Methods: 32 fresh patient samples and 4 different commercial hematology quality control (QC) materials were analyzed by two different cell counters, including Sysmex KX21 and Abbot cell-dyne Ruby. Results of six measurands, including white blood cell count (WBC), red blood cell count (RBC), hematocrit (Hct), hemoglobin (Hb), red cell distribution width (RDW), and platelet (Plt), were used for evaluating commutability of these QC materials. This study was relied on difference plot for patient samples to provide criteria for the evaluation. Results:. None of four QC materials showed commutability for all six analytes, and for WBC and Hct no commutability was found for all QC materials. Only Two controls showed commutability for RBC, Hb, RDW, and Plt. Conclusion: The control samples utilized in this study did not exhibit satisfactory performance for the devices used, particularly concerning common hematology parameters. Consequently, commercial hematology QC materials appear inappropriate for harmonizing different measurement procedures, at least in relation to these six analytes.

Keywords: Harmonization, Commutability, Quality Control Material, Hematology



021

## **External Quality Assessment Program (EQAP): are Biochemistry Samples Appropriate** for Harmonization?

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Background: Harmonization in measuring procedure has critical importance among medical laboratories. One approach to achieve this harmonization is participation in external quality assessment programs (EQAP). For this, commutable quality control (QC) materials are required which result in producing equivalent results by different measuring procedure of a given analyte. Thus, evaluation of commutability of QC materials in EQAP is important for determining their capability in harmonizing different measuring procedures of a given analyte. Methods: Results of measuring 18 common biochemical analytes on QC materials which were used in EQAP 44, 45, and 46 courses, were analyzed to evaluate the commutability of these QC materials with 8 different commercial kits. In this study, we used 95% confidence interval of total mean of the results of these kits for confirmation of commutability. Results: All three QC samples showed commutability for six analytes, including glucose, urea, uric acid, iron, phosphorus, and high-density lipoprotein-cholesterol (HDL-C), and nine analytes, including creatinine, total cholesterol, triglyceride, calcium, albumin, total protein, alkaline phosphatase, alanine transaminase, and lactate dehydrogenase, have only one non-commutable result among 24 possible results. Three analytes, including aspartate transaminase, total bilirubin, and direct bilirubin, have at least two non-commutable results. Conclusion: QC materials which were used in EQAP 44, 45, and 46 showed good commutability for 8 commercial kits in measuring 15 different analyte. So, EQAP is useful for harmonizing different participating laboratories for at least these 15 analytes. However, it is important to mentioned that different causes, except QC material and commercial kits, including data analyzing and imprecision of peer groups, have important effects on the results which should be considered when interpreting results of data analysis.

Keywords: Harmonization, Commutability, Control Material, External Quality Assessment Program, EQAP



### Lab Harmonization by Using Commutable Patient Samples in Peer Group Program

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Background: Participating in external quality assessment programs (EQAP) is an important approach for harmonizing medical laboratories. However, because of low frequency in Iran (3 times in a year) and noncommutability of most control materials, its effectiveness is not adequate. Peer group program with high frequency and by using unknown fresh commutable materials, can be more effective. Methods: 25 runs of peer group program was accomplished in Rasad Laboratory Network during 1402 and in each run one fresh pooled serum sample and one fresh whole blood with EDTA were delivered to each of about 25 participating laboratories. These unknown samples were analyzed like patient samples for routine biochemical tests and complete blood count (CBC). Results were recorded in RasadQM online software. Because of commutability of the samples, without considering the measuring procedure, all laboratories were added to one group. Data analyzing was done automatically and standard deviation index (SDI) and total analytical error were calculated. In addition, bias of the laboratory along with its 95% confidence interval for every run and total runs were calculated by using Excell software. Results: According to each analyte and each participating laboratory, results were different. For Rasad Pathobiology and Genetic Laboratory, calculated SDIs for nearly all cases were acceptable, and for most cases, 95% confidence interval of calculated bias relative to group mean encompassed zero and there was no significant bias. However in some other cases, significant bias was present. Conclusion: Generally, in comparison with EQA programs, peer-group program can detect relative bias in measuring procedures during shorter intervals, and because of using fresh commutable samples, can be used for relative bias evaluation among different measuring procedures.

Keywords: Harmonization, Commutable, Quality Control Material, Peer Group Program



### **Harmonization of Laboratory Tests**

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In the first medical diagnosis tests that were performed in the world, the differences in the results of one sample in two laboratories were significant. The issue of standardization of tests started from the same time. Global scientific centers for standardizing laboratory tests and actions by laboratories have been important developments. In spite of these efforts, the inconsistency of the test results of one test and one sample in different laboratories cannot be ignored. During the last decade, scientific centers such as CCLM (Clinical Chemistry and Laboratory Medicine) have conducted important studies on the harmonization of test results in various laboratories. In these studies, all aspects of a coordinated outcome have been considered \*From the activities before the test, test and after the test\*. From 2012 to this year, many researches have been conducted on the harmonization of test results and their articles have been published in reliable medical journals. With currency restrictions in the country and the import of laboratory kits and materials with the required frequency, it is necessary to harmonize laboratory tests inside the country. In Iran, it is more important to harmonize the kits or conduct the test first. It is suggested that 5 large laboratories or those with more than 300 visitors per day in Tehran should harmonize their consumable laboratory kits and gradually expand this effort to other private and public sector laboratories.

Keywords: Harmonization, Laboratory Tests



### Harmonization in Laboratory Medicine: More than Clinical Chemistry?

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The terms standardization and harmonization" are often used interchangeably, because their final endpoint is basically identical, i.e., providing laboratory results to stakeholders (i.e., clinicians and patients) that could be compared across different laboratories, over time. Although the importance of standardizing and/or harmonizing laboratory test results has been clear for four decades or more, adequate focus has only recently been given to the increasing need of pursuing these goals, particularly after the COVID-19 pandemic. Clinical laboratories can no longer work in isolation, and a wide effort is being proffered to foster standardization and harmonization in view of the challenges imposed by globalization, the historical need to improve patient safety and effectiveness of laboratory services, as well as for avoiding to reiterate unpractical recommendations that patients should always refer to the same laboratory for receiving equivalent results. Nonetheless, these two terms reflect in their essence to different concepts. Standardization should be used when test results are uniform across routine measurement procedures and traceable to a recognized standard reference material defined by the International System of Units (SI) through a high-order primary reference material and/or a reference measurement procedure. Harmonization, is instead aimed to make test results more comparable irrespective of the analytical procedure, mainly because neither a reference measurement procedure (RPM)or a primary reference material (RM) are available. Notably, this latter case involves the vast majority of the analytes measured in clinical laboratories, most of which represent an essential source of information for both clinical decision-making and patient care. In particular, standardization is difficult, if not impossible for measurands of complex molecular structures such as hormones and infectious disease serology testing. It is hence increasingly clear that efforts should not only be made for developing further standardization initiatives, but also to assure comparability of laboratory results and information for those measurands for which no RMP neither RM were, are and will be available in the near future. In addition, standardization and harmonization initiatives should be promoted not only in the analytical phase, but throughout all other steps of the total testing process (TTP), thus improving quality and safety of laboratory information.



# **Hematomorphology in Anemias**

**O25-O29** 



### Hematomorphology of Congenital Dyserythropoietic Anemias

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The congenital dyserythropoietic anemias (CDAs) are a group of rare hereditary disorders characterized by congenital anemia and ineffective erythropoiesis with distinct morphologic features in bone marrow late erythroblasts. Patients usually suffer from anemia, jaundice and splenomegaly at presentation. Suboptimal reticulocyte response for the degree of anemia is observed. Aniso-poikilocytosis and basophilic stippling are commonly observed in the peripheral blood smear. Based on the morphologic features of the bone marrow erythroblasts, three classic types have been introduced, which the second type is more common. Anisopoikilocytosis in peripheral blood smear is observed in all three forms but in type I usually macrocytosis is also evident, while in type II and III, RBCs are frequently normochromic. In bone marrow aspirate, type I reveal erythroid hyperplasia with up to 10% binuclear erythroblasts and pathognomonic chromatin bridges between nuclei, type II shows more than 10% (10-35%) mature binuclear erythroblasts and type III is characterized by presence of erythroid hyperplasia and large multinucleated erythroblasts. The rout of inheritance and genetic abnormality is also different. Most CDA patients are mildly or moderately affected and are not transfusion dependent, although may require blood transfusions in some situations. Patients with CDA-I may respond to interferon α and patients with CDA type II seem to benefit from splenectomy. Older patients should be monitored for probable requirement if iron chelators.



### Hematomorphology and Recent Advances in the Management of Microangiopathic Hemolytic Anemias (MAHA): A Narrative Review

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Background: Understanding of the pathophysiology of thrombotic microangiopathies, shch as TTP, HUS, DIC and a group of rare yet life-threatening hematologic conditions - has evolved in recent years along with better access to diagnostic testing. Identifying secondary causes requires a thorough diagnostic workup, but appropriate treatment of the underlying condition usually leads to resolution. Methods: I review evidence on the pathophysiology, diagnosis and management of this group of condition s forthe generalist. I searched MEDLINE, Embase and conference abstracts for my evidence review and presentation. Results: I summarize disease mechanisms and highlight controversies surrounding diagnosis and treatment of thrombotic microangiopathies, starting with a review of disease terminology. Conclusion: We will discuss the pathology, molecular pathogenesis, pathophysiology, clinical features, and management of MAHA using clinical cases to highlight management principles.

Keywords: Microangiopathic Hemolytic Anemias (MAHA), Thrombocytopenia, Anemia



### Hematomorphology in Hemolytic Anemia (Membranopathies)

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The phenomenon of hemolysis indicates that the destruction of red cells is accelerated with red cell defect in membrane. Increased red cell destruction is often completely matched by increased production in bone marrow, resulting in compensated hemolysis. Hemolytic anemia resulting in defects in the erythrocyte membrane proteins or lipids, both of which can alter the membrane's stability, shape, deformability, and/or permeability. In this Panel the hemolytic anemia that result from defect of erythrocyte's membrane is presented. These defects include spherocytosis, elliptocytosis, pyropoikilocytosis, overhydrated and dehydrated stomatocytosis, ovaloctosis, and acantocytosis.



### Hematomorphology in Hemoglobinopathies

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Background: Hemoglobinopathies are a group of genetic disorders characterized by abnormal structure or production of hemoglobin. The alterations in hematological parameters play a crucial role in the diagnosis and management of these conditions. The impact of hemoglobinopathies on hematological parameters can vary based on the specific type of hemoglobinopathy, emphasizing the need for detailed assessment and monitoring. Abnormalities in the size, shape, and structure of red blood cells are frequently observed in individuals with hemoglobinopathies. Understanding the distinct types of hematomorphology associated with various hemoglobinopathies is essential for the management of these conditions. Results: There are several types of hematomorphological changes observed in hemoglobinopathies, including alterations in erythrocyte size, shape, and hemoglobin content, as well as the presence of nucleated red blood cells and pronounced poikilocytosis. The morphological characteristics of abnormal red blood cells in hemoglobinopathies provide valuable insights into the underlying pathophysiological processes and clinical manifestations. These characteristics are often assessed through microscopic examination and play a critical role in the accurate diagnosis and classification of hemoglobinopathies. Common diagnostic methods for identifying hematomorphology in hemoglobinopathies include peripheral blood smear analysis, hemoglobin electrophoresis, and specialized staining techniques to visualize abnormal red cell features. Methods: All relevant English-language publications were searched in Medline. Conclusion: A detailed understanding of hematomorphology in hemoglobinopathies is pivotal for accurate diagnosis, disease monitoring, and personalized treatment approaches. Advancements in diagnostic techniques and therapeutic modalities continue to shape the management of hematological alterations in individuals with hemoglobinopathies, offering new avenues for improved patient care and outcomes.

Keywords: Hematomorphology, Hemoglobinopathy, Blood Cells



029

### Hematomorphol

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CBC, Diff and PBS panel tests are the basis of laboratory screening of blood diseases and especially anemias. In the CBC test, it is possible to find out the presence of anemia and to some extent based on MCV, MCH, RDW and RBC indices, but by examining the extent of peripheral blood and cell morphology, up to 90% of the diagnosis can be found. Each of the main anemias have their own specific and auxiliary morphology through which enzymopathies (G6PD deficiency with Bite cells, pyruvate kinase deficiency with echinocytes, pyrimidine 5' nucleotidase deficiency with punctate basophilic), membraneopathies (spherocytes, Elliptocyte, acanthocyte, stomatocyte and pyropoikilocytosis), hemoglobinopathies (target cell, irregular contracted cells, sickle cell, hemoglobin crystal), liver and kidney disease a anemia (acanthocyte and echinocyte), microangiopathic hemolytic anemia (schistocyte) and immune hemolytic anemias (spherocytes), megaloblastic anemias (macro-ovalocytes) and microcytic anemias such as iron deficiency anemia (microcyte, elliptocyte and teardrop cells). Of course, morphological changes in the number and shape of immature blood and bone marrow cells are also important in the diagnosis of some anemias. It was not possible to check the morphology of cells by cellcounter devices, but advanced microscopic scanners entered the market, which automatically check the extent of peripheral blood and identify the types of cells with the help of artificial intelligence (AI) and declare them as percentages. However, the person-centered diagnosis of cells by laboratory experts is very important, and in this panel, the etiology of cells, diagnostic criteria, matching them with cell counter indices, grading and how to report them are discussed. so that the harmonization between the laboratories is also created and the laboratories follow the same reporting style.



# **Immunohematology and Transfusion Medicine** O30-O32



## Noninvasive Prenatal Determination of Fetal RHD Status Using Cell-Free Fetal DNA in Plasma of RHD Negative Pregnant Women

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Background: The main cause of Hemolytic Disease of the Fetus and Newborn (HDFN) is the incompatibility of the RhD antigen between mother and fetus. Following the discovery of cell-free fetal DNA (cffDNA), noninvasive fetal RhD genotyping has also been made possible, which will help in the better management of immunized RhD negative mothers and in the targeted prenatal injection of Rho(D) Immune Globulin (RhIG). Aims: The aim of this study was to establish a reliable method with high accuracy to determine the fetal RHD genotype. Methods: The project was a prospective observational cohort study. Venous blood samples were collected from 70 RhD negative pregnant women from the 7th to 38th week of gestation, and after cell-free DNA (cfDNA) extraction from plasma, fetal RHD genotyping was performed by duplex Real-Time polymerase chain reaction (PCR) and examining exons 5, 7 and 10 of the RHD gene. SRY and RASSF1A were used as internal controls to confirm the presence of cffDNA in maternal plasma. Results: Out of the 70 samples, 59 were heterozygous positive for RHD and 11 were negative for RHD. In three cases where both the fetal RHD and SRY genotypes were negative, RASSF1A was amplified in their cell-free DNA sample treated with the BstUI enzyme, and the presence of cffDNA was confirmed. Conclusion: The findings reveal that the strategy used in this study is highly reliable and it is possible to determine the fetal RHD status with high accuracy in order to achieve the stated goals for RhD negative pregnant women.

**Keywords**: Hemolytic Disease of the Fetus and Newborn (HDFN), Rho(D) Immune Globulin (RhIG), Noninvasive Prenatal Diagnosis, Cell-Free Fetal DNA (cffDNA), Fetal RHD Genotyping



### The Alloimmunization Rate and it's Causes among Sickle Cell Disease and Sickle Thalassemia Patients in Iran

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Introduction: The alloimmunization following blood transfusion can be life- threatening. The production of alloantibody increases the chance of the multiple alloantibodies production by 20 times. This study aimed to evaluate the rate and causes of alloimmunization among sickle cell disease (SCD) and sickle thalassemia (Sβ). Materials and Methods: Our study included 104 SCD and Sβ patients referring to Baghaei 2 Hospital of Ahvaz in 2019 using a non- random simple sampling method. The blood samples were collected for Rh phenotypes, alloantibody screening and identification, and molecular tests. Results: The alloimmunization rate was 9.6% and 13.2% based on immunohematological tests and medical records, respectively. The main alloantibodies (90%) were anti- Rh, and 40% of the patients had multiple alloantibodies. A significant correlation was found between gender and alloimmunization. Conclusion: R0r′ and R1R0 genotypes were limited to our population in Iran. The alloimmunization rate was significantly increased from 7.6 % in previous study to 13.2 % and the rate of Rh alloantibodies had the higher percent of alloantibodies in comparison to other studies. Due to the differences in RH genotypes between our population and others, the blood transfusion from other ethnicities increased our total alloimmunization rate.

Keywords: Alloimmunization, RH Genotype, Rh Phenotype, Sickle Cell Disease, Sickle Thalassemia



### Immunohematology Changes in Hematopoietic Stem Cell Transplantation

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Allogeneic hematopoietic stem cell transplantation is a curative option for a variety of malignant and non-malignant hematological and congenital diseases. Due to the fact that the human leukocyte antigen system is inherited independently of the blood group system, approximately 40-50% of all HSCTs are performed across the ABO blood group barrier. Dependent on the kind of ABO mismatch, different effects on engraftment have been observed, e.g. delayed red blood cell recovery and pure red cell aplasia. Data on incidence of acute graft-versus-host disease (GVHD), non-relapse mortality, relapse, and overall survival are inconsistent. However, knowledge of clinician about expectable complications and close monitoring of patients helps to detect problems early and to treat patients efficiently; advanced immunohematology laboratory have a key role in both prevention and management of these cited complication. The risks of these complications can be prevented by graft manipulation (RBC and plasma depletion), typing of ABO/Rh group by molecular techniques, HLA typing, donor specific antibody screening by flow cytometry, lineage specific chimerism assay by sequencing and so on. Furthermore appropriate transfusion support according to the type of ABO incompatibility particularly for platelet component by immunohematology service via flow cytometry cross match help to prevent platelet refractoriness and management of bleeding risks in transplanted patient. Taken together having an advanced immunohematology laboratory besides using AABB standard transfusion policy in hematopoietic stem transplantation center not only help to prevent and also management of life threatening complication after transplantation but also leads to blood management in transfusion service and eventually aid to health economics.

Keywords: Immunohematology, Hematopoietic Stem Cell Transplantation



### **Infertility Due to Male Factor: Causes and Laboratory Diagnosis**

**O33-O37** 



# Identification of ITPR1 Gene as a Novel Predictive Biomarker for Non-Obstructive Azoospermia

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Background: Over 20% of infertile men were diagnosed with azoospermia which is driven by blockage of the excurrent ductal system, obstructive azoospermia (OA), or by abnormal/absent testes, non-obstructive azoospermia (NOA). It has been reported that microRNAs (miRNAs) were involved in the spermatogenesis process through the regulation of gene expression patterns. In particular, MiR-34b-5p has been reported as a non-invasive diagnostic biomarker for infertility. However, no gene targets regulating the mechanism of cation of this miRNA are known. Methods: Gene set enrichment analysis as well as qRT-PCR and immunohistochemistry were applied on fresh testicular tissues from NOA patients. Results: Using gene set enrichment analysis the ITPR1 gene was identified as the sole target for hsa-miR-34b-5p, and found significantly overexpressed in non-obstructive azoospermia (NOA) patients. This finding was confirmed by qRT-PCR on fresh testicular tissues from NOA patients. Then, pathway enrichment analysis as well as the diagnostic value analysis of hsa-miR-34b-5p/ITPR1 indicated ITPR1 as a hub gene in the calcium (Ca2+)-apoptosis pathway, and a valuable predictive biomarker for NOA. Moreover, gene expression and histological assays showed the association of the effects of ITPR1's increased expression on spermatogenesis failure through induction of apoptosis in NOA patients. Conclusion: These data suggested that the hsa-miR-34b-5p/ITPR1 axis could serve as a potential novel regulatory predictive biomarker for human spermatogenesis acting through the Ca2+-apoptosis pathway.

Keywords: MicroRNA, Non-Obstructive Azoospermia, ITPR1, Apoptosis, Calcium Pathway



# The Value of Semen Analysis in Assessment of Male Fertility: Past, Present and Future Mohammad Reza Sadeghi 1 \*

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About 15% of couples in reproductive age are suffering from infertility, which in Iran reaches 20% according to many studies, and the cause of about half of them is the male factor. Diagnosing infertility and its causes is the first and most basic step to choose the right treatment plan. In addition to clinical evaluation, the medical laboratory plays an essential role in diagnosing causes and monitoring the effectiveness of treatments through the evaluation of various biomarkers related to male fertility. Among the wide range of laboratory tests that have been offered for assessment of male fertility and the causes of infertility, semen analysis (SA) has maintained its position as the oldest and the cornerstone of male infertility diagnosis. Over the time, since 1677 when Antonie van Leeuwenhoek observed sperm with his preliminary designed microscope, until now, when sophisticated versions of microscopes accompany with computer software and even smartphones are using for SA, it has maintained its position as the frontline for evaluating male fertility. At the same time, the World Health Organization has tried to standardize the analysis methods at the global level. Although various tests have been developed to assess different aspects of male fertility and sperm functions, but most are insufficient for routine use and are mainly research-based. There is only weak evidence on relation of sperm chromatin integrity and male fertility. Therefore, assessment of sperm DNA fragmentation in infertile men is recommended as a complementary test. Despite the WHO standard guidelines for SA and its continues updating, most medical diagnostic laboratories do not follow these standards, resulting in significant differences in individual SA reporting between different laboratories. It leads to misdiagnosis and thus selection of inefficient treatment plan. The WHO seeks to identify barriers for using standardized protocol and attempt to implement them through quality control programs for SA at national and international levels. Although the development of computer-assisted sperm analysis (CASA)can almost solve this problem, but many existing software have several problems that need to be solved.



### Comparison of Spermogram Reports in Medical Diagnostic Laboratories with WHO Criteria

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Ordering semen analysis (SA) or spermogram is one of the oldest, most important, and even is requested before physical exam by physician, it is the first step in diagnosis of male fertility. However, SA results cannot exactly define male fertility status, but it provides valuable data of testis function and men's fertility. Macroscopic analysis of semen provides data about volume, color, odor, viscosity, etc., which has diagnostic value and does not show huge variation in reports of different laboratories. But in microscopic analysis of sperm counts, motility and morphology show a wide range of variation due to non-compliance with WHO criteria. this wide variation of SA reports of a man between laboratories lead to anxiety and worry about his health and also confused the physician in diagnosing the cause of infertility and selecting the most effective and less expensive treatment plan. Therefore, physician in the field of infertility treatment often refuse to refer their patients to medical diagnostic laboratories for SA. They prefer to refer their patients to IVF clinic where SA is performed according to WHO criteria. According to WHO criteria, sperm count should be done with appropriate dilution using Neobar slide or Makler Chamber. Assessment of motility should be reported immediately after liquefaction of seminal fluid without thermal shock to sperm by reporting four types of motility grades. The sperm morphology should be done by Papanicolaou staining of smear and reporting morphology of at least 200 sperm (1000X). Unfortunately, most of laboratories do not follow these standards and perform all evaluations and reports on a wet semen smear. Although the widespread use of the CASA system in medical diagnostic laboratories has reduced this variation to some extent, but CASA application also has its own problems and need more expertise



# Sperm DNA Fragmentation Index: Implications for Male Infertility and Assisted Reproductive Technology Outcomes

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Sperm DNA fragmentation index (DFI) has emerged as a significant parameter in the evaluation of male fertility potential, particularly in the context of assisted reproductive technology (ART) outcomes. High levels of DFI have been associated with reduced fertility rates, increased risk of miscarriage, and compromised embryo quality in ART procedures. Indications for DFI testing include unexplained infertility, recurrent pregnancy loss, and previous ART failures. There are several methods to assess sperm DFI including terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL), sperm chromatin structure assay (SCSA), sperm chromatin dispersion (SCD) test, and Comet assay. Each method offers unique pros, cons, and limitations, affecting its application in clinical scenarios. Inconsistencies in methodology and threshold determination hinder the routine utilization of DFI assessment in clinical practice. It seems that DFI evaluation plays a main role in predicting ART outcomes and guiding clinical decision-making in male infertility management. However, standardization of methodologies and interpretation criteria is essential to enhance the reliability and clinical utility of DFI testing in ART practice.

Keywords: Male Infertility, DNA Integrity, In Vitro Fertilization



### **Clinical Information of Male Infertility from Laboratories**

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The rate of male infertility is increasing throughout the world. It is now known that up to 30% of fertility problems may be because of the man alone and up to 90% of these are down to low sperm count or low sperm quality or both. These can be due to, environmental issues, genetic factors, delayed parenthood, drugs, etc., The diagnosis and prognosis of male subfertility has become a challenge. While the basic semen assessment has been performed for many years, a number of studies question the value of the traditional semen characteristics. Laboratories currently performing semen and endocrine assessment show great variability. The World Health Organization (WHO) manual for the evaluation of semen has been the core of andrology and fertility evaluation that has helped in further development of this field over many years. These tests also include male endocrine profile, biochemical evaluation of the semen, detection of antisperm antibodies in serum, the use of computer-aided sperm analysis (CASA), sperm DNA integrity, and its damage due to oxidative stress. Assisted reproductive techniques (e.g., IVF, ICSI) have shown great success but are too expensive. Further development in this field with newer techniques and extensive training/instructions can improve accuracy and reduce variability, thus maintaining the quality and standards of such an evaluation. There is an urgent need to have standardized training centers and increased awareness in this area of men's health for reproductive success.



### Interpretative Commenting in Clinical Laboratory: an **Academic Approach**

**O38-O41** 



### **Interpretative Comments in Complete Blood Count (CBC) Results**

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Clinical laboratory results have a significant impact on patient safety and disease management as more than 70% of all medical diagnoses are based on laboratory results. Three categories of variables including pre-analytical, analytical and post-analytical variables affect the laboratory results. In recent decades, by focusing on the variables of the analytical phase, a significant reduction in the amount of analytical errors has been achieved, but the pre- and post-analytical phases are still prone to errors, even to a greater extent. Paying special attention to post-analytical errors not only leads to the identification of problems before and during the reporting of results, but also is effective and beneficial in transferring data to the doctor, interpreting them and taking appropriate decision for the patient. Interpretive comments as a part of the post-analytical phase have recently attracted the attention of laboratories and clinicians and are considered an efficient strategy to improve the transmission and communication of laboratory results and the introduction of new and complex tests. Complete blood count (CBC) test results are one area in the clinical laboratory where interpretive comments are made by laboratory scientists. Here we will present some CBC reports with possible interpretive comments and a brief explanation of the comments.

**Keywords**: Interpretive Comments, CBC Test, Post-Analytics



# Interpretative Commenting on the Perspective of ISO 15189-2022: An Opportunity to Improve the Quality and Competence of Medical Labortatories in Iran

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Any process that affects patient care should be considered in the medical laboratory. There is evidence of errors in the interpretation of laboratory results at the bedside, and the goal of clinical interpretation is to reduce these errors and increase the quality of laboratory information and improve patient safety. According to the ISO- 15189 revised version 2022, interpretive commenting, when necessary, is the inclusion of interpretive comments in laboratory results that are mentioned in several clinical guidelines to improve the clinical application of laboratory information. The ultimate goal of interpretive commenting is to ensure appropriate interpretation. Laboratory results and information are important for effective clinical decision-making and efficient patient management.



### **Interpretative Commenting for Infectious Diseases Diagnostic Tests**

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A diagnostic medical laboratory service, in addition to analysis of patient samples and those results, may offer advice on appropriate test selection, interpretation as well as advice on further appropriate investigation. Interpretative comments in reports act as a bridge between clinical microbiology, infectiows disease and infection control. They help as choose the correct antibiotic, or sometimes no antibiotic when the situation demands it. In many centers the report has only the isolate and antibiotics tested. The additional comments if added give guidance to the clinicians to utilize the results. To offer interpretative comments for infectious disease tests like bacterial infections, antibiogram reports, viral infection like HBV, HCV, HIV, HPV, etc. fungal infections like candidiasis, cryptococosis, etc. and parasitic infections are definitely useful for treatment of diseases. The ultimate goal is to assure the appropriate interpretation and utilization of laboratory information for an effective clinical decision making process and valuable patient management.



### **Interpretative Commenting in the Clinical Laboratory**

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The aim of the clinical laboratory is to improve patient health through accurate diagnosis. While accurate and timely measurement of tests are crucial aspects of this service, the diagnostic laboratory also has a role and responsibility to assist clinicians in the interpretation of the results they generate in order to make the right diagnosis and management decisions. There is evidence that clinicians value interpretative advice from the laboratory due to gaps in their knowledge and abilities to select appropriate tests and make correct interpretation of laboratory results. There is wide variation internationally in the extent of provision of individualised narrative interpretative comments, even though there is evidence that interpretative assistance from the laboratory may improve clinical outcome. This lecture will outline the practice of interpretative commenting on results in the clinical laboratory, the needs of clinicians for interpretative support and the requirement for the clinical laboratory to improve the quality of the interpretative service currently offered, through education and training.



### **Laboratory Diagnosis of Common Parasitic Diseases** in Iran

**O42-O45** 



## Present Status of Leishmaniases in Iran with Emphasis on Principle Diagnostic Methods of Human Leishmaniases

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Leishmaniases are the most important of parasitic diseases are endemic in 99 countries of the World and also in 19 provinces of Iran. Cutaneous leishmaniasis (CL) is the old and prevalent parasitic disease with health significance. CL had been known in Iran even before Leishmania parasite was discovered. Abu Ali Cina is the Persian physician who mentioned to Kheyronieh (a long lasting skin sore) in his book named Ghanoon, most probably CL. CL occurs in two forms, zoonotic (ZCL) and anthroponotic (ACL). ZCL caused by L. major is endemic in northeast, south and central parts of Iran. ACL is produced by L. tropica and is prevalent in some of large and medium sized cities of Iran. Almost from 15,000 to 20,000 cases of CL (both ACL and ZCL) are annually reported from different parts of Iran. Based on epidemiological evidences, about 75% of reported CL in Iran is considered ZCL. Unlike CL, which accounts with high new cases per year, VL has been reported sporadically in Iran, but the disease is endemic in some parts of northwestern and southern areas of the country with about 50- 100 new symptomatic cases of VL reported annually. For the laboratory diagnosis of CL, parasitology (microscopy and culture) are used with 70-86 % sensitivity and 86-100% specificity. In the last decade, serologically test particularly direct agglutination test (DAT) has been currently used for diagnosis and seroepidemiological studies of VL in human and animal reservoir hosts in various parts of Iran particularly in the endemic areas with high sensitivity (96%) and specificity (95%), respectively. At this time, Molecular methods are used for Leishmania species and identification and their genotyping and also genetic resistance of the Leishmania parasites against antileishmanial drugs.

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



### Laboratory Diagnostic Methods of Intestinal Parasitic Infections in Human

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The cornerstone for the correct diagnosis of parasitic infections is based on a necessary knowledge thorough the patient is illness. Without a basic knowledge about the epidemiology, morphology and life cycles of the parasites, is difficult the diagnosis of parasitic infections. In addition to selecting the correct diagnostic procedures, laboratories staff must be ensured that specimens are collected properly and arrived at the laboratory promptly. Cyst of protozoan parasites and helminths ova can be kept in 10% formalin up to the tests. However, the trophozoites in fresh samples should be tested quickly. Refrigeration will preserve trophozoites for a few hours and protozoan cysts or ova for several days. Correct diagnosis of fecal samples is depended on both macroscopic and microscopic examination. Protozoan cysts may be found in formed feces, but, watery or loose fresh stools are likely to contain motile protozoan trophozoites and even their cysts. Microscopic examination of intestinal parasites in feces is not complete until direct wet mounts, concentration techniques and permanent stains have been properly applied. In recent years, extensive research focusing on serological, and molecular approaches has been done in parasitology for developing of newer diagnostic methods. Molecular methods based on PCR have made a fundamental development in the detecting and differentiation of intestinal protozoan parasites such as Entamoeba species, and for identifying subspecies and genotypes of pathogenic parasites.



### Toxoplasma Gondii Infection: Challenges and Prospects in the Diagnosis

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Background: Toxoplasma gondii is principal agent of one of the prevalent parasitic infection with a 30-35% seroprevalence in Iran. Despite its widespread occurrence and potential health impacts, Lab.diagnosing toxoplasmosis presents significant challenges due to the varied clinical manifestations and limitations of current diagnostic methods. Results: Diagnostic methods include parasitological, pathological, serological, and molecular approaches. Parasitological techniques involve the detection of tachyzoites in blood and body fluids. Pathological diagnosis relies on histologically identifying T. gondii in tissues, often unrelated to clinical symptoms. Serological methods based on detection of Anti-Toxoplasma antibodies play an essential role in diagnosis. Serological methods include the Sabin-Feldman Dye Test (SFDT), Agglutination tests, Western blotting, IFA, ELISA, and IgG Avidity. However, they face challenges due to producing specific and standard antigens, often prepared through mouse passages or cell culture systems, leading to inter-assay variability, biohazard, and high costs. Advancements in diagnostic antigen production, including recombinant antigens and stage-specific markers, enhance serological testing accuracy and standardization. Although standardization challenges persist, recombinant antigens offer improved discrimination between acute and chronic infections. Conclusion: The diagnosis of T. gondii infection remains challenging without the development of rapid, highly sensitive, and specific diagnostic methods. Current efforts are directed towards genotyping methods, advanced molecular and bioinformatics tools. These innovative approaches promise improved lab. diagnostic accuracy and efficacy in managing toxoplasmosis.

Keywords: Toxoplasmosis, Human, Serological Diagnosis, Iran



045

### **Laboratory Diagnostic Methods of Human Helminthic Diseases**

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Given the importance and prevalence of helminthic gastrointestinal diseases worldwide, and considering their occurrence in specific geographical areas, timely and accurate diagnosis of these parasitic agents is crucial. It not only holds therapeutic value and prevents severe complications but also plays a significant role in controlling and preventing such infections. According to the World Health Organization, helminthic gastrointestinal infections are generally categorized into those transmitted through soil, food, or snails. Among these, enterobiasis falls into the direct transmission category. Among the soil-transmitted helminths recently reported in Iran, Strongyloides stercoralis is notable for its considerable prevalence, particularly in immunocompromised patients, where the condition can deteriorate significantly. Helminthic diseases transmitted by snails in Iran include Fasciola hepatica and Schistosoma haematobium. Although no cases of Schistosoma haematobium infection have been reported in Iran since 2001, a notable number of fascioliasis cases have been referred to the laboratory of the School of Public Health at Tehran University of Medical Sciences in recent months.

Laboratory Diagnostic Methods: To search for and observe soil-transmitted parasitic agents, which include most gastrointestinal helminths, concentration methods such as sedimentation and flotation are emphasized. Concentration techniques like Formalin-Ether Concentration Technique (FECT), Formalin-Ethyl Acetate, and Formalin-Detergent are used to diagnose most helminthic infections, except for direct transmission helminths like enterobiasis. Given that the parasite's body, eggs, or larvae may not always be observable at all stages of pathogenesis in health-threatening parasitic infections like hydatid disease and fascioliasis, serological tests are essential for determining the treatment pathway in the clinic. Hence, regular evaluation of diagnostic tests and kits is crucial to ensure timely and accurate detection, preventing further harm to patients. This technical policy in clinical diagnostic laboratories can also prevent false negative or positive reports.



### **Novel Laboratory Diagnostic Methods of Cardio-Metabolic Disorders**

**O46-O49** 



#### Serum Levels of Fatty Liver Markers Including FIB-4, Ferritin, and SHBG

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In the diagnosis of fatty liver, three important parameters called FIB-4, Ferritin, and SHBG are used. Fatty liver is a disease caused by the accumulation of fat in liver cells and can lead to serious problems such as liver inflammation and cirrhosis. The FIB-4 test is a tool used to evaluate liver health and the severity of liver fat. In the FIB-4 test, the level of liver fibrosis is measured using serum albumin levels and ALT and AST enzymes in the blood. Ferritin is a protein that plays an important role in regulating iron levels in the body. Abnormal levels of Ferritin can be an indicator of fatty liver and liver damage. High levels of Ferritin are usually associated with problems such as fatty liver and liver inflammation. Additionally, SHBG, or sex hormone binding protein, is a blood protein that binds to sex hormones. Low levels of SHBG may indicate hormonal regulation problems in the body, which may also include fatty liver. In summary, the analysis of FIB-4, Ferritin, and SHBG is very important in the diagnosis of fatty liver. The results of these tests help the physician determine the severity of this disease and prescribe appropriate treatment.

Keywords: Fatty Liver, FIB-4, Ferritin, SHBG



#### Serum Levels of ApoB, LP (a), Cholesterol Remnants

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Apo B or apolipoprotein B is a type of protein that is on bad cholesterol or LDL, residual cholesterol or RC and lipoprotein (a) or Lp (a) particles. These particles can cause plaque buildup in blood vessels and cardiovascular diseases. High levels of apo B indicate many these atherogenic particles. Lp (a) is a special type of LDL that has an extra protein called apo (a). This protein is very similar to fibrinogen, which is a blood clotting factor. Therefore, Lp (a) can cause increased bleeding and blockage of blood vessels. High levels of Lp (a) are associated with a high risk of cardiovascular diseases. Remnant cholesterol or residual cholesterol is part of non-HDL or good cholesterol that has been reduced from LDL cholesterol. This cholesterol is usually found in small and fat-like particles such as VLDL and IDL. These particles can also cause plaque buildup in blood vessels and damage their walls. High levels of RC are also associated with a high risk of cardiovascular diseases

Keywords: apo B, Lp (a), Remnant cholesterol



### The Role of Serum Level of BNP, NT-proBNP in Evaluation of the Cardiac Function

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B-type natriuretic peptide (BNP) and its precursor, pro-BNP, have been well-established as biomarkers for heart failure and other cardiovascular diseases. However, recent research has also suggested their potential usefulness in diabetes. Elevated levels of BNP and pro-BNP have been found in patients with diabetes, particularly those with diabetic cardiomyopathy and diabetic nephropathy. These biomarkers have been associated with an increased risk of cardiovascular complications, including heart failure, and have been proposed as potential indicators of subclinical cardiac dysfunction in diabetic patients. Furthermore, BNP and pro-BNP have been shown to correlate with markers of insulin resistance and endothelial dysfunction, suggesting a potential link between these biomarkers and the pathophysiology of diabetes. In addition, studies have demonstrated the prognostic value of BNP and pro-BNP in predicting cardiovascular events and mortality in diabetic patients. This highlights their potential role in risk stratification and management of diabetic individuals at high risk of cardiovascular complications. Overall, the measurement of BNP and pro-BNP levels in diabetic patients may provide valuable clinical information beyond their established role in cardiovascular diseases. Further research is warranted to elucidate the precise mechanisms underlying the association between BNP, pro-BNP, and diabetes, as well as to determine their potential utility in guiding therapeutic strategies in this patient population.

Keywords: BNP, Pro-BNP, Diabetes, Cardiovascular Disease



## Serum Level of IL-6, PLR, NLR, hs-CRP in Evaluation of the Inflammation and Atherosclerosis

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IL-6, PLR, NLR, and hs-CRP are four important parameters that play a significant role in diagnosing inflammation. Inflammation has a crucial role in the development of atherosclerosis and cardiovascular diseases. IL-6 is a cytokine that increases in response to inflammation. Evaluating the level of IL-6 can help us determine the severity and presence of inflammation in patients. PLR, or platelet-to-lymphocyte ratio, indicates the balance between the immune system and inflammation. An increase in PLR may be a sign of inflammation. NLR, or neutrophil-to-lymphocyte ratio, is also an indicator of inflammation. An elevated NLR may indicate the presence of inflammation. hs-CRP is a measurable inflammatory marker found in the blood. High levels of hs-CRP may be a sign of inflammation. The importance of these markers in diagnosing inflammation lies in their ability to assess the level of each parameter in a patient, allowing us to determine the presence and severity of inflammation and prescribe appropriate treatment. These tests help us identify inflammatory diseases at an early stage and prevent serious complications.

Keywords: Inflammation, IL-6, PLR, NLR, hs-CRP



# Patients' Rights in Medical Laboratories **O50**



#### **Ethical and Legal Challenges of Laboratory Patients**

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The medical diagnostic laboratory plays an important role in the process of diagnosing diseases and maintaining health. The correct use of laws, guidelines, regulations and codes of ethics can help maintain and promote these programs. In this paper, an attempt is made to review the most important legal, disciplinary and ethical challenges observed from the point of view of monitoring medical laboratories, and to provide suggestions to solve them. Methods: In this article, an attempt has been made to review 750 cases of complaints from medical laboratories that have been registered in the Secretariat of the Vice President of Medicine of Iran University of Medical Sciences during the last five years (1398-1402). The cases categorized according to laws and regulations. Results: The complaints can be classified into six different groups. In this survey, among the registered complaints, 45% are related to the result of the test, 29% the cost of the test, 5% damage and complications of the test, 4% patient privacy, 2% the way the staff interacts with the client, and 15% include regulatory cases (institutions without license, advertising, physical space, unqualified people, etc.) Conclusion: The existing violations are not limited to these groups. There are some cases of violations that are either under-reported or are only noted for regulatory reasons. Despite their small number, these cases can have a profound impact on the existence and service delivery of laboratories. Conditions like: conducting tests by unlicensed and qualified persons and institutions, conflict of interest and non-transparent financial relationship between the laboratory and other persons. Establishing the necessary educational, supervisory and executive measures in preventing these cases will have a significant impact.

Keywords: Complaint, Regulations, Medical Laboratory



# **POCT: Innovations, Challenges and Opportunities O51-O54**



051

#### Point of Care Testing - from Policy to Implementation

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With the advancement of diagnostic technologies, new models of healthcare services are emerging. These services, provided without dependence on space and complex laboratory equipment, can easily be implemented at the point of care and in near patient setting. The rapid supply and increasing diversity of the technologies employed in their production, while offering significant benefits in expediting clinical care and therapeutic interventions, can also pose challenges by outpacing the necessary measures for designing appropriate management and accreditation systems. Utilizing the benefits of implementing these devices in diagnosis and care requires a multidisciplinary approach. This involves considering all aspects that need to be taken into account for the integration of these services into diagnostic systems, compliance with regulations, and generating reliable results and ultimately, increase the efficiency of processes associated with testing processes. Policies for the deployment of these devices in the laboratory diagnostics field need to consider the broad spectrum of their use outside the laboratory space by non-laboratory users. Potential interventions due to patient unpreparedness and emergency conditions should be taken into account. Important considerations include ensuring the appropriate and quality performance of this group of in vitro diagnostics, training and competency of operators and implementation of quality assurance programs.

**Keywords**: Point of Care Testing, In Vitro Diagnostics, Innovative Diagnostic Technology



#### Role of Point-of-Care Testing (POCT) in Pre-Hospital Setting

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Pre-hospital Point-of-Care Testing (PPOCT) refers to performing diagnostic tests in the scene of Emergency Medicine System and during transportation. This process provides test results in real time for EMT. POCT reduces the arrival-to-Treatment time (Door-to-Treatment time) and may change patient's medical plans and outcomes. The benefits of POCT on reducing Door-to-Treatment time are: 1. Increase the accuracy of diagnosis 2. Early start of treatment and Decrease in Door-to-Treatment Time 3. Reduction in Decision-Making Time 4. Work empowerment of EMTs 5. Reducing the duration of stay in the emergency department 6. Improving the overall results of treating patients in emergency situations Hospital emergency departments often face the problem of overcrowding. In two ways, POCT may reduce the length of stay (LOS) in the emergency department and reduce the time of determining the patient's assignment: Reducing the time of accurate clinical diagnosis due to access to necessary tests Reducing the assignment time due to the need to have comparative tests (for example, hemoglobin drop) Early treatments reduce complications and as a result, stabilizes the patient earlier It seems POCT can increase the percentage of patients who are discharged on time, improve and speed triage of patients from urgent to non-urgent, and reduce delays in initiation of treatment. Studies have shown that POCT, when used effectively, may reduce the adverse health effects of overcrowding, the effectiveness of treatment in the emergency department. Point-of-care testing (POCT) may reduce the number of tests requested from emergency department patients, thereby reducing the time to perform tests and potentially leading to shorter decision making times and ED length of stay (LOS). Finally, it seems that POCT can reduce treatment costs due to the reduction of time for diagnosis, care and early treatment and reduction of disease complications.



#### **Existing and Emerging Technologies for Point-of-Care Testing**

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Existing and Emerging Technologies for Point-of-Care Testing Point-of-care testing (POCT) enables rapid test results with minimal manual intervention near the point of patient care, leading to better health outcomes through rapid diagnosis, rapid clinical decisions, and earlier initiation of treatment. The last decade has seen significant advances in point-of-care testing (POCT) devices from lab-on-a-chip platforms, innovations in smartphone-based technology, and emerging wearable technology. And cloud-based deep learning systems promise a future revolution. COVID-19 has drastically changed the landscape of POC and Rapid Testing. And the point-of-care testing (POCT) market is expected to reach \$64.46 billion by 2029. Looking ahead, tumor markers, flow cytometry (mainly for chemotherapy monitoring), endocrine function tests, and drug monitoring will all benefit from recent technological advances in POCT. As POCTs become more sophisticated in terms of quality, speed and AI features, experts predict they will become part of the routine diagnostic process. These trials will be expanded across multiple therapeutic areas, even by patients themselves. In this lecture, we will discuss the current state of POCT and future trends.



# Point of Care Testing and New Developments in Technology and Information Management Siamak Mirab Samiee 1 \*

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In the future perspective of the health field, the advancement of technology and the integration of artificial intelligence will dramatically change diagnostic patterns, especially in the field of Point of Care testing and Self-testing and the transformative applications of artificial intelligence in advanced diagnostic technologies are increasing rapidly. Machine learning algorithms not only increase the speed and accuracy of tests at the point of care, but also have significant success in early disease diagnosis and prognosis prediction. Machine learning algorithms have shown significant achievements in the field of infectious diseases, where early detection is crucial for effective intervention. In the field of non-communicable diseases, artificial intelligence has made significant accomplishments in predictive analysis and prognosis. The integration of AI into point-of-care testing has led to improvements in early detection rates for chronic diseases, enabling people to proactively manage their health. However, logistical and infrastructure issues in implementation, data security and privacy concerns, cost implications as well as regulatory and ethical considerations are among its most important challenges.



### **Prenatal Screening and Diagnosis of Fetal Abnormalities**

**O55** 



#### **Prenatal Diagnostic Laboratory Methods**

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Prenatal Diagnosis is the most reliable way of preventing genetic diseases that has been implicated in many countries and has prevented the birth of newborns with different hereditary, congenital and genetic diseases during the past few years. Prenatal diagnosis is actually the use of various diagnostic methods to check the condition of the fetus during pregnancy, because postnatal genetic disorders are generally not treatable. In fact, many of the genetic diseases and birth syndromes that occur at birth in the fetus (congenital) such as Down syndrome or after birth, such as thalassemia and hemophilia, are easily identifiable before birth. With the advances made in molecular genetics, today, it is possible to detect before birth all genetic diseases that have been identified as pathogenic. Prenatal diagnosis allows for the presence of healthy children for couples carrying vector pathogens. In general, using non-invasive methods such as ultrasonography (three or four), the examination of fetal cells and DNA, as well as the examination of the mother's blood and ... many suspicious cases are detected. But invasive methods of pre-natal diagnosis require access to embryonic samples, which include amniocentesis, CVS, pre-implantation (PGD) implantation in pregnancies performed with IVF.

Keywords: Prenatal Diagnosis, Ultrasound, Amniocentesis, Cvs, Screening Tests



### Prerequisites for the Establishment of Smart Medical Laboratory: from Big Data to Human Resources

**O56-O58** 



# **Evolution in the Future of Laboratory Information Management (LIMS) With New Generation Intelligent Systems**

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In this lecture, we will delve into the advanced technologies that have fundamentally transformed the ecosystem of laboratory sciences. The main focus of this presentation is on clinical laboratory science information management systems (LIMS), which are the driving force behind new-generation smart hospitals. Utilizing advanced technologies such as machine learning, big data analysis, and artificial intelligence, these systems have optimized diagnostic processes to an unprecedented level. Highlighting these technologies, from laboratory automation to data mining and deep learning, and the unparalleled accuracy in sample analysis, represents a new era in laboratory science where clinical decisions are based on accurate and up-to-date data. This lecture aims to provide a clear picture of how clinical laboratory science is transformed by smart technologies and to discuss the future of this field. New generation LIMSs can communicate with other hospital systems such as patient management systems, drug management systems, medical management systems, and document management systems, and share laboratory data with doctors, nurses, patients, and other stakeholders. This collaboration helps create a harmonious, collaborative, and intelligent environment in hospitals. This relationship can increase the accuracy, speed, and security of diagnosis, prediction, prevention, and treatment of diseases and provide a higher level of satisfaction and quality of care. In short, LIMS is a powerful tool to elevate the standard of hospitals to smart hospitals and can lead to better and more effective medical services. In this presentation, we introduced and reviewed the new generation LIMS in clinical laboratory science and presented examples of its applications, challenges, and opportunities. We hope that this article or presentation can help increase awareness and interest in this field and inspire future research.

Keywords: LIMS, AI, Mechine Learning, Big Data



#### Medical Image Data Management in a Digital Clinical Laboratory

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Image-based clinical laboratory diagnosis is a key element in the overall setup of the facility. Digital transformation of a clinical laboratory should embrace this component. The digital image acquisition is the start point where a wide range of options exist to capture the images in diverse formats, from camera-enriched microscopes to a sophisticated digital microscope. The automation of image acquisition in a high throughput lab is the next major issue which owns mechanical as well as electronic complexities in order to eliminate the role of human based slide handling. When the image is acquired, there should a seamless access to image management software which is not following the same principles as radiological image management systems. The DICOM format for microscopic images has specific features that make image storage, retrieval and viewing completely different from radiology discipline. So, the microscopic image PACS is an inevitable component in digital transformation of a clinical laboratory which should comply with whole-slide image format as well as color photos. Decision support tools to analyze the microscopic image have proven added value to a digital lab. AI solutions to automate image analysis are now commercially available for the most common microscopic services including peripheral blood smear, urinalysis, POP smear and spermatogram. Generative AI has a great potential to prompt relevant images and diagnoses using patient data to serve as a decision support. Digital reporting is another element which coverts the text production in an electronic manner hence facilitating the final step in documentation of the lab results, particularly the free-textbased reports and interpretations.



#### From Data to Knowledge and Intellingence in Clinical Labs

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In the realm of modern medicine, clinical diagnostic laboratories play a vital role in the diagnosis and management of diseases. With recent advancements in information technology and artificial intelligence (AI), these laboratories are now capable of utilizing big data to generate deeper knowledge and insights that can significantly improve the quality of healthcare. On one hand, the clinical data collected by laboratories are a rich source of information that can be analyzed by advanced AI algorithms. These analyses aid in identifying patterns and relationships that may not be discernible to humans. With the intelligent deployment of artificial intelligence, clinical laboratories can become future hubs of innovation where advanced diagnostics and data-driven treatments become a reality. This can contribute to increased diagnostic accuracy, the provision of personalized treatments for patients, and therapeutic efficiency, while reducing the costs associated with healthcare. In this presentation, we will explore how knowledge and artificial intelligence are formed in clinical diagnostic laboratories, their importance and impact, and the challenges and opportunities of this approach. We will also discuss the transformation of clinical diagnostic laboratories as one of the main pillars in ensuring health and improving the quality of life for individuals in society



### Role of Resource Management in Effectiveness & **Quality Improvement of Medical Labs**

**O59-O62** 



#### New International Perspectives of HRM in Medical Laboratories

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The new global perspective in resource management is the optimal and effective use of artificial intelligence in the field of human resource management of leading and successful organizations. The role of artificial intelligence in improving the productivity and efficiency of human resources processes is as follows. The process of recruitment and hiring of medical laboratory staff: quick scanning of resumes and basic electronic application forms and individual and skill abilities of people through machine learning algorithm and comparative analysis of resumes in line with a smarter choice with the least error and the lowest possible cost The process of evaluating the competence of medical laboratory employees:rapid analysis and evaluation of the skills, experiences, and special characteristics of employees individually and comparing them through machine learning algorithms in line with the best selection of employees upon arrival. The process of personal development of medical laboratory staff: artificial intelligence can provide personalized training for staff and adjust it based on individual needs and skills, and by providing quick, customized and confidential feedback to staff, identify the functional strengths and weaknesses of staff and to plan The process of non-compliance and risk management of medical laboratory employees: artificial intelligence, by accurately analyzing the patterns of common errors by employees, also predicts possible errors in the future and provides appropriate patterns to the human resources manager in designing effective corrective action and preventive action. Finally, it accurately calculates and reports the managed costs through error management The efficiency process or employee productivity: artificial intelligence can adjust the efficiency level of employees based on education, experience, performance and skills with practical basic information in a way that is based on real data and the exact implementation of fairness and justice in the payment of efficiency from this path It will definitely increase the motivation and productivity of employees



# AI and Data Analysis in Laboratory Evidence-Based Diagnoses and its Role in Improving the Productivity in Medical Laboratory

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For years, Iran's laboratory diagnosis system has been suffering from a lack of experts and laboratory scientists. Today, artificial intelligence has covered all fields of science, culture and medicine, and it is easily able to improve the management of human resources in the laboratory by simulating laboratory diagnosis processes. The use of artificial intelligence and machine learning technology in diagnoses based on laboratory evidence is very attractive, possible and efficient. Many medical laboratory diagnoses are based on the analysis of images and data by experienced laboratory staff. Artificial intelligence, as a powerful tool, can provide more accurate diagnoses by analyzing images, and with reproducibility, better precision than routine visual diagnoses for laboratory professionals. Artificial intelligence by analyzing laboratory data, producing recommendations and interpretation services. Furthermore, the added value it has for laboratory reports; It can play a valuable role in improving time management and personnel productivity in the medical laboratories of Iran".



#### **Functional Payment of Employee Salaries**

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One of the most important things that make employees stay and feel good in a center is the appropriate salaries that match their performance. According to the upstream rules, the centers that have more than 50 employees must comply with the job classification and adjust their payment based on the tables that are announced and notified annually. And the centers that have less than this number of employees are required to respect the minimum rights of the labor law for everyone. But this type of payment, which is based on educational qualification and service record, although it is mandatory according to the law, it does not create job satisfaction. On the other hand, we all confirm that when the employees are present at their work, they do not use all their capacity for their job. By proper encouragement and better payment, the satisfaction of both the employee and the employer will definitely be achieved. In this article, an attempt has been made to derive a fair formula by complying with the labor law and protecting the rights of employees and their dignity as well as the rights of employers to obtain the maximum satisfaction of both parties. Of course, this method, like all other methods, has weaknesses and strengths, which are tried to be addressed. First, it is necessary to separate and schedule the work of each department. For this, perhaps the easiest and fastest way is to use the average sample of the department and the previous working hours during a specific period of six months. In the next step, a figure is determined for each test in such a way that the performer knows exactly what figure will be paid to him by performing each test. With this, even the working hours will be changed from dry and daily wages to fluid and functional. In this method, at the end of each month, after counting the tests performed and the final calculation of each person's salary, the basic salary of the individual, which is determined by the labor law, is separated and paid separately. And the second part of salary is paid as performancebased salary. One of the disadvantages of this method is the increase in work speed, which may harm its quality, and it should be controlled by monitoring and setting indicators.



## The Role of Artificial Intelligence in Controlling Laboratory Diagnostic Equipment Costs to Meet ISO 15189 Standards

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Introduction: Challenges such as cost management and equipment efficiency in medical diagnostic laboratories are among the most critical issues in medical environments. Improving these challenges is a fundamental priority for specialists and managers of these laboratories. Therefore, the use of artificial intelligence technology as an advanced and scientific tool can provide effective solutions for improving performance and reducing equipment-related costs. Research Methodology: This study adopts a mixed-method approach to investigate the role of artificial intelligence (AI) in cost control and performance improvement in medical diagnostic laboratories. Through a pre-test/post-test experimental design, the impact of AI implementation on performance and costs is evaluated. Additionally, semistructured interviews with laboratory managers and AI experts are conducted to gather qualitative data. Quantitative data from laboratory systems are also collected. This research methodology aids in achieving a deeper understanding of the role of AI in enhancing performance and controlling costs. Results: Research indicates that the use of artificial intelligence in medical diagnostic laboratories leads to significant improvement in process efficiency and cost reduction associated with equipment management. By applying artificial intelligence algorithms to laboratory data, significant improvements can be made in data analysis accuracy, equipment needs prediction, and reduction of financial and time resources consumption. Furthermore, the vital role of laboratory equipment in ensuring the accuracy and reliability of medical test results underscores the importance of these equipment in providing healthcare services. Further research also demonstrates that the use of artificial intelligence can improve the performance of equipment such as biochemical analyzers, blood analyzers, microscopes, and quality monitoring and control systems. Conclusion: Based on the findings, the use of artificial intelligence as an advanced and scientific tool in medical diagnostic laboratories can lead to significant improvements in cost control and performance enhancement of these centers. This technology can not only help continuously improve processes related to laboratory equipment but also enhance the quality of healthcare services.

Keywords: Artificial Intelligence, Standard 15189, Laboratory Equipment, Quality Control



### Sustainable Development of Laboratory Information Management System: Prospects, Challenges and **Solutions**

**O63-O66** 



# The Challenges That Suppliers of LIS Systems Face in the Framework of the Country's Digital Health Development Programs

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1. A look at the history of LIS system usage in Iran (without guidance - without RFP).2. Development of systems according to the management needs of private sector laboratories (an endless cycle of trial and error).3. Development of systems according to the needs of third parties (insurance organizations - early 80s).4. Development of systems according to the needs of third parties (Ministry of Health - HIS evaluation and the first indicators document for LIS under HIS in the early 90s and the Health System Transformation Plan).5. A look at the business relationships between software service providers and laboratories (NASSR's role).6. Interventions by third parties in the relationships between LIS service providers and laboratories (scientific and professional associations - Ministry of Health - insurance organizations).7. Development of systems according to the needs of third parties (e-prescription and e-dispensing programs by insurance companies from 1400).8. Development of systems according to national needs (Digital Health Development Program - Electronic Health Record) led by the Ministry of Health as the main authority and the Reference Health Laboratory as the specialized program center.



# Implementation of Semi-Automated Cancer Registry System Based on Integration of Pathology Reports and National Electronic Health Record System

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Today, health information technology plays a significant role in the exchange and transfer of patient data. Hospital Information Systems (HIS) and Laboratory Information Systems (LIS) in pathology labs and the Iranian Electronic Health Record System (SEPAS) are among the technologies that can be used in a wide range of health programs. After collecting and integrating information from HIS, LIS, and other health service software, the data can be stored in SEPAS. Using this data in disease registration programs to improve the quality of patient care and research can be highly impactful. Using HIS and LIS software for semi-automated pathology reporting has been practical. Pathology reports are the most reliable method for cancer diagnosis. Since the population-based cancer registration program has been mandatory since 1365, and the cancer registration program is a crucial component of cancer control, the data can be connected to the SEPAS system. Using a dashboard prepared for the population-based cancer registration program, the incidence and prevalence of cancer can be calculated quickly and cost-effectively, facilitating cancer control planning. The existing systems for disease registration programs offer benefits such as reusing registered data, reducing costs, and minimizing errors. In this context, an initiative within the country involved modifying existing systems in pathology laboratories to produce standardized reports with ICD-O codes. Additionally, in collaboration with the Ministry of Health, guidelines for exchanging pathology data with SEPAS were developed. In this infrastructure, pathology report data is sent to SEPAS, and the pathology report is generated. Finally, using the designed dashboard on the SEPAS system, cancer patients are identified and made available to cancer registration centers. This article presents the report of this completed project.



#### **Basic Functions of Laboratory Information Management System (LIMS)**

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The widespread use of laboratory information management systems (LIMS) as important and effective components on the performance of medical laboratories dates back to more than 50 years ago. Registering and accepting test requests, collecting, recording and reporting laboratory results and organizing and archiving them were the most important functions of these systems in the beginning, but focusing on generating information for the purpose of financial management of the laboratory was a priority. While almost from the beginning, the focus was on efforts to improve the quality of laboratory operations and automation, including pre-examination, examination and post-examination phases, but by acceleration and advancement of hardware and software in the field of information technology, artificial intelligence and its applications are also considered. In explaining the basic functions of laboratory information systems, different approaches can be used, but data security, test request, specimen management, laboratory analysis, recording laboratory results and ensuring their validity, reporting laboratory results, notification management, data archiving and Information and access to them, the ability to prepare various cross-sectional reports, quality assurance, administrative and financial functions are among the most important topics.



#### Cloud-Based LIMS: A Sustainable Model for Accessibility and Agility

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In the evolving landscape of scientific research, the emergence of cloud-based Laboratory Information Management Systems (LIMS) heralds a new era of data management, emphasizing sustainability, accessibility, and agility. This presentation examines the transition from traditional, on-premises LIMS to their cloud-based counterparts and highlights the numerous benefits this change offers to facilities and research laboratories. By adopting cloud-based solutions, laboratories can achieve scalable, flexible, and efficient operations essential for fostering innovation and streamlining workflows. The journey of LIMS from inception to modern cloud-based models illustrates technological advancements and the evolving needs of scientific research. Initially designed as internal systems, LIMS were constrained by physical infrastructure limitations, leading to challenges in scalability, accessibility, and cost. The shift towards cloud-based solutions, driven by the need for more adaptable and cost-effective systems, has transformed data management in laboratories. These systems, built on the Software as a Service (SaaS) model, offer unparalleled accessibility, allowing researchers to access data anytime, anywhere. One of the primary advantages of cloud-based LIMS is their ability to provide enhanced accessibility and scalability. Laboratories can easily adjust the volume of data and size of various projects without significant initial investments in hardware and software. This agility enables laboratories to quickly respond to changing research demands and opportunities. Moreover, adopting cloud-based systems reduces physical infrastructure and energy consumption associated with on-site systems, contributing to environmental sustainability. However, the transition to a cloud-based LIMS is not without challenges. Concerns regarding data security and privacy, integration with existing systems, and managing organizational changes must be carefully addressed. Additionally, laboratories must consider potential issues related to vendor lock-in and ensure interoperability between different systems and platforms. Looking ahead, cloud-based LIMS are poised to continue evolving with emerging trends and technologies shaping their development. The integration of artificial intelligence and machine learning promises to revolutionize data analysis and decisionmaking processes in laboratories. As cloud technology advances, it empowers scientists to focus more on innovation and discovery, making cloud-based LIMS an essential tool in the quest for scientific advancement. In conclusion, the shift towards cloud-based LIMS represents a strategic move towards more sustainable, accessible, and agile laboratory management. Leveraging the power of cloud technology, laboratories can not only enhance their operational efficiency but also contribute to environmental sustainability. This chapter aims to equip laboratory managers, IT professionals, and researchers with a comprehensive understanding of cloud-based LIMS, providing them with the knowledge to effectively navigate the transition and fully exploit the potential of cloud technology in their operations.



### The Challenges of Training and Providing Technical and Managerial Human Resources for Medical Laboratories

**O67-O71** 



#### **Key Challenges Facing Clinical Laboratory Sciences Practice Training**

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The increasing number of tests and the diversity of technologies employed in clinical laboratories necessitate a heightened focus on the training of proficient personnel in the field of laboratory science. Generally, the educational curriculum for laboratory science students, in terms of skill acquisition, encompasses fundamental practical training within faculty laboratory science departments and an internship program conducted in university-approved laboratories. The integration of these two practical training components should be orchestrated in a manner that facilitates the acquisition of essential skills for laboratory science professionals. Skill training in this profession entails several key challenges. A number of these challenges are associated with teaching skills within the CLS department and executive faculty, primarily encompassing limitations in financial and human resources. The insufficient allocation of adequate space, equipment, and cutting-edge technologies, as well as a shortage of skilled manpower, are the consequences of these limitations. A significant challenge related to internship courses is the limited numbers of clinical laboratory sites dedicated to student training, as well as the constraint in using motivated and capable CLS educators who have sufficient time to instruct students in various skills. In conclusion, financial support to strengthen educational infrastructure, the recruitment of experienced educators and all-round support for them, as well as the establishment of close and reciprocal communication between faculty educational department and CLS educators at the internship site, can be instrumental in addressing these challenges.

Keywords: Clinical Laboratory Science, Practical Training, Internship, Challenges



#### An Overview of the Medical Laboratory Science Bachelor's Program and its Applications in Developed Countries

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Medical laboratory science (MLS) is a complex field embracing a number of different disciplines such as Microbiology, Hematology, Clinical Chemistry, Urinalysis, Immunology, Serology, Histopathology, Immunohematology and Molecular biology and others. Many critical medical decisions that are life-changing are based on laboratory results generated by medical laboratory professionals. To provide high-quality, reliable analyses, laboratory professionals must have extensive knowledge of pathophysiology, correlation of laboratory data extensive knowledge of instrumentation diseases, and and test principles specific methodologies. The MLS Program curriculum, leading to eligibility for certification and licensure as a MLS practitio ner, requires students to engage in diverse, complex and specific experiences critical to the acquisition and practice o f essential laboratory professional skills and functions. Students in the Medical Laboratory Sciences program are eli gible for student membership in the American Society for Clinical Laboratory Science (ASCLS) and several other pr ofessional organizations.

**Keywords**: Laboratory Sciences, Bachelor, Curriculum, Developed Countries



### Brief Introduction of Doctorate in Medical Laboratory Sciences Program in the USA

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Education is the process of facilitating learning, or the acquisition of knowledge, skills, values, beliefs, and habits and these studies help advance knowledge in a particular field or even any experience that has a formative effect on the way one thinks, feels, or acts may be considered educational process. Also, academic education is generally defined as education that has learning as its primary purpose. The laboratory director is responsible for the overall operation and administration of the laboratory, including the employment of personnel who are competent to perform test procedures, record, and report test results promptly, accurately, and proficiently, and for assuring compliance with the applicable regulations. The laboratory director qualifications in Iran by Iran authority include: being a doctor of medicine and being certified in pathology, having a doctorate in medical laboratory sciences, being a medical laboratory specialist, being a PhD in laboratory sciences fields (biochemistry, laboratory hematology, microbiology, immunology) and being a licensed in medical laboratory sciences fellowship. The Doctorate of Medical Laboratory Sciences degree program was approved in 1989 and was started a year later in 1995. On the s first doctorate other hand, a similar educational program was commenced at Rutgers University in 2014 the nation s first doctorate in clinical laboratory science graduate received her degree in May 2018. This program has been launched to address an ongoing need for greater accuracy and cost efficiency in lab testing due to a gap between practicing physicians and labs not understanding the correct tests to order or how to interpret them and for patient safety in several universities across the US.



# Career Challenges and the Importance of Employing Laboratory Sciences Graduates in Medical Diagnostic Laboratory

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In many developing countries, the job market for laboratory professionals is often characterized by limited access to qualified experts, low demand in the public sector, and relatively modest salaries. Consequently, there is significant employee turnover and highly skilled workers often seek employment in the private sector. This study presents the criteria for recruiting laboratory science professionals in Iran and other countries, along with their challenges, and proposes strategies to address these issues based on a review of existing literature and studies. In Iran, there are specific laws and regulations for employing laboratory professionals to ensure that qualified and experienced individuals are hired. Key requirements include having a university degree in laboratory sciences, relevant professional experience, participation in continuous education programs, and adherence to ethical standards. However, differences exist in other countries, which will be discussed. For example, the Clinical Laboratory Scientist (CLS)certification exam is a valid national credential for laboratory specialists working in clinical laboratories. Administered by the American Society for Clinical Pathology (ASCP) it covers a comprehensive range of clinical laboratory science knowledge. Participation in this exam requires a bachelor's degree in clinical laboratory science or a related field, at least one year of full-time laboratory experience, background checks, and compliance with other ASCP requirements. The exam covers topics such as clinical chemistry, hematology, immunology, microbiology, molecular diagnostics, and transfusion medicine. Passing the exam leads to obtaining the CLS certificate, which is valuable for career advancement and higher salaries in clinical laboratories. Globally, job challenges include competing with a large number of job seekers for limited positions, hiring individuals from unrelated fields without relevant skills, lack of strong communication networks between laboratories and jobseeking professionals, geographical constraints, long working hours, and job burnout for some employees. Other challenges include work-life imbalance, gender bias in the selection of professionals, and the need to maintain technical skills in rapidly evolving laboratory fields. To address these issues, enhancing university curriculum programs aligned with current advancements in the laboratory domain and improving human resource recruitment planning are crucial. Collaboration with the private sector to leverage their expertise and experiences is essential. Additionally, creating transparent career progression paths with clear growth opportunities is necessary for attracting and retaining employees in the public sector.

Keywords: Medical Laboratory Scientist, Career, Medical Diagnostic Laboratory Sector



# The Role and Career of Medical Laboratory Sciences Graduations in Health Care System Mohammad Javad Gharavi 1 \*

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Nowadays, 70 to 80 percent of healthcare decisions in the field of epidemiology of common diseases around the world rely on laboratory results. Therefore, it should be believed that the graduates of different levels of laboratory sciences play a very important and valuable role in planning and organizing the process of medical services, and without considering their position, laboratory results and outcomes will not be credible. Although technological advances, inventing modern equipment and high-tech devices are necessary and will enhance the appearance of laboratories in improving technical knowledge and updating the laboratory space significantly, but without the active presence of skilled, efficient, and capable employees, and competent managers, progress and development of service delivery in this organization will not be feasible. One of the prominent examples of this claim was the unparalleled role of laboratories in diagnosing and fighting the pandemic disease of coronavirus. This congress will attempt to present the innovative role of laboratory science graduates at all educational levels from bachelor's to fellowship in laboratory sciences and pathology, and their esteemed position in serving the goals of the healthcare system.

Keywords: Medical Laboratory Graduates, Health Care System, Lab Career



The Position of Medical Laboratories in Health Policy **O72** 



# Health Insurances and the Value-Based Care Model: the Experiences of the Iran's Social Security Organization

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Community health is influenced by numerous factors and results from the collaboration of a diverse array of organizations and specialists in related fields. Laboratory science specialists play a crucial role in improving and promoting community health by aiding in the accurate and timely diagnosis of diseases. The increasing reliance of physicians on diagnostic and laboratory services, alongside the rising costs of the health system, necessitates optimal use of laboratory facilities and equipment. Efficient resource utilization requires attention to the quality of services in addition to quantity, and payments should be based on the outcomes of health interventions and services. Valuebased care has been a focus of health system policymakers for years. Health insurance organizations play a significant role in achieving a value-based care model. Conversely, establishing a value-based care model is crucial for optimizing the use of limited resources for insurance organizations. Initial studies indicate that approximately 5.5 to 7.6 percent of the Social Security Organization's resources are spent on diagnostic services and tests. In 1401, CBC tests were performed over 17 million times, making them the most frequently conducted tests. The TSH test, with over 13 million orders, was the most expensive laboratory service. The quality of purchased services and their impact on maintaining and improving the health of insured individuals is always a concern for insurance organizations. Insurance organizations implement various policies, restrictions, and incentives to enhance the quality and performance of diagnostic and therapeutic service providers, but it appears that there is still a long way to go to achieve a value-based care model. In the absence of family physicians and gatekeepers in the health system, controlling unnecessary services for health insurance is not easily possible. Repeated requests for certain services and tests due to the lack of health records and clinical history access for physicians have always been a concern for the health system and insurance organizations. However, implementing electronic prescriptions and providing physicians access to patient records in prescription systems gradually facilitates demand management. Undoubtedly, reducing unnecessary and repetitive laboratory services and preventing resource wastage requires coordination and collaboration between clinical and paraclinical physicians. Implementing a performance-based payment system instead of the fee-for-service (FFS) model by insurance organizations paves the way for achieving value-based care. A significant measure that can improve the value of health service purchases is measuring the quality of laboratory services, which in turn enhances the performance of providers and improves health system outcomes. Insurance organizations can enhance efficiency and satisfaction in the health system by improving data mining capacity, identifying, and collaborating with high-quality laboratory.



### The Role of the Microbiology Laboratory in an Era of **Increasing Antibiotic Resistance**

**O73-O75** 



### **Effective Antimicrobial Agents in ICU Crisis**

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CIAI and CUTI- and sepsis are the worst clinical Conditions which lead to death if not Diagnosed, and Treated. Mlain Causative agent's MDR Superbugs of Enterobacteriales, Pseudomonas aeroginosa and Acinetobacter bowmannii Blood Stream infection (BSI) is invitable in ICU crisis, and beside The mentioned bacteria, MRSA, VISA, VRE, CRE others may Enter blood Stream from internal closed abscess, ruptured appendix Stabwounds infection. Klebsiella pneumonia producing Carbapenemare Carbapenemase producing non fermenters Extended Spectrum Beta lactamase Gram Negative bacilli - are the main Causes of mortality and morbidity. These bacteria produces potent Beta lactamases. Which destroy Beta Lactam Rings in all Types of penicillins and Cephalosporins. Beta Lactam & Beta lactamase inhibitor (BBLi) are in the way for efferent therapy. Amoxicillin- Clavulanate Moraxella Catarrhalis harmophilus influenzar Ampicillin -Sulbactam⊠ for Staphylococcal infection piperacillin -Tazobactan MDR -g (-) Bacilli Ceftazidime clavulanate MDR - gram Negative Bacilli Ceftazidimeavibactam good activity on Parudo Moncis ceftozolane -Tazobactam good activity on pacndomon. Imipenem cilastatin-relebactam Meropenem Vabrobuctam effective against CRE cefiderocol active against CRE and Prendommas Ervacyclin-a halogenated tetracycline (Teigecycline)- against Gram Negative Gram positive Superbugs.. Pluzomicin - Neo-aminoglycosides. Active against Acinetobacter Cefturoline - active against MRSA Dalbuvancin, oritavancin active against VISA, VRSA Delfafloxacin flouroquinolone active against MRSA With new inoviation for rapid diagnosis of AMR production of New antimicrobes, good hygiene and persuing antibiotic steword Ship hopefully Super bugs become under the Control.

**Keywords**: CIAI: Complicated Intraabdominal in Fection, CUTI: Complicated Urinary Tract in Fection, Carbapenemase



### **Invasive Fungal Infections: Diagnosis and Sensitivity**

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Pathogenic fungi can cause infectious disease in patients with immunocompromised conditions, such as solid and bone marrow transplantation, acquired immunodeficiency syndrome, hematologic malignancy, and usage of immunosuppressant drugs. The most etiologic agents of such infections are Candida, Aspergillus, Mucorals, and Cryptococcus species. Invasive fungal infections are defined according to the revised EORTC/MSG definitions based on host factors and clinical, radiological, and laboratory findings of infections. The outcomes of these infections have been poorly described. The diagnosis methods for these infections are direct smear and culture, histopathology, culture-independent methods such as the use of serological methods like galactomannan and β-D glucan assays, and identifying the nucleic acids of fungi. Antifungal susceptibility tests are essential tools to identify the local and global sensitivity patterns of pathogenic fungi for the treatment guide of fungal diseases. The goal of these tests is to identify the MIC values that may be used to treat patients and track rates of antifungal resistance species. Different methods have been presented by standards development organizations: broth microdilution tests using the CLSI standard methods or the EUCAST standard, disk diffusion, and agar screening for Aspergillus resistance, gradient diffusion strips, sensitive yeast one assay, Vitek 2 yeast panels. The miscellaneous methods include flow cytometry, MALDI-TOF mass spectrometry, agar-based antifungal screening, and isothermal microcalorimetry. Invasive fungal infection presence of certain patients with risk factors. Early diagnosis and appropriate antifungal therapy can be helpful in the treatment and best management of patients.



### Artificial Intelligence's Role in Clinical Microbiology

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Artificial intelligence (AI) improves patient care, choices for therapy, and diagnostic precision in clinical microbiology. Al's performance and role in clinical microbiology include the following: Automated Image Analysis: To identify and categorize microorganisms, artificial intelligence (AI) can examine images of pathology slides, microbial cultures, or other diagnostic samples. This may reduce the possibility of human error and greatly accelerate the diagnosis process. Pathogen Identification and Classification: AI can assist in the identification and classification of pathogens based on their genetic or phenotypic characteristics. This is particularly valuable in identifying antibiotic-resistant strains and guiding appropriate treatment strategies. Antimicrobial Susceptibility Testing (AST): AI can improve AST speed and accuracy, which can help identify the best antimicrobial agents to treat infections. This is crucial in the era of increasing antibiotic resistance. Clinical Decision Support Systems (CDSS): CDSS powered by artificial intelligence (AI) can assist doctors in analyzing complex microbiological data and providing treatment plans based on patient characteristics and infection-causing microorganisms. Epidemiological Surveillance: AI can track and predict infectious disease spread using large datasets. Public health programs need this to detect outbreaks early and execute control measures. Data Integration and Interoperability: AI can help integrate data from electronic health records, laboratory information systems, and imaging platforms. Better patient health understanding and decision-making result from this holistic approach. Despite these developments, validation, ethics, and AI integration into healthcare workflows remain challenges. Clinicians, microbiologists, and data scientists must work together to optimize AI in clinical microbiology.



## **Platelets in Thrombosis and Hemostasis**

**O76-O82** 



#### Platelet Function Analyzer (PFA-100/200) Compared to Platelet Aggregometry

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Physiological hemostasis relies on a complex interplay between blood vessels, platelets, and coagulation factors. Platelet aggregation at the site of vascular injury prevents hemorrhagic events during primary hemostasis. Moreover, quantitative or qualitative platelet defects can also lead to bleeding disorders. At the same time, in patients subjected to antiplatelet therapies, improper responses to these drugs may increase the risk of thrombotic events. Although the physiological mechanisms behind platelet activation are well understood, their translation into diagnostic levels by laboratory analysis remains a significant challenge for health providers. Thus far, several methods have been introduced to analyze platelet functional activities, of which bleeding time, Light/ impedance aggregometry, lumiaggregometry, and flow cytometry-based platelet activation assays are primarily used in specialized labs for diagnostic purposes and patient management. However, point-of-care testing (POCT) dedicated to platelet functional analysis, including devices like PFA-100, VerifyNow System, and Multiplate Electrode Aggregometry (MEA), has also emerged, offering more straightforward and faster assessments usable in emergency clinical settings. However, amongst all the methods mentioned above, Light transmission aggregometry (LTA) versus recent point-of-care testing (POCT) systems (such as PFA-100) draw much attention as the former is still considered to be a gold standard laboratory test for platelet functional analysis. In contrast, the latter claimed it was better to simulate platelet function dynamically under physiological conditions. Therefore, this lecture compares each method's strengths and weaknesses, effectiveness, application, and structural and functional features. Moreover, interpreting the results obtained from these methods presents a challenge that underscores the importance of a comprehensive understanding of the molecular mechanisms involved in the different stages of platelet plug formation. Since each technique has limitations in evaluating inherited and acquired platelet disorders, their establishment and utilization require a comprehensive understanding of the device's mechanism and patient requirements based on the type and prevalence of platelet disorders.

**Keywords**: Hemorrhage, Light Transmission Aggregometry, Platelet Disorders, Platelet Function Analyzer (PFA)-100, Point-of-Care Testing



### **Interpretation of Various Platelet Indices Provided by the Cell Counters**

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Various models of automated cell analyzers are considered as one of the main laboratory devices, used to quantitatively measure blood cells and analyze their general characteristics, such as cell volume and distribution indices. Today growing advances in technology have led to the development of sophisticated devices that provide more details about the cytomorphology and complete differentiation of blood cells. In this regard, impedance analysis, optical light scattering/fluorescence analysis, and flow cytometry technique are the main analytical methods that have been used so far to evaluate platelets. Typically, platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and platelets -large cell ratio (P-LCR) are the common platelet indices calculated with most cell analyzers. Indeed, ensuring an accurate platelet count is very important in identifying and managing bleeding complications in individuals suffering from thrombocytopenia or platelet dysfunction. Therefore, an accurate platelet count is essential for clinicians to monitor thrombocytopenia, therapeutic responses, and also to avoid unnecessary transfusions, where in addition, platelet-related indices may provide important information about the initial hemostasis status. In this regard, while the analysis of platelet graph and indices may experimentally assist the laboratories in identifying potential errors in platelet count or morphology, on the other hand, the interpretation of the platelet histogram and relevant indices can help clinicians gain more information about abnormalities that affect platelet function or indicate underlying diseases. Moreover, using more developed cell analyzer, other indices such as immature platelet fraction (IPF) may provide further information about platelet reconstitution under different pathophysiological conditions. As a result, it is worth noting that platelet indices obtained from routine blood tests can also be recognized as valuable parameters for the evaluation of hemostatic status, while on the other hand, as an advantage for clinical research, these indices may provide valuable diagnostic and predictive information in various conditions without incurring additional costs.

Keywords: Cell Counter, Histogram, MPV, Platelet Function, Platelet Indices, Thrombocytopenia



#### Clinical Approach to Thrombocytopenia

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Idiopathic thrombocytopenic purpura (ITP) is a condition characterized by low platelet counts and bruising or bleeding in the skin and mucous membranes. The management of ITP typically involves a combination of observation, medical therapy, and, in some cases, surgical intervention. 1) Observation: In cases of mild ITP or when the platelet count is above 30,000/µL, a wait-and-see approach may be appropriate. This involves closely monitoring the patient's platelet count and symptoms, with the aim of avoiding unnecessary intervention. 2) Medical therapy: When the patient's platelet count is below 30,000/µL or they are experiencing bleeding symptoms, medical therapy may be considered. The primary goal of medical therapy is to increase the patient's platelet count while minimizing the risk of side effects. a. Corticosteroids: Prednisone is the most commonly used medication for ITP. It can be effective in raising platelet counts, but its use is often limited by side effects such as weight gain, mood changes, and increased risk of infections. b. Immunosuppressive therapy: Other medications that can be used to treat ITP include azathioprine, cyclosporine, and mycophenolate mofetil. These medications work by suppressing the immune system, which can help reduce the destruction of platelets. c. Romiplostim and eltrombopag: These medications are used in patients who are intolerant to or have a contraindication to corticosteroids, or who have had an inadequate response to corticosteroids. 3) Surgical intervention: In rare cases, patients with ITP may require surgical intervention. This is typically reserved for patients with severe or chronic ITP who have not responded to medical therapy or who have significant bleeding or bruising. Surgical options include splenectomy (removal of the spleen) or plateletpheresis (removal of platelets from the blood). It's important to note that the approach to ITP can vary depending on the patient's individual circumstances, including their platelet count, symptoms, and medical history. It's crucial to consult with a healthcare professional experienced in managing ITP to determine the most appropriate course of action for each patient.



### Laboratory Approaches in Immune Thrombocytopenia (ITP): PIFT vs. MAIPA

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Immune thrombocytopenia (ITP)is an autoimmune disorder characterized by the destruction or reduced production of platelets. There are two types of ITP: primary (without a secondary cause or underlying disorder) and secondary, which are usually linked to other autoimmune conditions, infections, medication or malignancies. Several lines of evidence have suggested a key role for antiplatelet antibodies(APAs)in both the pathogenesis and development of ITP, where macrophages within the reticuloendothelial system effectively phagocyte platelets coated with antibodies through Fcy receptors, leading to an accelerated clearance of platelets. In addition, there is a positive correlation between the increase in serum levels of APAs and the clinical symptoms observed in ITP patients, which doubles their importance in the clinical course and treatment of the disease. Hence, it seems that the development of laboratory tests capable of detecting APAs can be useful in improving the management of ITP, while it may also help to distinguish this disease from other cases of thrombocytopenia in certain conditions. In this regard, important laboratory approaches in ITP testing include Monoclonal Antibody-specific Immobilization of Platelet Antigen(MAIPA) and Platelet Immunofluorescence Test (PIFT). MAIPA enables the detection of APAs specificity using antigen-specific antibodies against distinct platelet antigens. However, it is important to note that, the detection of all APAs in MAIPA can be essentially impossible due to the difficulty of performing multiple tests and the high cost of obtaining antigen-specific antibodies for all platelet antigens. This is what overshadows the use of this method as a routine laboratory test, especially since it may also not lead to the potential diagnosis of all ITP patients. In contrast, PIFT offers a more feasible and cost-effective alternative that allows the detection of a larger number of patients in a one-shot analysis with the general detection of anti-platelet antibodies, while eliminating the need for multiple antigen-specific anti-platelet antibodies. This is an advantage that can suggest PIFT as a suitable screening test for ITP, although it lacks the capabilities of the MAIPA in the specific detection of anti-platelet antibodies.

**Keywords**: Antibody, Immune thrombocytopenia, Monoclonal Antibody-Specific Immobilization of Platelet Antigen (MAIPA), Platelet Immunofluorescence Test (PIFT)



### **Recent Updates on Thromboinflammation**

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Thrombotic events and inflammatory responses are closely related pathophysiological conditions that involve multicellular crosstalk between platelets, leukocytes and endothelial cells. Heterotypic adhesive interactions between platelets and neutrophils are important for a number of physiological responses including thrombus formation, wound healing, innate immune reactions, inflammation and allergic responses. Dysregulation of these interactions is also relevant to a range of human diseases including atherosclerosis, acute myocardial infarction, ischemic stroke, acute respiratory distress syndrome and deep vein thrombosis. Co-occurrence of endothelial injury, thrombus formation and leukocyte recruitment at the site of vascular damage creates a conserved milieu that supports an intimate cellular crosstalk between these effector cells. In such a specific milieu, regardless of the classic multistep pattern of platelet adhesion to the site of injury and leukocyte recruitment to the inflamed or injured endothelium which are well described, two novel observations are also occurring that add more complexity and interest including: 1) The observation of neutrophil extracellular traps (NETs) formation in leukocytes adhered to thrombi and their involvement in pro-inflammatory and pro-coagulant functions, which has inspired researchers to investigate the clinical importance of leukocyte recruitment to the sites of vascular injury, particularly in deep-vein thrombosis (DVT). 2) A recent observation, in which we showed how secondary leukocyte recruitment to thrombi in a distinct pattern, termed "Directed Intravascular Conveyance" can lead to extensive accumulation of leukocytes a sites of vascular injury. Taking all the facts into consideration, this lecture first presents an overview of the classical multi-stage mechanism of thrombus formation in different pathophysiological conditions, in which some defects in the functional capacities of platelets are also generally discussed. It then focuses on intricate interplays between proaggregatory, pro-coagulant and pro-inflammatory functions during thrombosis linking thrombus formation to inflammation.

**Keywords**: Adhesion, Cell Migration, Endothelial, Inflammation, Leukocyte, Platelet Activation, Pro-Coagulant Activity, Thrombosis



081

#### **Diagnostic Algorithm of Platelet Functional Disorders**

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Medical diagnostic laboratories play a prominent role in the diagnosis of inherited and acquired platelet disorders. An accurate diagnosis not only improves the effectiveness of treatment but also aids in assessing response to treatment. Any quantitative or qualitative abnormalities in platelets can predispose individuals to bleeding. In this regard, inherited platelet disorders are heterogeneous group of rare diseases affecting platelet production or function. In addition to inherited disorders, acquired causes such as medications, infections, autoimmune diseases, liver disorders, or certain cancers also contribute significantly to platelet disorders. Aside from the assessment of platelet count, specialized tests like platelet function analysis, evaluation of platelet surface markers by flow cytometry, and ultimately genetic testing for detecting genetic mutations involved in disease pathogenesis are utilized. Evaluation of liver function tests, viral serology, and autoimmune tests particularly assist in identifying underlying conditions causing acquired platelet disorders. In order to diagnose platelet disorders, it can be extremely beneficial to use standardized diagnostic algorithms, but these algorithms are not always applicable in routine laboratories due to operational complexity and the need for specialized equipment and experienced technicians.



### **Novel Preclinical Models to Investigate Thrombolysis and Stroke Outcomes**

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Stroke remains the second largest cause of death and disability globally; with the majority of strokes are ischaemic in nature. Treatment of ischaemic stroke(stroke)relies on successful recanalisation of occluded cerebral arteries through intravenous thrombolysis or endovascular thrombectomy(thrombectomy). Unfortunately, often after the initial clot is treated and blood flow restored, damaged vessel(s)rapidly reocclude, necessitating use of antithrombotic (antiplatelet/anticoagulant) therapy. However, acute administration of antithrombotics in the setting of stroke thrombolysis presents unique challenges, due to unacceptably high rates of intracerebral bleeding. Therefore, the identification of antithrombotic adjunctive therapies that can be safely used to enhance thrombolysis in stroke remains an elusive goal. A focus of our research program is to(i)Develop novel antithrombotic agents with unprecedented safety profiles, and(ii)Establish preclinical mouse models that can examine the effect of these novel adjunct therapies in combination with thrombolysis to improve stroke outcomes. In proof-of-concept studies, we have used these models to demonstrate the effect of the direct thrombin inhibitor argatroban as adjunct to rtPA. Real-time assessment of thrombolysis revealed recanalization rates of ~30% in rtPA-treated animals with high rates of rethrombosis. Addition of argatroban increased recanalization rates to 50% and reduced rethrombosis. Paradoxically, this was associated with increased cerebral ischemia and stroke-related mortality(25%-42%). Serial analysis of carotid and cerebral blood flow showed that coadministration of argatroban with rtPA resulted in a marked increase in carotid artery embolization, leading to distal obstruction of the middle cerebral artery. Real-time imaging of carotid thrombi using fluorescence macroscopy revealed that argatroban destabilized platelet-rich thrombi at the vessel wall, leading to dislodgement of large platelet emboli. These studies confirm the benefits of anticoagulants in enhancing thrombolysis and large artery recanalization; however, in this instance the effect of argatroban is offset by increased incidence of carotid artery embolization and distal middle cerebral artery occlusion. These models will provide important new insight into the effects of adjunctive antithrombotic agents on real-time thrombus dynamics during thrombolysis and their correlation with stroke outcomes.



**Young Scientists** 

**O83-O87** 



### Regeneration of Beta Cells in Type 1 Diabetes Via Pharmaceutical Induction

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Background: Treatment strategies for type 1 diabetes encompass insulin therapy, pancreas transplantation, and  $\beta$  cell regeneration. Antimicrobial peptides have shown potential in enhancing insulin release and improving glucose tolerance. However, the mechanism underlying their promotion of damaged pancreatic cell regeneration into functional  $\beta$ -like cells remains elusive. Method: The in vivo effects of magainin-AM2 (Mag) and growth hormone (GH) were assessed in normal and Streptozotocin (STZ)-induced diabetic mice on pancreatic  $\beta$  cell regeneration. Fasting blood sugar (FBS) and glucose tolerance test (GTT) were measured. The western blot and histopathology experiments were used to evaluate beta cell regeneration in removed mouse pancreases. Results: Mag and GH treatment mitigated STZ's impact on FBS and GTT values. It also led to a significant increase in total cell counts ( $\alpha$  and  $\beta$ ), insulin+ and glucagon+ cells per islet, and a decrease in T and B cells. Furthermore, we observed a 1.43- and 2.21-fold increase in paired box 4 expression, a key factor in  $\alpha$  to  $\beta$ -like cell conversion, in normal- and diabetestreated mice, respectively. Similarly, expression of P-S6 and extracellular signal-regulated kinases 1 and 2, essential for cell proliferation/differentiation, increased by 3.27- and 2.19-fold among diabetes-treated and control diabetic mice, respectively. Notably, Mag treatment followed by GH administration exhibited the greatest amelioration across all experiments. Conclusion: This in vivo data supports the potential of pharmaceutical induction of  $\alpha$  cell production and their trans-differentiation into functional  $\beta$ -like cells.

**Keywords**: Differentiation, Growth Hormone, Magainin, β-like Cells



# The High Frequency of Carbapenem-Resistant Acinetobacter Baumannii (CRAB) in Central Iran

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Background: We assessed the frequency of occurrence for infections caused by wild-type A. baumannii, multidrugresistant (MDR) or XDR A. baumannii, and CRAB. We detected different antibiotic resistance genes in the genomes of infectious A. baumannii strains from central Iran. Methods: This study investigated 546 clinical patient samples for the presence of A. baumannii by using conventional culture methods and PCR. Antibiotic resistance profiles, and the phenotypic and genotypic characteristics of various antibiotic genes were analyzed. Results: Out of 546 samples, 87 (15.9%) A. baumannii isolates were obtained using culture and all culture positive samples were also positive by PCR. The most effective antibiotics were polymyxin B (n=84 strains) (96.6% susceptibility), colistin (n=81) (93.1%), and ampicillin/sulbactam (n=18) (20.7%). All clinical A. baumannii isolates were ESBL-positive. The number of CRAB was 84 (96.5%). All CRAB isolates were both MDR and XDR. Of all CRAB isolates, 78 out of 84 (92.4%) produced metallo-β-lactamase (MBL) by phenotypic diagnosis. The most abundant genes were blaPER (32/87; 36.7%), blaTEM (29/87; 33.3%), blaVEB (26/87; 29.8%) for ESBL and Ambler class D β -lactamases included blaOXA-23 (69/84; 82.1%), blaOXA-24 (46/84; 54.7%), MBLs included blaVIM (51/84; 60.7%), and blaIMP (28/84; 33.3%) for carbapenemase. Conclusions: High frequencies of XDR A. baumannii and CRAB (96.5%) were detected in central Iran. Quick and accurate diagnosis, appropriate isolation of patients colonized or infected by CRAB isolates, application of accurate and effective infection control policies and programs, and appropriate preventive measures are deemed helpful in preventing the further spread of these resistant and clinically highly relevant strains.

**Keywords**: Extensively Drug, Resistant (XDR), Carbapenem, Resistant A. Baumannii (CRAB), blaOXA-23, blaVIM. Iran



085

# Implementing Echinococcus Granulosus Derived MicroRNAs as Biomarkers for Diagnosis and Follow up of Cystic Echinococcosis Patients

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Background: Cystic echinococcosis (CE) is a neglected tropical disease caused by the larval stages of Echinococcus granulosus (E. granulosus). MicroRNAs (miRNAs) are small noncoding RNAs acting as mediators in host-parasite interaction. Recently, numerous studies have been conducted on miRNAs in infectious diseases; however, little data are available about the role of miRNAs in pathogenesis and early diagnosis of CE. Methods: The current study evaluated the expression of four E. granulosus-derived miRNAs, including egr-miR-125,5p, egr-let-7,5p, egr-miR-2, and egr-miR-71 in fibrotic and healthy liver tissues of 31 CE patients with active and inactive hydatid cysts by qRT-PCR. Results: Of the 31 patients, 48.4% had active cysts (CE1 and CE2), while the remainder had transitional (16.1%) and inactive (35.5%) CE types cysts. The qRT-PCR analysis revealed a significant increase of 11.2, 9.91, 6.2, and 13.1-fold in the fibrotic tissue group for egr-miR-125,5p, egr-let-7,5p, egr-miR-2, and egr-miR-71, respectively. Among these miRNAs, egr-miR125-5p exhibited the highest area under the curve (AUC) value of 0.8050 for predicting liver fibrosis. Conclusions: Our findings provide new data about the role of E. granulosus-derived miRNAs in pathogenesis of CE. The high AUC of egr-miR125, 5p reflecting the possibility of using egr-miR125,5p as biomarker in CE diagnosis. Further studies on serum of CE patients are needed to confirm the potential role of circulating egr-miR-2a-3p and egr-miR-125-5p in the early diagnosis of CE.

Keywords: Cystic Echinococcosis, Echinococcus Granulosus, MicroRNA, Real-Time PCR



# Royal Jelly Induced ROS-Mediated Apoptosis in Naml-6 Cells: an Emerging Perspective for ALL Treatment

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Background. Considering that the chemotherapy regimen of Acute lymphoblastic leukemia (ALL) is accompanied by various challenges, there is require novel agents for ALL treatments. Honey bees' royal jelly (RJ) is one of the most appreciated natural products that reveal anti-tumor activity in humans. This study aimed to evaluate the antileukemic properties of RJ on ALL-derived Nalm-6 cells. Methods. The metabolic activity was measured by MTT assay. Apoptosis and intracellular reactive oxygen species (ROS) levels were investigated using flow cytometry analysis. Moreover, quantitative real-time PCR (qRT-PCR) was performed to scrutinize the expression of various regulatory genes. Afterward, the RJ effect on peripheral mononuclear cells (PBMC) was examined to evaluate its safety. Results. RJ significantly decreased the viability of Nalm-6 cells in a concentration and time-dependent manner. RJ caused a 50% reduction in Nalm-6 cell proliferation (IC50) in 2.267±0.026 concentration after 48 h. In addition, RJ vigorously increased the percentage of apoptotic cells in a dose-dependent way by activating ROS production. According to qRT-PCR results, RJ induces mitochondria-mediated apoptosis through increased levels of Bax and Bad but not Bcl-2 and Bcl xL and upregulates Bax and Bcl-2 ratio. Additionally, the ROS-related gene expression analysis showed the expression of FOXO4 and Sirt1 genes raised after treatment. Noteworthy, RJ has no apoptotic effect on PBMC as normal cells, as indicated in MTT and flow cytometry investigation. Conclusion. This study sheds light on the potent anti-leukemic effects of RJ and provides evidence for the pharmaceutical application of this agent in the treatment of ALL which requires further in vivo experiments.

Keywords: Acute Lymphoblastic Leukemia (ALL), Royal jelly (RJ), Apoptosis, Nalm-6, PBMC



# Identification of Reactive Proteins in Patients with Triple-Negative Breast Cancer (TNBC) using 2D Immunoblotting and Mass Spectrometry

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Background: Triple negative breast cancers (TNBCs) include 12 to 24% of breast cancers. Their most important feature is high prevalence at a young age, more aggressive phenotype and worse prognosis. Due to the absence of estrogen and progesterone receptors and Her2, target therapy is not used for these patients, so the aim of this study is to identify new protein biomarkers by immunoproteomics technique. Methods: In this study, which was conducted using immunoproteomics followed by mass spectrometry, 50 serum specimens were taken from patients with triplenegative breast cancer (TNBC) and control subjects, and their demographic and pathological characteristics were collected to provide antibody sources. The PARI-ICR cell line was cultured in DMEM-12 medium to prepare theantigen source, and thus 50 million cells were collected by the physical method and lysed using the thiourea method. The concentration of protein obtained from cell lysate was also measured using the Bradford method. These proteins were then separated by Isoelectric focusing (IEF) and SDS-page. After 2DE, the proteins were transferred from the gel surface to the PVDF paper and were stained by ECL solutionafter exposure to the primary and secondary antibodies, finally, the protein spots reacting with the specific antibody were determined by mass spectrometry. Furthermore, functional analyses and interaction of the proteins were carried out using Gene Ontology (GO), PANTHER, Gene MANIA, and STRING databases. Results: This study introduced a total of 9 protein biomarkers, namely Statherin, Stathmin, LAMTOR1, Galectin-1, COP9, MDH2, Prohibitin, Ras-related protein Rab-11B, and PSME1. Conclusion: These biomarkers can be used for vaccine preparation or treatment managementin the future. Furthermore, it is possible to diagnose cancers from serum earlier by detecting serum autoantibodies that are produced against tumor proteins and also designing a suitable ELISA kit.

Keywords: Cancer, Biomarker, Immunoproteomics, Triple-Negative Breast Cancer (TNBC)



# **Keynote Speech**

**O88-O91** 



088

### Tehran Lipid and Glucose Study: A National Legacy

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The year 2024 marks 26 years since the landmark Tehran Lipid and Glucose Study (TLGS) was designed in the Islamic republic of Iran. With rapid economic and demographical transition in Iran in the last decades of twentieth century, a dramatic risk in non-communicable disease (NCDs) especially cardiovascular disease, as the major cause of morbidity and mortality occurred. This legacy research project was approved by the National Supreme council for Scientific Research in 1977 periodic examination and follow up of over 15000 people, 3-80 years of age, and every 3 years was a great opportunity to find they trend of various risk factors of TLGS population in a country in nutrition transition with substantial change in life style. Continuation of a cohort study, especially in a developing country is a major challenge. In the TLGS, following the collection of baseline data, a community-oriented life change has been implemented. This intervention has been effective in decreasing the incidence of type 2 diabetes and in diminishing the prevalence of metabolic syndrome and its components. Therefore, TLGS has added the aspect of intervention for health benefit, which has been lacking in many cohort studies, such as Framingham. More recently, TLGS has conducted studies involving genomic and biomarkers of NCDs and has performed the first whole-genome sequence version and announced the Iranian Reference Genome Research Project. Having information in genomes and metabolomics of this cohort with 20 years phenotypic findings could disclose many aspects of personalized medicine in endocrinology and other domain of medicine in Iran.

Keywords: Communicable disease, Tehran Lipid and Glucose Study, Life-Style Change, Iran



089

# Standardization and Harmonization of Clinical Laboratory Test Results: Essential to Achieving Optimal Quality

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The current landscape of laboratory systems and reference standards for interpreting diagnostic test results lacks consistency, posing a risk to patient care. Even laboratories using the same instruments and reagents exhibit high variability and poor harmonization in test result interpretation. This inconsistency, often unnoticed by those involved in laboratory processes, especially when results are transferred between laboratories, has the potential for inappropriate patient care due to differing interpretations based on reference intervals. Harmonizing reference intervals is deemed crucial for patient safety, supported by factors such as widely accepted diagnostic cut-offs for certain tests across laboratories. While progress has been made in assay harmonization and standardization by organizations such as IFCC, reference interval harmonization lags behind. Global initiatives, such as NORIP, Pathology Harmony, AHRIA, and AHRIP, aim to address this issue with unique approaches. In Canada, the Canadian Society of Clinical Chemists has formed a national Working Group to coordinate efforts to harmonize reference intervals. Proposing harmonized reference intervals and common reporting formats as the preferred option, the group utilizes direct reference value data and retrospective patient data from multiple provinces to develop Canadian harmonized reference intervals. Despite challenges in implementing harmonized reference intervals at the national level, there is a pressing need for their development, requiring the involvement and commitment of various stakeholders, including physicians, accreditation programs, quality assurance programs, clinical chemists, and other laboratory professionals, to ensure widespread implementation and success.



#### **Pharmacogenomics**

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Pharmacogenomics is the study of how genes affect a person se response to drugs. This field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications that can be prescribed based on a person us genetic makeup. Many drugs that are currently available are uone size fits all," but they don't work the same way for everyone. It can be difficult to predict who will benefit from a medication, who will not respond at all, and who will experience negative side effects (called adverse drug reactions). Adverse drug reactions are a significant cause of deaths in the world. Researchers are learning how variants in genes affect the body's response to medications. These genetic differences will be used to predict whether a medication will be effective for a particular person and which dose will help prevent adverse drug reactions. The field of pharmacogenomics is growing, and new approaches are under study in clinical trials. In the future, pharmacogenomics will be used to develop tailored drugs to treat a wide range of health problems, including cardiovascular disease, Alzheimer's disease, cancer, and asthma. Pharmacogenomics is part of the field of precision medicine. This is treatment that's personalized based on genes, environment and lifestyle. Pharmacogenomics can help your healthcare provider prescribe a medication that leads to fewer side effects or that may work better for you. Providers typically use a blood sample for pharmacogenomic testing. A provider sends sample to a laboratory where a technician checks DNA for specific changes. Which gene or genes they check depends on which test provider has ordered, which condition they're trying to treatment and which medications they're considering.

Keywords: Pharmacogenomics, Drugs, DNA, Lifestyle, Treatment, Precision Medicine



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# Reference Intervals of Biochemical Markers in a Multiethnic Iranian Population: The IRLAR project

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Background and aim of the study: The significance of clinical laboratory test results cannot be overstated. Approximately 80% of a physician's medical decisions rely on the data presented in laboratory reports. However, a test result lacks meaningful value unless it is accompanied by the necessary information for proper interpretation. This crucial context is usually conveyed through the inclusion of a reference interval (RI) or a medical decision limit. In contrast to the direct method, which is costly, time-consuming, and challenging due to the definition of health, indirect methods are easy to perform and employ statistical techniques to determine a range of values that encompasses 95% of the population. This method is appealing because it relies on readily available data, leading to time and cost savings. Our goal in this national project is to establish RIs for 17 routine lab tests by the refineR method Methods: More than 24 million lab records for 17 biochemical lab tests including FBS, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, SGOT, SGPT, ALKP, urea, creatinine, uric acid, total protein, albumin, total bilirubin, direct bilirubin, LDH and TSH from 2015-2015 were collected from 60 outpatient medical laboratories after getting approval from the National Institute for Medical Research and Development (NIMAD) and IACLD. Laboratories were selected based on the results of the External quality assessment program (IOAP) conducted by IACLD. Only those laboratories with high scores in three successive assessments were selected. Data was cleaned for any inconsistency in national code, sex, age, lab name, province, test principle, or test unit. Results that fell outside of predefined criteria for outliers were excluded from the calculation of the reference interval. The central tendency (e.g., mean or median), and variability (e.g., standard deviation or interquartile range) of the results and RIs were then calculated by refineR. Results: Based on test result variation, RIs were established for different age groups in both genders. More importantly, RIs were established for children, adolescents age, and adults. While RIs for some lab tests had very close distribution at different age and sex groups, there were great age- and sexdependent variations in other lab tests. Our results showed a great variation in RIs in different Iranian ethnic groups and provinces, while established RIs, in general, were reproducible in four years of data collection. Indeed, our established RIs for some lab tests were to some extent different from those already established by other studies, which may stem from different lab test principles and ethnicity. Conclusion: This is the first national RI project encompassing a large Iranian population from different provinces with different ethnicities. The results of this national project will help doctors to better interpret the laboratory results of the Iranian population and will provide them with a more reliable source of reference sources.

Keywords: Reference Interval, Iranian Population, Indirect Method, RefieR, Medical Laboratory



# Laboratory and General Guide of Professional Ethics for Medical Practitioners and Affiliates of the Medical Council of Islamic Republic of Iran

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Introduction: Professional medical ethics have evolved and manifested throughout history in documents such as medical oaths, which have been prominent writings in this field over the centuries. These oaths, advisories, and guidelines have aimed to define the ethical duties expected from medical professionals and affiliates, specifying the necessary ethical standards, principles, and rules relevant to their time and the challenges in the medical profession. On the other hand, by adhering to these professional standards, medical professionals have fostered public trust in their caregivers, positioning the medical profession in a special societal status. These documents, while mandating serious adherence to public moral norms, also enumerate specific ethical duties from a specialized behavioral guide perspective and strive to provide clear answers to professionals' questions. It is often seen that what is commendable but non-mandatory for the general public is a necessary norm for medical professionals, and failure to adhere to it could lead to moral and professional reproach. Method: This study examines the relevant sections of the General Guide of Professional Ethics for Medical Practitioners and Affiliates of the Medical Council of the Islamic Republic of Iran, focusing on the expected duties from the laboratory community in Iran. Findings: Several clauses in the aforementioned guide directly and indirectly refer to biomedical ethics principles and the specific ethical duties of laboratory professionals. Discussion and Conclusion: Professional behavior and adherence to the expected ethical duties by the laboratory community, as highlighted in this guide, not only enhance the quality of services provided to health service recipients but also increase the efficiency of these professionals and public trust by respecting patient rights. Ultimately, this will reduce instances of behaviors contrary to medical conduct (as per Article 6 of the Disciplinary Regulations of the Organization), potentially decreasing complaints with ethical implications.

Keywords: Professional Ethics Guide, Medical Council



### Reciprocal Rights of Recipients and Providers of Service in Medical Diagnostic Laboratories

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In today's world, the relationship between medical and affiliated professions and society is extensive, leading to significant benefits and advancements in diagnostic and therapeutic methods. Ensuring the legal interests of all individuals involved in these interactions results in various perspectives. Health service providers expect conditions that preserve and protect their legal interests, while society, regulatory organizations, and patient rights advocates expect policies and actions that do not contradict public and patient interests. Considering that the service delivery system and interactions with laboratory clients differ somewhat from other healthcare sectors, addressing specific aspects of this field, alongside the comprehensive Patient Rights Charter issued by the Ministry of Health, can enhance individuals' commitment and dedication to their specialized work. The main principles of reciprocal rights for recipients and providers of laboratory services are based on five core principles:

1. Receiving appropriate laboratory services, 2. Receiving adequate and satisfactory information, 3. The right to free choice and decision-making, 4. Respecting privacy and confidentiality, 5. Access to an efficient complaints handling system. Addressing these issues is a step towards implementing and enforcing the Charter of Rights for clients of medical diagnostic laboratories.

Keywords: Patient Rights, Medical Diagnostic Laboratories, Medical Ethics



# **Poster Presentation**



## A Laboratory Guide to Diagnosis of Rash-Inducing Viruses

**P1** 



# Prevalence of HBsAg and Anti-HCV in Referred to the Laboratory of Afshar Hospital, Yazd

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Introduction: This research was conducted in order to evaluate the prevalence of hepatitis B and C in a clinical training center in Yazd city during seven consecutive years. Methods: A retrospective study was conducted from 1396 to 1402 on the results of the tests of people referred to the laboratory of Afshar Hospital in Yazd. Serum samples were evaluated for the presence of HBsAg and Anti-HCV by ELISA method and were confirmed using Vidas kits. Results: Out of 39,699 serum samples examined for HBsAg, 20,941 were women and 18,758 were men. The average age was 53.8 years. 26,713 samples were in wards and the rest were outpatients. The highest number of investigated cases was related to the year 1401 (8869) and the lowest was to the year 1399 (3879). 437 samples (1.1%) were HBsAg positive (1.2% outpatients and 1% from wards). 261 cases (59.7%) were men. The prevalence rate was 1.04% in 1396 and 1.02% in 1402. Out of 39186 serum samples, 116 samples (0.3%) were positive for Anti-HCV. The average age of these people was 52.7 years. 26652 samples were from wards and the rest were outpatients. 18,685 people were men (96 positive samples) and the rest were women. The prevalence of Anti-HCV in wards and outpatients was 0.32% and 0.28%, respectively. The most cases of investigation were related to 1401 (8849) and the lowest was 1399 (3840). The prevalence rate was 0.33% in 1396 and 0.25% in 1402. The rate of positive cases in terms of HBsAg and Anti-HCV was different between women and men. Conclusion: The rate of prevalence and lack of significant decrease in positive cases of hepatitis B and C during the years under review and the difference in its rate in men and women should be the attention of the health authorities.

Keywords: HBsAg, Anti-HCV, Yazd



### **Accreditation in Medical Laboratories**

**P2-P6** 



### **Enhancing Medical Laboratory Standards via Continuous Professional Development**

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Background: Accreditation and continuing professional development (CPD) are critical to maintaining high-quality medical laboratory services. However, integrating CPD into accreditation standards remains a challenge. This review aims to propose a more robust accreditation model by examining current practices and suggeding systemater CPD approach for enhance laboratory excellence. By incorporating CPD into accreditation standards, we can create a more rigorous and world-class medical laboratory system. Methods: The methodology of this review article involves a multi-faceted approach, including a literature review, expert interviews, survey research, case studies, and data analysis to investigate the integration of Continuous Professional Developmen (CPD) into accreditation standards for medical laboratories. Results: Medical laboratory standards are greatly improved by continuous professional development (CPD), which leads to increased analytical accuracy and compliance with best practices. However, implementation varies globally due to financial, resource, and cultural barriers. Conclusion: Continuous professional Development (CPD) is critical for improving laboratory standards and ensuring precision, efficiency, and adaptability to technological advances. Despite challenges in resourcelimited settings, its strategic integration can enhance patient outcomes and global healthcare quality.

**Keywords**: Continuous Professional Development (CPD), Medical Laboratory Standards, Quality Assurance, Competency Assessment



Р3

# The Necessity of Ranking Domestically Produced Laboratory Diagnostic Kits Based on Brand and Lot Number

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Although various factors such as equipment, methods of conducting tests, the level of proficiency of personnel, etc., play a role in the correct presentation of test results in medical diagnostic laboratories, but the role of kits and consumables in presenting the results of laboratory tests cannot be overemphasized. denied The consecutive review of the external quality control results (EQAP) shows well that the group (CV) in different brands are very different for each test. Although the work method, the type of equipment and some other factors in the correlation of the answers The tests are effective, but the above factors are almost the same for all brands, so the quality of the kit is the most important reason for the high (CV) of the group. The more important issue is that different brands do not have the same (CV) in consecutive periods. And it is different from one lot number to another lot number and has a significant ups and downs. What is important in this is the production of wrong results, which, of course, is a major loss in addition to distorting the face of the laboratory, it also affects the patient and surprises the doctor, and sometimes prolongs the course of the disease treatment. It seems that instead of visits and low-result inspections, which the energy and power of the laboratories and that department lead to, as the main task and based on the results of external quality control and the correlation of the answers, the ranking kit should be used. Laboratory tests based on type and brand and to test their specificity and sensitivity. For this, the Six Sigma method or similar methods can be used. In a case study conducted by the author and based on the results of external quality control.

Keywords: Coefficient of Variation of the Group, External Quality Control, Brand Kit



Assessmenting the Performance of Microscopists and Experts of the Laboratories Responsible for the Microscopic Diagnosis of Malaria at Jiroft University of Medical Sciences Through the Conduct of the Professional Qualification Assessment Test (PT)

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Introduction: Since the professional qualification test program is one of the pillars of the quality assurance system, it is necessary to implement this program to improve the qualification and performance of malaria microscopists. Method: Determining the composition and order of the slides used in the test of common pathogenic plasmodium and coding them based on a random table, then labeling the slides and sending the slides with a special form to the selected laboratories, then collecting the panel of slides along with the results. From the laboratories and reviewing and summarizing the results, finally determining and reviewing the weaknesses and strengths of the microscopists and solving their problems Out of a total of 25 people, the largest number of participants were in the age group of 30-39 (60%). In terms of gender, there are 11 men and 14 women. In terms of work experience, most of them were in the range of 5-9 years, and (45.8%) succeeded in obtaining a rank, (29.2%) B rank, and (25%) C, rank in the validation test. The average percentage of the total score of microscopists is 90.1%. The average percentage of sensitivity of microscopists was 99%, the average percentage of parasite detection specificity was 100% and the average percentage of parasite detection among microscopists was 82.7%. In terms of parasite count, In the end, the status of microscopists in this period was calculated according to the qualification evaluation program, 11 people (72%) were excellent, 10 people (40%) were very good, 3 people (12%) were good, and 1 person (4%) was poor. Conclusion: The PT test results can be used to compare each microscopist with himself, to compare covered laboratories with each other during consecutive periods for planning, how to train and improve the qualification and performance of microscopists.

**Keywords**: Quality Assurance, PT Test, Performance Evaluation, Malaria, Jiroftquality Assurance, PT Test, Performance Evaluation, Malaria, Jiroft



# Examining the Level of Awareness and Knowledge of the Technical Departments of the Laboratories of Tehran Metropolis with the Concepts of Quality control and Quality Assurance in the Laboratory

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For establishing the Quality control and Quality assurance in laboratories, in addition to the knowledge of the laboratory managers, knowledge of the personnel of the technical departments of the laboratories is also required. so we decided to investigate the level of the knowledge of the personnel of the laboratories during this research. The present research is a descriptive-analytical study and the population of the research consists of all the personnel of the technical departments of the selected laboratories in the city of Tehran, numbering people. In this research, with the help of a 70-question questionnaire, information was collected in four sections: demographic information, the knowledge about the laboratory safety principles, the knowledge about the general concepts of quality assurance and quality control, and the knowledge about the quality control of different parts of the laboratories. The validity of this questionnaire was reported as favorable by and experts. Data analysis was done using SPSS version 24.

Keywords: Quality Assurance, Quality Control, Laboratory Personnel



### The Frequency and Type of Preanalytical Errors in Hematology Laboratory for Two Large Academic Hospital of Shiraz University of Medical Science

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Background and Objectives: Laboratory reports play a vital role in patient management. Improving the quality of laboratory tests deserves high attention. The pre-analytical phase of laboratory testing is a decisive step in quality assurance plans. Special attentions are needed to record and reduce the pre-analytical errors in the hematology laboratory. Our study was designed to investigate retrospectively, the type and frequency of pre-analytical errors in the hematology laboratory of two large academic hospitals. Methods: We conducted a cross-sectional study in the hematology laboratory of two academic hospitals by collecting and analyzing data within a certain period of time. The study focused on pre-analytical variables. Both inpatient and outpatient departments were included. Results: A total of 195161 samples were received in the hematology lab during this period. In overall, pre-analytical errors were found in 887 samples, which composed 0.45% of the total samples. The most common error in both mentioned Hospitals was clotted CBC (655/195161, 0.33%). wrong container in ESR test has the lowest amount of errors (3/195161, 0.001%). Conclusion: Pre-analytical errors continue to pose a significant challenge to hematology laboratories. These errors are predominantly attributed to flawed specimen collection procedures that eventually compromise the quality of the specimen. It is important to continuously train and adhere to standards and principles in order to prevent errors during the pre-analytical stage and achieve control over this stage.

Keywords: Pre-Analytical Errors, Hematology Laboratory, Quality Management



### Application of NMR and LC/MS in Clinical Laboratories

**P7-P8** 



#### Tyrosinemia Type III

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Background: Tyrosinemia is a congenital metabolic abnormality whose symptoms include liver and kidney disorders as well as mental retardation, and if left untreated, it can cause the patient's death. There are three different types of tyrosinemia. Type3 tyrosinemia is caused by a defect in the enzyme 4-hydroxyphenylpyruvate dioxygenase. The characteristic features of type 3 tyrosinemia are mental retardation, seizures, intermittent ataxia, and self-destructive behaviors. Methods: The 5-day-old newborn had abnormal tyrosine in metabolic disease screening by LC-MS/MS method. The parents were related and had a healthy child. For follow-up and confirmation, an amino acid profile was requested by HPLC and LC-MS/MS that the results of tyrosine increased until the age of nine months. The baby did not have any special clinical symptoms. The result of urinary succinyl acetone test by GC-MS was normal. Genetic test was done for further investigation, and tyrosinemia type3 was confirmed. Results: The result of newborn tyrosine in the initial screening by LC-MS/MS in the dry blood spot sample is equal to 286 micmol/L.In order to follow up, the test was repeated three times at intervals of several months and the results of tyrosine 268,450 and 936 were obtained respectively. The evaluation of organic aciduria by GC-MS for succinyl acetone excretion was negative. Tyrosinemia type3 variant C.308-64 G>A was confirmed in the whole exome sequencing (WES) genetic test. Conclusion: Screening of metabolic diseases in 2-7-day old newborn is done using MS/MS method. Tyrosine is one of the primary screening markers for tyrosinemia. The secondary marker in tyrosinemia type3 is an increase in the ratio of tyrosine to citrulline.diagnosis of typeIII tyrosinemia, moderate and permanent increase of tyrosine in the measurement of amino acids by HPLC and LC-MS/MS method, investigation of 4-hydroxyphenylpyruvate dioxygenase(HpPD)enzyme activity in liver biopsy sample and molecular investigation of 4-hydroxyphenylpyruvate dioxygenase enzyme mutation. Treatment in typeIII tyrosinemia includes a diet with phenylalanine and tyrosine restriction. Also, treatment with vitaminC is considered as a cofactor of 4-hydroxyphenylpyruvate dioxygenase.

Keywords: Tyrosinemia, Succinyl Acetone, 4-Hydroxyphenylpyruvate Dioxygenase, LC-MS/MS



# Detection of Antigenic Determinants from Tumor Tissues of Breast Cancer Patients Aged under 40 and over 40 Years by Two-Dimensional Electrophoresis and Mass Spectrometry

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Background: Breast cancer (BC) is the most common malignancy and the leading cause of cancer-related death among women worldwide. Individuals under 40 years old have a worse prognosis and unfavorable molecular subtypes compared to the post-menopausal period. The aim of this study is to recognize biomarkers, which are differentially expressed in two age groups and stages of BC patients. Methods: The proteome of tissue samples of 40 BC patients (=<40y n=20 and >40y n=20) was subjected to two-dimensional electrophoresis (2-DE) combined with Liquid chromatography mass spectrometry (LC MS) system to identify differentially expressed proteins. The intensity of protein spots was compared with SameSpots software. Functional, pathway, and interaction analyses of identified proteins were performed using geneontology (GO), PANTHER, Gene MANIA, and STRING databases. Results: Ten proteins showed differential expression (over1.5-fold) by LC-MS, including 6up-regulated in =<40y BC often in the early stages of the disease and 4 up-regulated in >40y BC patients. Among the proteins identified in the group over 40 years old, Prohibin 1 was of great importance because the production of antibodies against it were also confirmed by immunoproteomics. Proteins involved in the catalytic activity, binding, transcription regulator activity, biological regulation, cellular process, nucleobase biosynthetic and metabolic process, cellular detoxification, showed the most significant changes in BC patients. Additionally, the most potential functions related to these detected proteins were associated with the proliferation, migration and invasion of cancer cells, oxidoreductase, and antioxidant activity. Conclusion: In this study, several changes in protein expression were identified in people under 40 years of age, especially in the early stages of the disease, which can be useful as promising biomarkers for early diagnosis and prognosis of breast cancer.

**Keywords**: Breast Cancer, Proteome, Biomarker, Mass Spectrometry



#### **Challenges in Laboratory Diagnosing and Reporting HPV Infection**

P9-P13



Р9

#### Investigating the Analytical Characteristics of Two Human Papilloma Virus Genotyping Kits Based on PCR-Hybridization and Real Time PCR Methods in a Clinical Study

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Background: Human papillomavirus (HPV) is the name of a group of 200 known viruses. In 90% of people the body controls the infection by itself. Persistent HPV infection with high-risk HPV types is the cause of cervical cancer and is associated with cancers of the vulva, vagina, mouth/throat, penis and anus. HPV infection causes about 5% of cancers worldwide. The two main ways to diagnose are cytology and HPV testing. Methods: In the clinical study conducted in this research, 100 positive clinical samples were evaluated. These samples were checked using the High + Low Papillomastrip Kit (OPERON®) and reported positive. In the following, these samples were evaluated in parallel with the real-time PCR method. All primers and probes were designed to identify 19 high-risk and 19 low-risk genotypes and were evaluated with positive clinical samples. Results: The comparative results showed that all the genotypes that had positive results with the operon kit were also identified by the real time PCR method, but in 5 clinical samples, genotypes were evaluated as positive by the real time PCR method that were not detected by the operon kit. In this way, the analytical feature of the real-time PCR method was evaluated at 100% and the Operon kit at 95% (p<0.001). Also, the Kappa Agreement was calculated to be 0.65. Conclusion: It is recommended to use the real-time PCR method for genotyping clinical papilloma samples. Of course, the advantages and disadvantages of both methods should also be considered.

Keywords: HPV, PCR-Hybridization, Real Time PCR



#### **HPV and Skin Cancer: Are Non-Coding RNAs Completing the Puzzle?**

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Oncogenic viruses, such as human papillomavirus (HPV), have been increasingly recognized for their potent carcinogenic properties, particularly in relation to the rising global incidence of skin cancer. The complex interplay between viral genes and host cells contributes to the pathogenesis of HPV-induced skin cancer. Noncoding RNAs (ncRNAs), which constitute a significant portion of the human genome, have emerged as key regulators in various malignancies. This review explores the potential involvement of ncRNAs in the development of skin cancer triggered by HPV, focusing on their diagnostic and therapeutic implications. Current diagnostic methods for HPV-associated skin cancer often lack accuracy and invasiveness. NcRNAs show promise as biomarkers for early detection and prognosis. Evaluating viral and human ncRNA profiles in normal and cancerous skin tissue may offer a practical approach to pre-diagnosing skin cancers. Various classes of ncRNAs, including miRNAs, lncRNAs, and circRNAs, have been implicated in HPV-related skin cancer pathogenesis. By identifying specific ncRNAs that are dysregulated in skin cancers, they can be utilized as diagnostic biomarkers. Additionally, targeting these ncRNAs may open new avenues for therapeutic interventions. Notably, the diagnostic potential of ncRNAs extends beyond HPV-related skin cancers, encompassing other cancer types such as lung, breast, and prostate. Therefore, assessing ncRNA profiles provides a comprehensive approach to cancer diagnosis and prognosis.

Keywords: Human Papillomavirus, Skin Cancer, Cutaneous Cancers, Non-Coding RNA



## Molecular Detection and Association of Human Papilloma Virus in Paraffin-Embedded Tissue Samples of Patients Suffering Ovarian Cancer in Ahvaz, Iran: a CaseControl Study

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Background: Human papillomavirus (HPV), the causative agent of cervical cancer, is associated with several other epithelial malignancies. Previous reports on HPV infection and its association with ovarian cancer are highly contradicting. Reports on HPV association with ovarian cancer in Iranian women are also rare. Hence, the purpose of this study was to screen women with epithelial ovarian cancer for possible HPV infection and its genotyping. Methods: In this case-control study, 45 Paraffin-embedded ovarian tissue specimens served as the case group and 45 FFPE tissues from ovarian cysts served as the control group were included from March 2017 to February 2021 and subjected to DNA extraction. The β-globin gene was amplified using PCR to confirm the quality of the extracted DNA. The genomes of HPV were identified, using specific primers, by PCR. The genotyping of positive samples was then done using a Real-Time PCR technique. SPSS version 22.0 was used to perform all statistical analyses. Results: A total of 40/90 (44.4%) samples had HPV DNA. Regarding the presence of HPV DNA, there was no discernible difference between ovarian cancer and ovarian cystic tissues (P>0.05). Among the 40 genotyped strains, the predominant genotype was 16 (67.5 %), followed by 31 (47.5%), 18/45 (17.5%), 68 (15%), 59 (10%), 51 (7.5%), and 6/11 (5%). 95.65 percent of the positive samples (22/23 samples) in the case group and 94.11% of the discovered viruses (16/17 samples) in the control group were High Risks (HR)-HPV. Conclusion: The present study shows a high frequency of HPV infection in epithelial ovarian cancer and cystic tissues in our region. It is highly recommended to get vaccinated against HPV to reduce the risk of cancer. The result of the current investigation supports the results of earlier research that, HPV is not associated with ovarian cancer.

**Keywords**: Human Papillomavirus- Ovarian Cancer, Ovarian Cystic, Genotyping, Carcinoma, Ovarian Epithelial Cancer, HPV Infection, Malignancy, PCR, Real-time PCR, Nested PCR



#### Detection of High-Risk Human Papillomavirus DNA in Invasive Ductal Carcinoma Specimens

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Background: According to several studies, there is an association between human papillomavirus (HPV) and breast cancer. Therefore, detection and genotyping of HPV seem important. The present study aimed to investigate the presence of HPV DNA in breast tissues by analyzing the L1 gene. Methods: This case-control study was conducted on 63 formalin-fixed paraffin-embedded (FFPE) tissues of invasive ductal carcinoma (IDC) as the case group and 32 FFPE tissues of fibroadenoma as the control group. HPV DNA was detected using the polymerase chain reaction assay. Positive samples were then subjected to genotyping. All statistical analyses were performed in SPSS version 22.0. Results: The patients age ranged from 15 to 92 years, with a mean age of 43.54±16.36 years. HPV DNA was detected in 17/95 (17.89%) samples, including 9/32 (28.12%) fibroadenoma samples and 8/63 (12.69%) IDC samples. No significant difference was observed regarding the presence of HPV DNA between the IDC and fibroadenoma tissues (P=0.08). However, a significant difference was found in the detection of high-risk HPV (HR-HPV) between the case and control groups (P=0.03). In the case group, 87.5% of the detected viruses (7/8 samples) were HR-HPV, while in the control group, 22.22% of positive samples (2/9 samples) were HR-HPV (P=0.03). Based on the results, HR-HPV and low-risk HPV genotypes were detected in 53% (9/17) and 47% (8/17) of positive samples, respectively. Conclusion: In this study, 12.69% of IDC samples were positive for HPV genomes, and HR-HPV was detected in 87.5% of these samples. The present results suggest the important role of HR-HPV in the development of breast cancer.

Keywords: Human Papillomavirus, DNA, Invasive Ductal Carcinoma



## Human Papilloma Virus and Risk of Lung Cancer Correlation: A Case-Control Study at Imam Khomeini Hospital, Ahvaz, Between 2011 and 2019

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Abstract: Human papillomavirus (HPV) is a well-established causative factor for various human malignancies, accounting for approximately 8% of all cancer cases. This study aimed to investigate the prevalence of different HPV types in lung cancer patients, utilizing a cohort of 61 individuals who received treatment at Imam Khomeini Hospital in Ahvaz between 2011 and 2019. Methods: Paraffin-embedded tissues were used for molecular analysis, with the primary goal of comparing the incidence of HPV using the Nested PCR assay followed by sequencing. Results: Among the lung cancer patients, HPV DNA was detected in 10 individuals, while three individuals in the control group of healthy individuals were found to have HPV infection (16.3% versus 12.1%, P=0.65). Importantly, all identified HPV types were classified as high-risk type 16. Additionally, the researchers investigated potential associations between age, sex, smoking habits, and lung cancer in patients with and without HPV infection. The study findings revealed that age, sex, and smoking habits did not show statistically significant associations with the presence of HPV (P>0.05). Moreover, the presence of HPV infection did not significantly correlate with the occurrence of lung cancer (P>0.05). Conclusion: Therefore, based on these findings, it can be concluded that there is no significant correlation between the incidence of lung cancer, HPV infection, and smoking.

Keywords: Human Papilloma Viruses, Lung Neoplasms, Polymerase Chain Reaction, Tissues, Iran



#### Dynamic Change in Laboratory Diagnosis and Follow Up of patients with Myelodysplasia Neoplasms

P14-P22



### The Role of Cell-Free DNA in the Detection and Monitoring of Treatment in Hodgkin Lymphoma Patients

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Background: Cell-free DNA (cfDNA) refers to fragments of DNA that originate mainly from leukocytes and result from various cellular processes, including apoptosis, necrosis, or active secretion of extracellular vesicles and exosomes. Circulating tumor DNA (ctDNA) specifically refers to the fraction of cfDNA derived from cancer cells, and is responsible for the significant concentration of cfDNA in the plasma, often observed in patients with hematologic neoplasms such as Hodgkin Lymphoma (HL). HL is a type of cancer characterized by the presence of abnormal lymphocytes called Reed-Sternberg cells. The objective was to assess cfDNA as a biomarker for diagnosis and monitoring of HL patients. Methods: This search was based on PubMed and Google Scholar databases with Hodgkin lymphoma and cfDNA keywords. Articles published between 2020 and 2024 were considered. Results: Studies have shown that despite the successful treatment of most HL patients with chemotherapy, 10-20% of patients under 60 years of age and approximately 50% of patients over 60 years of age will relapse after treatment. HL relapse is generally associated with unfavorable prognosis. CfDNA testing, compared to other classical methods such as biopsy and direct tissue sampling, provides a non-invasive, standardized, and easily accessible sampling method. In HL, Hodgkin and Reed/Sternberg (HRS) له DNA is released into the bloodstream in large amounts. It can be used to identify mutated STAT6 gene (the most common mutation in HL identified) and 106 other mutated genes using advanced sequencing techniques such as NGS. The observations also show a direct correlation between the reduction in ctDNA levels during chemotherapy and treatment outcomes, consistent with standard PET/CT scan results. Conclusion: Non-invasive evaluation of ctDNAis suitable with high sensitivity for monitoring treatment process and predicting relapse or chemotherapy resistance. This assessment, in combination with other complementary tests, may also complete PET/CT scans in the management of HL patients.

Keywords: Hodgkin Lymphoma, cfDNA



# Acute Myeloid Leukemia Induces Bone Marrow Mesenchymal Stromal Cells to Express Wnt/β-catenin Genes through Exosome Secretion

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Background: While a wide range of therapeutic approaches have been developed for acute myeloid leukemia (AML), refractory disease and relapse are still common. Currently, it is well known that the components of the bone marrow microenvironment (BMM), including mesenchymal stromal cells (MSCs), play a crucial role in leukemia growth and survival. Evidence reveals that the leukemic exosomes alter the components of BMM in a way that favor leukemia survival, leading to therapy resistance. In this study, we assessed the effect of AML-exosomes on human bone marrow mesenchymal stromal cells, especially alteration in the expression of the Wnt/β-catenin signaling genes, as a leukemia-supporting pathway. Methods: Exosomes were isolated from the HL-60 cell line and characterized by TEM (Transmission Electron Microscopy), DLS (Dynamic Light Scattering) technique, and flow cytometry. Exosomes' concentration was estimated using a BCA protein assay. MSCs were co-cultured with different concentrations of AML-exosomes. MTT, apoptosis, and ki-67 assays were used to achieve our data. Gene expression analysis was also performed by qRT-PCR. Results: Our results showed higher metabolic activity, decreased apoptosis, and enhanced proliferation in MSCs treated with 50 µg/ml of AML-exosomes compared with the control group. qRT-PCR data demonstrated that Wnt1, β-catenin, and LRP genes were upregulated in MSCs treated with 50 μg/ml of exosomes in comparison to their untreated counterparts (P<0.05). Conclusion: Since Wnt/βcatenin signaling is involved in leukemia progression, our findings suggest that AML-exosomes induce MSCs to activate this pathway, which may cause chemotherapy resistance and poor prognosis in the patients.

Keywords: Acute Myeloid Leukemia, Exosome, Mesenchymal Stromal Cell, Wnt/β-Catenin Signaling Pathway



### The Evaluation of P53, BAX, and BCL2 Apoptotic Genes' Expression in HL-60 Cells after Treatment with Human Bone Marrow Mesenchymal Stem Cell Exosomes

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Background: Acute myeloid leukemia (AML) is a predominant clonal hematological malignancy with high mortality and severe morbidity which urgently needs new advanced treatments. Mesenchymal stem cells (MSCs) have been proposed to have potential for cell therapy due to their ability to secrete numerous paracrine factors, including exosomes. Exosomes containing proteins or nucleic acids, such as lncRNAs, participate in intercellular communication and serve as key modulators of various cancers. Our study aims to investigate the effects of BM-MSC exosomes on the expression of P53, BAX, and BCL2 apoptotic genes in HL-60 AML cells. Methods: Normal BM-MSCs were cultured with serum-free culture media to isolate exosomes from their supernatants by using a precipitation-based method. The validation of exosomes was performed in three phases: flow cytometric CD marker identification, TEM morphological analysis, and DLS size evaluation. Later, the MTT assay was performed to specify the proper dose of exosomes for further analysis. Then, HL-60 cells were treated with exosomes, and RTq-PCR was operated to determine the gene expression of P53, BAX, and BCL2 apoptotic genes. Finally, analytical tests were used to calculate the statistically significant differences. Results: MTT assay results demonstrated that within 24 hours of treatment, BM-MSC exosomes could effectively decrease the metabolic activity of HL-60 cells at a concentration of 100 µg/mL. Additionally, the expression levels of P53 and BAX were significantly elevated, while the BCL2 level decreased in treated HL-60 cells compared to their untreated counterparts. Conclusion: BM-MSC exosomes suppress the metabolic activity of HL-60 cells while simultaneously affecting apoptosis by increasing the expression levels of P53 and BAX and decreasing the BCL2 level. These findings suggest that BM-MSC exosomes may serve as potential supportive therapies for hematological malignancies like leukemia.

Keywords: Exosome, P53, BAX, BCL2, Mesenchymal Stem Cell



#### Increased miR-155 in K562 CML Cell Line Causes Down-Regulation of BCL2 Expression

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Background: Chronic Myeloid Leukemia(CML) is a myeloproliferative neoplasm with an incidence of 1-2cases per100,000 adults.CML is characterized by a balanced genetic translocation,t(9;22)(q34;q11.2).The resulting BCR/ABL1 chimeric protein is a constitutively active tyrosine kinase that activates multiple signaling pathways, which collectively lead to malignant transformation. MicroRNAs (miRNAs) are short non-coding regulatory RNAs that control gene expression and play an important role in cancer development and associated with CML.One such miRNA,miR-155,has been found to be downregulated in CML.Downregulation of this miRNA is presumably mediated by BCR-ABL tyrosine kinase activity. In this study we aimed to investigate the effect of miR155 on bcl2 expression in K562 CML cell line. Methods: The K562 BCR-ABL positive cell line was cultured in RPMI1680(90%),FBS(10%) and pen/strep.The cells were subcultured when confeluented,2.0 x 106cells were transfected with PLentiIII-miR155-GFP construct through electroporation Twenty-four hours later,transfection was verified by flow cytometric analysis. Then total RNA was extracted from transfected K562 cell lines. Then the quality and quantity of RNA was determined by nanodrop device and electrophoresis.cDNA of total RNA was synthesized.qRT-PCR was performed for bcl2 and miR-155.Relative expression was calculated for target gene using the ΔΔCT method. Results: Fluorescent color was observed in 35% of cells, this means that 35% of the cells were transfected.qRT-PCR results showed increased 20 folds in compare to control.A decrease in bcl2 expression to 0.25 fold were seen. Conclusion: In this study, we showed that overexpression of miR-155 can decrease the expression of bcl2, and as a result, the survival of leukemic cells decreases and they undergo apoptosis. We propose a new potential anti-leukemia agent in K562 CML cell line,i.e. miR-155.

Keywords: Apoptosis, Bcl2, CML, K562, miR155



#### Investigating Alterations in Local and Circulating Expression Profile and Diagnostic Value of IGF-1 Axis and its Related Proteins in Patients with Osteosarcoma Tumor

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Background: Osteosarcoma, the most prevalent type of malignant primary bone tumors, originally arises from osteoblasts. Due to their general symptoms such as pain, and swelling, these tumors are diagnosed late and cause mortality. Insulin-like growth factor-1 (IGF-1), Insulin-like growth factor binding protein-3 (IGFBP-3), and IGF-1 receptor (IGF-1R) are components of the IGF axis that are involved in different normal and pathological statuses. Methods: 90 human samples (30 tumor tissues, 30 normal adjacent tissues, and 30 blood samples) of osteosarcoma patients were assessed. Serum levels of IGF-1 and IGFBP-3 were measured by ELISA. Moreover, qRT-PCR and immunohistochemistry were used to investigate the gene and protein expression of IGF-1R in cancerous tissues and their noncancerous tumor margins. Results: Osteosarcoma cases revealed significantly increased circulating levels of IGF-1, IGFBP-3, and expression of IGF-1R in comparison with controls. Additionally, the results indicate that the more severe conditions patients have, the higher levels of the markers they have. Indeed, IGF-1, IGFBP-3, and IGF-1R had an elevation in patients with high-grade, metastasis, whose received chemotherapy, and experienced tumor recurrence. Especially, osteosarcoma patients with metastatic tumors had significant enhancement of IGF-1, IGFBP-3, and IGF-1R. Also, ROC curve analysis revealed that the IGF axis is of potential to differentiate osteosarcoma patients from controls. Conclusion: Collectively, the data suggest the IGF axis's possible role in the aggressiveness of osteosarcoma neoplasm. Although more investigations are required to clarify the underlying molecular mechanisms, our study proposes their potential to serve as biomarkers in patients up monitoring and ever targeted therapy.

Keywords: Osteosarcoma, IGF-1 Axis, Metastasis, Malignancy



### The Importance of CD44v6 in both Malignant and Benign Primary Bone Tumors from a Clinical Perspective

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Background: The objective of this study was to assess the expression profile of CD44v6, a potential cancer stem cell marker, and its diagnostic and predictive significance in three distinct types of primary bone tumors. Methods: In this study, we utilized real-time qRT-PCR and immunohistochemistry to examine the gene and protein levels of CD44v6 in a total of 138 fresh bone tissues. This included 69 tumor tissues comprising osteosarcoma(N=23), chondrosarcoma(N=23), and GCT(N=23), as well as 69 corresponding non-cancerous tumor margins. Furthermore, we investigated the circulating level of CD44v6 by isolating PBMCs from 92 blood samples. Among these, 69 samples were obtained from patients diagnosed with primary bone tumors, while the remaining 23 samples were from healthy donors. Results: In patients with osteosarcoma and chondrosarcoma tumors, both the gene and protein expression of CD44v6 were found to be significantly higher compared to the GCT group. Furthermore, the circulating level of CD44v6 was notably elevated in patients diagnosed with osteosarcoma and chondrosarcoma in comparison to the GCT group and patients with malignant tumor characteristics. Additionally, we observed a strong correlation between the gene and protein levels of CD44v6 and important tumor indicators such as tumor grade, metastasis, recurrence, and size at the tumor site. CD44v6 shows potential in differentiating patients with bone tumors from both control groups and tumor groups with severe and invasive characteristics from those with nonsevere features. Importantly, the expression level of CD44v6 also demonstrated predictive value for determining tumor grade and the likelihood of recurrence. Conclusion: CD44v6 is likely to play a role in the development of primary bone tumors and has the potential to serve as a diagnostic biomarker for bone cancer. However, to obtain more accurate and conclusive findings, further mechanistic investigations involving larger population samples are necessary.

Keywords: CD44v6, Osteosarcoma, Chondrosarcoma, Giant Cell Tumors, Malignancy



#### Sorafenib Decreases Gene Expression of TSC1 Tumor Suppressor in ALL; a Resistance Mechanism

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Introduction: Acute lymphoblastic leukemia is the most common blood cancer in pediatric patients. Despite the enormous progress in ALL treatment, there are still patients that cannot be saved. Therefore, new treatment strategies are needed to improve patient outcomes. One of the drugs suggested in the treatment of ALL is sorafenib, which does not have FDA approval. Several studies in various types of solid tumors, especially hepatocellular carcinoma, showed that sorafenib creates drug resistance and one of the mechanisms of resistance is the reduction of TSC1,2. TSC1,2 are tumor suppressors that are inhibited by sorafenib by activating the P13K/AKT pathway. The aim of this study was to investigate the effect of sorafenib on the expression of TSC1,2 genes in the NALM-6 cell line. Methods: NALM-6 cell line were treated with 5μM concentrations of sorafenib, then TSC1,2 expression was measured by Rq-PCR. Data analysis and fold change calculation were done using ΔΔCT method. Results: TSC1 gene expression in NALM-6 cells decreased by 0.04 (fold change) after drug treatment (p<0.05). TSC2 gene expression in NALM-6 cells after drug treatment was 0.58 times (fold change) of control (p<0.05). Conclusion: Our study showed that Sorafenib has a negative effect on the expression of TSC1 as an effective tumor supressor, whereas it had no effect on the expression of TSC2. So it is confirmed that sorafenib resistance in ALL occurs through TSC1 downregulation. Therefore, new therapies targeting molecular abnormalities hold promise for achieving better initial remission, with the hope of preventing relapse.

Keywords: NALM-6, Sorafenib, TSC1, TSC2



# Serum Levels of Interleukin-1β and Disease Progression in Multiple Myeloma Patients: A Case and Control Study

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Bakground: Multiple myeloma (MM) is known as an incurable heterogeneous plasma cell malignancy that presents with a variety of clinical manifestations. Inflammation plays an important role in this disease. Cytokines and Chemokines cause the progression of the disease. One of them is interleukin- $1\beta$  (IL- $1\beta$ ), which may be involved in the pathogenesis of MM. Other markers such as calcium, albumin, creatinine, globulins, and total protein are also used to diagnose and prognosis patients. The main purpose of this study was to evaluate the serum level of IL- $1\beta$  and various forms of calcium (total calcium, ionized calcium, and corrected calcium), albumin, creatinine, globulin, and total protein on stage-I of MM patients and healthy controls

Methods: Serum samples from 30 stage-I MM patients and 30 healthy subjects as controls were examined in this study. The protein concentrations of serum IL-1 $\beta$  was assessed by enzymelinked immunosorbent assay (ELISA), total calcium, albumin, creatinine, total protein, and globulin Measured by auto analyzer BT3000, an electrolyte analyzer was used to measure ionized calcium (Ca++) and a special equation was used to calculate the corrected calcium

Result: The mean level of IL-1 $\beta$  was significantly elevated in stage-I MM. The mean levels of IL-1 $\beta$  were 7.04 $\pm$ 1.15 ng/ml in stage-I MM and 3.12 $\pm$  0.90 ng/ml in controls (p<0.001). The mean levels of total calcium (total Ca) were 9.45 $\pm$ 0.56 mg/dl in stage-I MM and 9.09 $\pm$ 0.43mg/dl in controls (p=0.008). The mean levels of ionized calcium (Ca++) was 4.65 $\pm$ 0.28mg/dl in stage-I MM and 4.75 $\pm$ 0.33mg/dl in controls (p=0.2). The mean ratio of serum ionized calcium to total calcium (Ca++/ total Ca) was 0.49 $\pm$ 0.054 in stage-I MM and 0.52 $\pm$ 0.047 in controls (p=0.02). The mean ratio of serum ionized calcium to corrected calcium (Ca++/ total Ca) was 0.42 $\pm$ 0.033 in stage-I MM and the Mean ratio of serum ionized calcium to calcium total (Ca++/ total Ca) was 0.52 $\pm$ 0.047 in controls, Comparison of the mean of the two groups shows a significant difference.

Conclusion: The results of the study indicate the possible involvement of IL-1 $\beta$  at stage-I MM and it can indicate the role of chemokines in the disease process, especially in the early stages. Changes in the chemical profiles mentioned can help in the diagnosis and prognosis of the disease.

**Keywords:** Multiple Myeloma, Interleukin, 1β- Total Calcium, Ionized Calcium, Corrected Calcium, Albumin, Creatinine



## PD-1/PD-L1 Interaction Regulates BCL2, KI67, BAX, and CASP3, Altering Proliferation, Survival, and Apoptosis in Acute Myeloid Leukemia

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Introduction: Programmed death ligand-1 (PD-L1) is a pivotal inhibitory checkpoint ligand known to induce T-cell exhaustion via interaction with the programmed death-1 (PD-1) receptor. Beyond this, PD-L1's intrinsic signaling pathways within cancer cells warrant further exploration. Methods: This study aims to elucidate the effect of PD-L1 stimulation on the proliferation, survival, and apoptosis of acute myeloid leukemia (AML) cell lines. Two human AML cell lines, HL-60 and THP-1 were cultured and treated with phorbol 12-myristate 13-acetate (PMA) to induce PD-L1 overexpression. Post-treatment PD-L1 expression was confirmed via flow cytometry. Subsequently, cell surface PD-L1 was stimulated using a recombinant PD-1, 24 hours post-PMA treatment. The expression alterations in pivotal genes including BCL2, MKI67, BAX, and CASP3 were monitored using quantitative real-time polymerase chain reaction 24 and 48 hours post-treatment. Additionally, annexin-V through flow cytometry. Results: Findings reveal that PD-L1 stimulation augments AML cell proliferation and survival by enhancing MKI67 and BCL2 expressions while concurrently inhibiting cell apoptosis due to decreased BAX and CASP3 expression following PD-L1 stimulation. Notably, stimulated cells expressed exhibited reduced annexin-V compared to control cells. Conclusion: This study underscores that PD-L1 stimulation fosters AML cell proliferation and survival while impeding cell apoptosis. The results hold potential implications for targeting PD-L1 in AML treatment strategies.

Keywords: Acute Myeloid Leukemia; Apoptosis; Cell Proliferation; Programmed Death-Ligand 1



#### **Harmonization in Medical Laboratories: Challenges** and Solutions

P23-P25



#### A Qualitative Study on Treatment among Women with Vulvovaginal Candidiasis

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Background: Non-adherence of patients with vulvovaginal candidiasis (VVC) to treatment recommendations leads to treatment failure and recurrence of infection. Therefore, this qualitative study was conducted to identify barriers and facilitators of observance of treatment among women affected with vulvovaginal candidiasis. Methods: This qualitative study was conducted through 26 in-depth unstructured interviews with 24 patients and 2 gynecologists using purposeful sampling with maximum variation in Ahvaz, southwest Iran. Interviews were conducted in person at health centers and the gynecologist\_s offices. MAXQDA 10 software and conventional content analysis were used for data analysis. Results: The findings showed barriers and facilitator factors of adherence to treatment in women with VVC. Some of these factors lead to increased adherence to treatment, and others play the role of hindering factors. These factors were classified into two main categories: patients\_beliefs and fears and concerns. Conclusion The results of this study showed that many of the behaviors of patients from the acceptance of the diagnosis process to treatment are rooted in the patient\_s beliefs and fears. Therefore, it seems necessary to design and carry ou interventions based on the findings of this study, which can be used in developing appropriate solutions, and treatment guidelines, and adopting a policy for treatment adherence.

Keywords: Recurrent Vulvovaginal Candidiasis, Qualitative Research, Treatment Failure



#### High Level of Serum Lead in Patients Referring to a Clinical Laboratory in West Part of **Tehran Province between 2017-2024**

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Introduction: Lead toxicity results in chronic adverse changes in metabolism and behavior in adults and nervous system damage in children under 5 years old. The aim was to evaluate the lead toxicity between patients referring to a clinical laboratory in west part of Tehran province.

Method: 1651 serum Pb data (determined by atomic absorption) were evaluated among patients between 21 March 2017 to 15 January 2024. Analysis of variances used to compare sex groups for lead serum levels. Results: Mean±SD of serum Pb levels were equal to 9.7±7.6 μg/dL in male, 6.86±4.07 μg/dL in female, and 4.92±4.22 μg/dL in children (p= 0.001). Considering serum lead higher than 3.4 μg/dL as the cut -off value for screening of unsafe children (according to CDC recommendation), 51.09% of 5 years old and younger children were screenpositive. Older patients had significantly higher serum lead level; 0-10 years= 5.07±4.58, 11-20 years= 4.89±2.49, 21-30 years= 6.95±4.45, 31-40 years= 7.77±5.84, 41-50 years= 7.75±4.8, and age> 50= 8.99±6.65. Conclusion: Serum lead toxicity should be evaluated in Iranian population, especially in children. Redefining the cut-off and reference intervals of serum lead helps to find toxic cases with higher sensitivity. Insensitive reference intervals that are currently used in clinical laboratories, results in missing patients, and promoting chronic consequences in upcoming generations.

Keywords: Serum Lead, Reference Interval, Central Nervous System, Behavioral Changes



## Implementation of External Assessment of Biochemical Quality among 205 Medical Diagnostic Laboratories of Mazandaran University of Medical Sciences - 1402

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Introduction: Quality control between medical laboratories is one of the most important methods in determining and evaluating the quality of laboratory results. Method: In this study, the control serum sample based on the human sample, the entire sample was prepared from one patient, was distributed among 205 public and private laboratories in Mazandaran province to check 15 basic and routine biochemistry tests, and the results of the tests at the same time of referral, time It was obtained that the autoanalyzers were on and performing daily tests. After distributing and obtaining the results in the shortest time, the results of the collected data were entered into the SPSS software and after removing the outliers and grouping the participating laboratories based on The kits used, the average indicators of the group, the standard deviation (SD) of the group, the number of participants in each group and finally the result of each laboratory and the DI index were calculated and determined. After the final analysis of the result sheets of each laboratory, the preparation was presented in writing in less than three weeks from the beginning of the study. Findings: In this study and the results of all the biochemical tests of 205 laboratories based on the DI quality index, about 11% of the DI index is at an unacceptable level, 19% is at an acceptable level but needs further investigation, 24% is at a good level, 38 The percentage was at a very good level and finally 8% were at an excellent level. Conclusion: In this method, due to obtaining the results at the same time as the sample delivery and providing the results in the shortest time, satisfactory results were observed for checking and calibrating the devices.

Keywords: External Assessment, Quality, Biochemical, Laboratory



#### **Hematomorphology in Anemias**

**P26** 



# Hemoglobin Constant Spring Interference with Hb A1C Measurement in HPLC Method Atefeh Bahmei 1, Gholam Hossein Tamaddon 1 \*

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Background: Hemoglobin Constant Spring (Hb CS) is a type of hemoglobin variant associated with thalassemia, characterized by its overproduction and ineffective function. It is considered a non-deletional α-thalassemia with mild symptoms compared to other forms of thalassemia. The patient with controlled diabetes was referred to the laboratory for a check-up with fasting blood sugar (FBS) and 2-hour postprandial (2hpp) blood sugar which were normal, and with the High-performance liquid chromatography (HPLC) method, the Hb A1C test was reported to be 9.2%, which was not consistent with the patient's history. His sample was sent to the hematology department. This case aimed to find the interfering factor in the A1C test. Methods: HPLC, electrophoresis capillary, CBC count, and peripheral blood smear (PBS) were performed for this patient. Results: The patient's CBC showed normal values for most parameters, except for the mean corpuscular volume (MCV:74.8 fL) and red cell distribution width (RDW-CV:20%), suggesting variability in the size of red blood cells. The PBS was examined and revealed the presence of few ovalocytes, few target cells, anisocytosis, and slight polychromasia. The hemoglobin (Hb) electrophoresis initially reported an A1C level of 5.5% and a sharp peak for Hb Constant Spring (Hb CS) at 6%. Subsequent HPLC and electrophoresis confirmed the presence of Hb CS. Conclusion: Hb CS may interfere with accurately measuring Hb A1C using the HPLC method, leading to a false increase in Hb A1C levels. Herein, electrophoresis capillary testing can help distinguish between these two factors.

Keywords: Hb CS, HPLC, PBS, Electrophoresis Capillary



# Immunohematology and Transfusion Medicine P27-P36



#### Haemovigilance System: Past, Present and Future

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The transfusion of blood and blood components is a life-saving intervention. However, there are risks of adverse events related to the donation of blood or its components, and with the transfusion of blood or blood components to patients. Haemovigilance is a set of surveillance procedures for the assessment of adverse events along the entire blood transfusion chain to prevent their occurrence or recurrence. Today, the haemovigilance system is implemented in many European, American, Asian and African countries, and according to the latest report of the World Health Organization (WHO), 49% (84 out of 171) countries had a national haemovigilance system (NHS) in 2018. In Iran, a national haemovigilance system namely the Iranian national haemovigilance system (INHS) was established in 2009. The current haemovigilance systems are basically classified according to legal status, application field and organizational structure. These systems show significant conceptual and organizational differences. Despite the importance of haemovigilance in the quality and safety of the blood transfusion process, many countries do not have an effective national haemovigilance system. Specific challenges are encountered, depending on the organization of the blood transfusion system in a country. The purpose of this study was to raise awareness of all those involved in the field of blood transfusion, especially physicians, nurses and hospital blood bank staff, about the history, concepts, implementation levels and models, challenges and developments of the haemovigilance system.

**Keywords:** Blood Transfusion, Haemovigilance System, Haemovigilance, Blood Safety, Adverse Events



### Comparison of the Amount of mtDNA DAMPs in Platelet Concentrates (PCs) Prepared from Male and Female Blood Donors During the PCs Storage

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Background: Platelet transfusion is a common treatment for the prevention of hemorrhage and thrombocytopenia. During storage of platelet concentrates (PCs), platelets undergo a series of morphological and functional changes that are called platelet storage lesion (PSL). Oxidative stress (OS) and mitochondrial damage are the main causes of PSL. Oxidative conditions and mitochondrial function vary significantly among individuals. Therefore, it is likely that one of the contributing factors to the development of PSL is the donor segender. In this study, we investigated the relationship between the genders of donors with mtDNA release in PC during storage. Methods: In this observational cohort study, 40 PCs were collected from healthy donors (20 male, 20 female). Sampling from the PCs was taken on days zero, 3, and 5 of PC storage." The platelet count and the level of free mtDNA were measured in the aforementioned days using a cell counter and real-time PCR assay. Results: According to the Friedman test results, there was a significant difference between the quantitative levels of mtDNA on aforementioned days (p<0.001). Additionally, there was no significant interaction between the time and the groups, indicating that the quantitative levels of mtDNA did not differ significantly between groups over time (p>0.05). Furthermore, the Mann-Whitney test did not reveal a significant difference in the mean levels of mtDNA between the mentioned groups. Conclusion: The results indicate that the level of mtDNA is not associated with the gender of blood donors and is independent of it.

Keywords: Gender, Blood Donors, Platelet Concentrate, Platelet Storage, Free Mitochondrial DNA



#### Investigation of the Epidemiological Trend of Brucellosis in Kermanshah Province from 1397 to 1401

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Introduction Brucellosis is of special attention from the economic and public health aspects, and it is one of the most important diseases that can be transmitted between humans and animals in Iran, and contaminated animal milk and unpasteurized products prepared from it are the most common sources of brucellosis transmission. study method It has been done retrospectively and descriptively in 1401 findings In 2017, the number of patients was 696 - the incidence was 35.6 per hundred thousand people In 2018, the number of patients was 612 - the incidence was 31.5 per hundred thousand people In 2019, the number of patients was 341 - the incidence was 17 per hundred thousand people In 1400, the number of patients was 414 - the incidence was 22.6 per hundred thousand people In 1401, the number of patients was 649 - the incidence was 32 per hundred thousand people Conclusion The most important and common way of contracting the disease in Kermanshah province is through digestion and consumption of unpasteurized dairy products. Therefore, in order to prevent the disease, it is necessary to educate and inform the general public with a wide spectrum. Also, effective measures should be taken by the veterinary department regarding the destruction of infected animals and monitoring, which unfortunately, due to the lack of financial resources, this important task is not carried out in the best way in some cases.

**Keywords**: Kermanshah, Malta Fever



# Assessment of the Prevalence of Iron Deficiency With Out Anemia (IDWA) and Iron Deficiency Anemia (IDA) Among Regular Blood Donors Visiting Tehran Blood Transfusion Center

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Background: Regular blood donors may experience iron deficiency due to repeated blood donation. The aim of this study was to assess the prevalence of iron deficiency without anemia (IDWA) and iron deficiency anemia (IDA) among regular blood donors. Methods: This cross-sectional study was conducted from Bahman 1401 to Farvardin 1402 at the Tehran Blood Transfusion Center among 130 male regular donors. CBC tests using Sysmex K1000, serum iron using the Ferrozine method, ferritin using the Elisa method, and Total Iron Binding Capacity (TIBC) using the Direct method were performed on blood samples. All collected data were analyzed using R software for statistical analysis. A significance level of 0.05 was considered in this study. Results: 13 individuals (10%) of regular blood donors had serum ferritin levels less than  $12 \mu g/L$ , and 117 individuals (90%) had serum ferritin levels higher than  $12 \mu g/L$ . 105 individuals (80.8%) had serum iron levels higher than  $160 \mu g/dL$ , 9 individuals (6.9%) had serum iron levels lower than 50  $\mu g/dL$ . Among the 13 individuals with serum ferritin levels less than  $12 \mu g/L$ , 9 had serum iron levels less than 50  $\mu g/dL$ , and 4 had normal serum iron levels. Conclusions: 13 individuals (10%) of donors had low serum ferritin levels. 9 individuals (7%) had IDWA, and 4 individuals (3%) had iron deficiency anemia.

Keywords: Blood Donation, Blood Donor, Iron-Deficiency Anemia, Serum Ferritin



#### Assessing the Role of Thromboelastography in Optimizing Transfusion Therapy for Thalassemia Patients

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Background: Studies have consistently shown that individuals with major beta thalassemia are at a greater risk of thrombosis due to factors including the procoagulant activity of thalassemic erythrocytes, decreased liver synthetic function, heightened platelet activity, and vascular damage from prolonged stress. Currently, there are no tests available to predict the risk of thrombosis in these patients. Thromboelastography (TEG) is a laboratory test that comprehensively assesses a patient's coagulation status, including the dynamics of blood clot formation, strength, and breakdown. TEG can offer a rapid assessment of coagulation status and guide product transfusions in adult patients with thalassemia. Our objective is to evaluate the role of thromboelastography in transfusion management for thalassemia patients. Methods: We conducted a literature review using specific keywords and searched the PubMed and Google Scholar databases for relevant scientific literature published within the last years. Results: Thromboelastography, when compared to conventional coagulation tests, has played a crucial role in improving patient blood management by reducing transfusions, optimizing blood product utilization, and enhancing resource management. TEG-guided therapy has demonstrated benefits such as reduced bleeding rates, length of hospital stays, and mortality rates. The comprehensive depiction of the coagulation process and the availability of point-ofcare testing are advantages favoring these devices, which may assist physicians in making rapid diagnoses and instituting early interventions. These tests may also help predict bleeding and rationalize the use of blood products in these patients. Conclusion: Screening thalassemia patients with TEG may help identify those at high risk for thrombosis. By using TEG, clinicians can gain a better understanding of each patient is individual coagulation status enabling tailored transfusion therapy to optimize coagulation function while minimizing the risk of complications. This personalized approach to transfusion management can help improve outcomes for thalassemia patients.

Keywords: Thalassemia, Thromboelastography, Transfusion, Hemostasis, Coagulation



### The Deployment of Rapid Coagulation Testing Devices in Resource-Limited for Optimizing Transfusion Management

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Background: Patients with high perfusion disorders face the challenge of transfusion-related complications. In addition, the limited availability of blood products in society underscores the importance of managing blood product transfusions in these patients. Hence, investigating the developing of rapid coagulation testing devices including the CoaguChek system, i-STAT system, ROTEM (Rotational Thromboelastometry) and TEG (Thromboelastography) systems might hold the potential to revolutionize the approach to transfusion management by providing timely and accurate coagulation assessments. This study aims to explore the application of these devices in transfusion management. Methods: Searching across PubMed, Web of Science, and Google Scholar databases over the past few years, papers relevant to the specified keywords were included in this study. Results: In a prospective cohort, rapid TEG proved to be a better predictor of bleeding and red blood cell transfusion requirements than PT or PTT, with the α-angle showing superiority over fibringen for predicting plasma transfusion, and maximum amplitude surpassing platelet count for predicting platelet transfusion. Furthermore, a study comparing TEG or ROTEM with standard laboratory test-guided transfusion demonstrated a significant reduction in patients needing FFP. Additionally, the CoaguChek system, particularly the CoaguChek XS system, emerged as a valuable tool in transfusion by providing rapid and accurate PT/INR monitoring, allowing for timely adjustments and contributing to improved patient outcomes through effective anticoagulation therapy. The i-STAT system was highlighted for its versatility and portability, offering a wide range of tests on a single instrument, especially coagulation tests such as INR. Its capacity to deliver prompt and precise diagnostic information makes it an invaluable asset for healthcare providers, ensuring timely and accurate patient care. Conclusion: ROTEM and TEG systems, CoaguChek system, and i-STAT system can help identify patients with coagulopathy, guide blood product transfusions, and improve patient outcomes leading to optimizing transfusion management.

Keywords: CoaguChek System, i-STAT System, ROTEM, TEG, Transfusion Management



### Rapid Detection of N-RAS Gene Common Mutations in Acute Myeloid Leukemia (AML) Using High Resolution Melting (HRM) Method

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Objective: This study aims to utilize the High Resolution Melting (HRM) method to rapidly detect common N-RAS gene mutations in patients diagnosed with Acute Myeloid Leukemia (AML). The presence of mutations in genes such as N-RAS plays a crucial role in AML prognosis and treatment response. The objective is to identify the distribution of common N-RAS mutations at codons 12, 13, and 61 in AML patients using the HRM method. Additionally, the study aims to confirm the efficiency of the HRM method for mutation detection by comparing its results with the sequencing data, which is considered the gold standard method. Methods: A total of 50 newly diagnosed AML patients were included in this study. Peripheral blood samples were collected from these patients, and mononuclear cells were isolated. The HRM method was employed to detect the distribution of common N-RAS mutations. To validate the HRM method, the results were compared with the sequencing data, which serves as the gold standard method for mutation detection. Peripheral blood samples were obtained from 50 newly diagnosed AML patients. Subsequently, mononuclear cells were isolated from the samples, and DNA extraction was performed. The HRM method was employed to investigate the presence of mutations. To assess the efficacy of the HRM method in mutation detection, a comparison was made with direct sequencing. Results: Among the 50 samples, N-RAS mutations were detected in 7 cases (14%. The majority of mutations were observed in codon 12 (57.14%, while codons 61 and 13 accounted for 28.57% and 14.28% of the mutations, respectively. Statistical analysis did not reveal any statistically significant association between the HRM results and the demographic data of the patients. Conclusion: Based on the near same results of HRM and direct sequencing, this method is recommended as efficient, cost-effective, and rapid approach for detecting common mutations.

**Keywords**: HRM, AML, N-RAS



## High-Resolution Melting Analysis Compared to Direct Sequencing for the Identification of DNMT3A Mutations in Patients with Acute Myeloid Leukemia

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Objective Abnormal gene expression is major cause of Acute Myeloid Leukemia (AML). AML-associated mutations often contribute to gene instability and a diminished response to treatment. Notably, the DNMT3A mutation holds particular significance, given to its pivotal role in methylation and expression of other genes. Methods Peripheral blood samples were taken from 50 patients with AML. DNA was extracted mononuclear cells and Then, HRM method was conducted with aim to detect gene mutation. Results were compared to direct sequencing as gold standard to determine the HRM efficacy. Results Mutations in codon 23 of the DNMT3A gene were identified in 5 patients (10%), all of which were of the missense type. A comparison between direct sequencing and HRM analysis revealed complete agreement in mutation detection. Conclusion Given the perfect agreement observed between HRM and direct sequencing results, HRM emerges as a preferable alternative to conventional, labor-intensive techniques for detecting gene mutations.

Keywords: HRM, AML, DNMT3A, Leukemia



### Impact of Horsetail, Alfalfa, Nettle, Oak, and Aleppo Oak Extracts on Hemostasis in Laboratory Coagulation Studies

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Objective: Historically, plant extracts were applied for different purposes, such as preventing bleeding or treating wounds, and they are still common among indigenous and tribal populations. Methods In this research, extracts of Horsetail, Alfalfa, Ortie, Chane, and Aleppo oak were prepared by the maceration method. The extracts were mixed with platelet-poor plasma and platelet-rich plasma with aim to conduct Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), and Platelet Aggregation tests. Results Although alfalfa, horsetail, and Ortie showed reductions in APTT, the effects were not statistically significant compared to the control group. The combined extract demonstrated the most substantial impact compared to the single extracts in a dose-dependent manner. Horsetail and Alfalfa prompted platelet aggregation in response to arachidonic acid but not collagen. In the case of Ortie, no aggregation occurred with arachidonic acid, and only incomplete aggregation was observed in response to collagen. Intriguingly, blood clotting occurred immediately upon the addition of the Chane, Aleppo oak and the pooled extract, resulting in the gelation of both platelet-poor plasma (PPP) and platelet-rich plasma (PRP) Conclusion Oak, Aleppo oak, and the combined extract were more effective in activating both primary and secondary coagulation pathways by decreasing the duration of PT and APTT, as well as the stimulation of platelet aggregation process.

Keywords: Coagulation, Platelet aggregation, Horsetail, Ortie, Alfalfa, Chêne, Aleppo Oak



### Application of Artificial Intelligence in Blood Transfusion: From Blood Donating to Blood Receiving

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Background: The blood transfusion process involves several steps: donor identification, blood collection, screening and grouping tests, blood product preparation, compatibility testing, and post-transfusion complications monitoring. Proper storage, classification, and interpretation of the diverse data generated at each stage are crucial for ensuring safe and high-quality transfusions. Therefore, employing artificial intelligence (AI) in this field is essential. This study aims to explore the application of AI and machine learning algorithms from blood donation to reception. Method: We reviewed existing research in databases like PubMed and Scopus from 2014 onwards to evaluate AI-related algorithms' types, applications, advantages, and disadvantages in this context. Results: Our review shows that machine learning (ML), a core AI component, holds significant promise for blood transfusion. Artificial Neural Networks (ANNs) can estimate blood donation probability and issue donor calls. Deep Learning (DL) and Convolutional Neural Networks (CNNs) assess blood product quality. K-Nearest Neighbors (KNN) predict screening test results, and Support Vector Machines (SVMs) interpret blood grouping tests. Additionally, Multilayer Perceptrons (MLPs) accurately estimate blood units required for surgeries. Conclusion: Overall, AI application can substantially reduce blood wastage and enhance transfusion quality and safety. AI algorithms can be widely used in estimating blood requirements, donor selection, product compatibility determination, predicting blood units for surgeries, and anticipating post-transfusion complications.

Keywords: Artificial Intelligence, Machine Learning, Blood Transfusion, Blood Donation



#### **Infertility Due to Male Factor: Causes and Laboratory Diagnosis**

P37-P38



# Probiotic Microorganisms Affect Reproductive and Nervous Systems of Male Rats Treated with Acrylamide

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Background: Probiotic microorganisms reduce carcinogenic compounds in vivo and prevent tissue damage through their ability to physically absorb carcinogenic compounds such as acrylamide (Acr). This study was designed to evaluate the protective effects of probiotic microorganisms on reproductive and nervous systems of male rats treated with Acr. Methods: Thirty-two rats were randomly divided into one control and three experimental groups (n=8/group). The control group received normal saline through gavage, group 2 received 20 mg/kg Acr, group 3 received 20 mg/kg Acr+20 mg/kg probiotic microorganisms, and group 4 were given 20 mg/kg Acr+200 mg/kg probiotic microorganisms. After 30 days, testis, prostate, seminal vesicle and cerebellum were removed and fixed. Sections of tissues 5-6 µm thick were stained with hematoxylin-eosin (H&E). Results: The testis weight (P<0.0001) decreased significantly in the Acr-treated group in comparison with the other groups. The number of spermatogonia, spermatocytes, spermatids and Leydig cells in the Acr group were significantly (P<0.05) less compared with the control and Acr+200 mg/kg probiotic groups. The mean Johnsen score in the Acr treated group was lower than in the control group (P<0.0001). There were Acr-induced changes in the prostrate and seminal vesicle: congestion, vacuolization in the secretory epithelial cells, and epithelial rupture. The volumes of cerebellar layers were decreased in the Acr group vs. the control group while recovered in both Acr-receiving groups. Conclusion: Acr has toxic effect on the male rat reproductive and cerebellar tissues which may be prevented by the use of probiotic microorganisms.

**Keywords**: Acrylamide, Cerebellum, Probiotics, Rats, Testis



#### Investigation of Oxidative Stress Parameters in Smoking Men in Kermanshah

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Introduction: Most of the studies on the effect of smoking on the phenomenon of oxidative damage and plasma antioxidant changes are in elderly people with a long history of smoking, and there are few reports in young people. Plasma oxidant and testosterone level in young smokers and compared with non-smokers. Method: In this case-control study, men referred to infertility centers in Kermanshah were included in the study. The criteria for entering the study were male smokers. 5 ml of blood was taken from the patients. Testosterone and TAO tests were done by ELISA method and uric acid and zinc tests were done by calorimetric method with autoanalyzer. Finally, data analysis was done with SPSS statistical software. Results: The results show that a total of 36 patients participated in the present study. Of these, 24 were in the case group (smoking men) and 12 were in the control group (non-smoking men). The parameters of testosterone, uric acid, zinc and TAO in the case group (smoking men) are significantly lower than the control group (non-smoking men) (P<0.05). Conclusion: Smoking has a significant effect on oxidative stress parameters in men. It is essential for doctors and specialists to educate their patients about the negative consequences of smoking on their health, and regular monitoring of uric acid and zinc levels in smokers is recommended.

Keywords: Uric Acid, Zinc, Oxidative Stress, Smoking



### **Laboratory Diagnosis of Common Parasitic Diseases** in Iran

P39-P44



#### Molecular and Serological Prevalence of Toxoplasma Gondii among Breast Cancer Patients in Jahrom, South of Iran

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Bakground: Toxoplasma gondii is an intracellular parasite with a worldwide prevalence among warm-blooded animals and humans. Humans are mainly infected through ingestion of water or food, which is contaminated with oocysts shed by cats or by eating raw or undercooked meat containing T. gondii tissue cysts. In healthy individuals, the infection is usually self-limiting and asymptomatic. However, toxoplasmosis in immunocompromised patients (e.g., cancer patients, organ transplant recipients, and HIV/AIDS-positive individuals) could be a life-threatening infection with fatal outcome. Furthermore, reactivation of latent infection may cause severe infection in immunocompromised patients, which results in encephalitis or disseminated infection. In this regard, reactivations of latent toxoplasmosis have been reported in patients with different types of cancer. Methods: One hundred and seven women with breast cancer (aged 34 to 80 years) were screened for anti-T.gondii antibodies (IgG and IgM) during 2019£2020. A questionnaire regarding demographic factors was filled out by participants. Molecular detection was performed by polymerase chain reaction (PCR) using the primer pair targeting the repetitive element (RE) gene of T. gondii. The risk factors and demographic data were analyzed by SPSS software (ver. 20, Chicago, IL, USA) using the Chi-squared test. Conclusion: Our findings showed a high seroprevalence rate of anti-T.gondii IgG in breast cancer patients. Although we did not detect active infection, reactivation of chronic infection due to immunosuppression should not be neglected among patients with malignancies. Nonetheless, such studies need to be done in a larger sample. Screening programs for detection of toxoplasmosis (due to reactivation of chronic infection) could be recommended as a routine follow-up among breast cancer patients.

**Keywords**: Toxoplasmosis, Breast Cancer, Elisa, PCR



#### Assessment of Interleukins 33 and 5 and in Strongyloidiasis

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Introduction: Strongyloides stercoralis (S. stercoralis) is a serious threat to human health, particularly in immunocompromised individuals. In current study the levels of interleukins IL-33 and IL-5, along with eosinophilia, neutrophils, and basophils were evaluated. Materials and Methods: 41 S. stercoralis -infected patients and 15 healthy individuals were included. Infection was confirmed using direct smear, nutrient agar culture, and SSU gene PCR. Subsequently, the serum levels of interleukin 33 and 5 were assessed using the ELISA method. Additionally, The white blood cell count, neutrophils, eosinophils, and basophils were measured with Giemsa staining. Results: Out of the 41 study participants, the WBC count did not show a difference compared to the control group. However, the percentage of eosinophils showed a significant increase in the patient group, with an average of 21 compared to the control group. The percentage of neutrophils and basophils in both groups fell within the normal range. Nevertheless, the interleukins 33 and 5 revealed no significant change in their serum levels within the patient group. Conclusion: In the patient group, there was an increase in the number of eosinophils in the peripheral blood compared to the control group, while the number of basophils and neutrophils in the peripheral blood remained unchanged. It appears that the absence of an increase in neutrophils and basophils may be attributed to the hypothesis of their accumulation around the larvae in the tissue rather than in the peripheral blood. Moreover, the average serum levels of interleukin 33 and 5 did not show an increase in the patient group. This lack of increase could be linked to the disease phase of the patients under examination, their immune system status, or underlying conditions, contributing to the parasite's persistence in the host's body.

Keywords: Strongyloidiasis, IL-33, IL-5



#### Case Reported of Lung and Fungus Ball Lesions Associated with Cladospotium Subcinereum A48 in a Diabetic Patient

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Due to recent advances in diagnostic methods, fungal diseases are diagnosed more than in the past. Infections with less-known fungi like Cladosporium are rarely reported globally in the lungs. In addition, susceptible patients, such as those with compromised immune systems and diabetes, contribute significantly to the escalation of reported cases. We report the first case of lung and fungus ball lesions associated with Cladosporium subcinereum A48. A chronic fungal mass caused a Cladosporium subcinereum A48 infection in a rural woman with diabetes, fever, and bloody sputum. CT scans, Bronchio-alveolar lavage (BAL), culture, and molecular methods were used to confirm the disease and the cause of infection. The infection was probably caused by the patient not taking insulin during the last few months of their life. Failure to use insulin caused acidosis and decreased the patient's immunity level, as a result, the fungal agent settled in the patient's lung and created a fungus ball in the patient's lung.

**Keywords**: Infections, Cladosporium, Fungus Ball



# Isolation and Molecular Identification of Leishmania spp. Agents in Patients with Cutaneous Leishmaniasis in Yazd Province, Endemic Region of Central Iran

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Background: Cutaneous Leishmaniasis (CL) is a major health problem in many parts of Iran. Many methods have been introduced for the detection and identification of Cutaneous Leishmaniasis. The purpose of this study was isolation and molecular identification of Leishmania spp. agents in patients with CL from the endemic region of central Iran. In this study, one of the main loci of central Iran named Yazd will be assessed for CL identification using PCR-RFLP. Methods: For this cross-sectional study, sampling was done from 372 suspicious patients with CL who were referred to the Health Centers of Yazd Province from 2016 to 2017. After collecting samples of patients, DNA extraction was done from samples on slides. Genus detection was done using specific primers by PCR. RFLP analysis was done for species identification Results: Out of 372 samples, 159 samples were positive using PCR based method. Out of 159 samples, 87(54.7%) L. major and 72 (45.3%) L. tropica were identified using RFLP analysis. The number of lesions in each patient was different but 119 (74.8%) patients showed a number of 1-3 lesions, and more lesions (more than10 lesions) were shown in 4 (2.5%) person Conclusion: The CL found in Yazd province resulted from L. major and L. tropica as the agents of rural and urban types, respectively. The prevalence of L. major and L. tropica was almost the same. This indicated that control programs could be designed for treatment and vector and reservoir control.

Keywords: Cutaneous Leishmaniasis, Iran



# The Polymorphism of TGF-β1 (rs1800469) and Susceptibility to Visceral Leishmaniasis

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Background: Leishmania infantum is a intracellular protozoan that invade mainly the reticulo-endothelial system and cause visceral leishmaniasis(VL). The feature of the disease in different individuals vary from infection without any clinical signs to a sever disease with clinical manifestations. The immunological background and cytokines of the individuals plays the main role in the progression and severity of clinical manifestations in VL. Since it has improved the role of TGF- $\beta$ 1 in visceral leishmaniasis, and due to the regulatory effect that some SNPs have on the function of the genes, we designed to study the role of TGF- $\beta$ 1 SNP (rs1800469) on outcome of the visceral leishmaniasis(VL). Methods: The study was performed on 114 VL patients and 210 healthy residents of endemic areas as controls, in East Azerbaijan district. DNA was extracted using PAK-GENE-YAKHTEH kit (cat. No. 2050) based on its protocol. The amplification refractory mutation system (ARMS)-PCR was used to determine the genotypes of TGF- $\beta$ 1 SNP (rs1800469). Results: The frequency of CC, CT and TT genotypes among patients were 6.15%, 87.7% and 6.15% whereas these amounts for healthy individuals were 28.1%, 66.19% and 5.71% respectively. Statistical analysis of distribution of genotypes among groups was performed using Chi-Square test and revealed a significant difference (P < 0.01). Conclusion: Based on the findings of this study, CC genotype of TGF- $\beta$ 1 SNP (rs1800469) is statistically associated with immunity to VL and Individuals with the transforming growth factor- $\beta$ 1 (rs1800469) CT and TT genotypes may have increased susceptibility to Visceral leishmaniasis.

**Keywords**: Visceral leishmaniasis, TGF-β1, polymorphism, SNP



#### Norwegian Scabies in an Immune- Compromised Patient: A Case Report

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Background: Norwegian scabies (hyperkeratosis scabies) is an acute form of skin disease seen in immune-compromised patients. This study aimed to describe a Norwegian scabies from Ahvaz, southwest of Iran in 2024. Methods: A 74 year old disable and diabetes male with autoimmune disease, complained of dermatitis lesions and itching with sever hyperkeratosis, several macula and papules on trunk, buttocks, groin, legs, thighs, fore ad upper arms and armpits for more than one year duration were referred to a Iran Zamin Medical Diagnostic Laboratory in Ahvaz, Southwestern Iran in 2024. Scraping from the crusted lesions of skin and slide preparation with 20% KOH was done. Reults: Microscopic examination presented that huge infestation of Sarcoptes scabiei in all forms of parasite included adult female, nymph stage and eggs. The disease was diagnosed with Norwegian scabies and the patient successfully treated with topical 5% permethrin ointment for two weeks continuously. Conclusion: Overall, Norwegian scabies should be considered in immune- compromised patients with contaminated areas.

Keywords: Sarcoptes Scabiei, Norwegian Scabies, Diabetes



# **Laboratory Diagnosis of Inborn Errors of Immunity** P45-P49



#### **New Diagnostic Tests for Autoimmune Diseases**

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Introduction and Method: Rheumatoid arthritis (RA), diabetes 1, psoriatic arthritis, Sjogren's syndrome, systemic lupus erythematosus (SLE) are examples of autoimmune diseases that affect different organs in the body. Production of autoantibodies, activation of immune cells, increased expression of pro-inflammatory cytokines and activation of interferons are signs of the onset of autoimmune diseases, which are called biomarkers. Basically, biomarkers are little signs in the body that can be used to definitively diagnose the disease, the sickness period, disease prevention and treatment. One of the most important advantages of biomarkers is the early diagnosis of the disease before it causes serious damage to the body. Results and Discussion: In the laboratory diagnosis of Rheumatoid Arthritis (RA), which mostly affects the joints, one of the markers which showed a high capability in diagnosing the disease was GZMA; Or in case of type 1 diabetes, damage to the liver, eyes and other organs can be prevented by early detection of the disease by biomarkers such as macrophage inflammatory protein-16 (MIP-16). Various biomarkers for other autoimmune diseases can be mentioned, such as increased Anti-U1 ribonucleoprotein and Granzyme B in the diagnosis of SLE, which involves almost all organs of the body; high abundance of anti-extractable nuclear antigen (ENA) and CD4+ TRAV13-2+ in Sjigren's syndrome, which mostly affects the exocrine glands and lacrimal glands; increased GlycA, I-FABP and kallikrein 8 in psoriasis in which mostly affects the skin. Recently, newer and more specific biomarkers have been found. The aim of this manuscript is to increase the speed and accuracy in the diagnosis of rare or common diseases by providing a comprehensive encyclopedia in the field of diagnostic biomarkers, so that finally, with quick and easier diagnosis, additional pain and suffering can be prevented.

Keywords: Diagnostic Tests, Autoimmune Diseases



# The Association between Various Viral Infections and Multiple Sclerosis: an Umbrella Review on Systematic Review and Meta-Analysis

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Background: Multiple Sclerosis (MS) is one of the immune-mediated demyelinating disorders. Multiple components, including the environment and genetics, are possible factors in the pathogenesis of MS. Also, it can be said that infections are a key component of the host's response to MS development. Finally, we evaluated the relationship between different pathogens and MS disease in this umbrella research. Methods: We systematically collected and analyzed multiple meta-analyses focused on one particular topic. We utilized the Scopus, PubMed, and Web of Science databases starting with inception until 30 May 2023. The methodological quality of the analyzed meta-analysis has been determined based on Assessing the Methodological Quality of Systematic Reviews 2 and Grade, and graph construction and statistical analysis were conducted using Comprehensive Meta-Analysis. Results: The Confidence Interval of effect size was 95% in meta-analyses, and p < 0.05 indicated a statistically meaningful relationship. The included studies evaluated the association between MS and 12 viruses containing SARS-CoV-2, Epstein Barr virus (EBV), Hepatitis B virus, varicella zoster virus (VZV), human herpesvirus 6 (HHV-6), HHV-7, HHV-8, HSV-1, HSV-2, Cytomegalovirus, Human Papillomavirus, and influenza. SARS-CoV-2, with a 3.74 odds ratio, has a significantly more potent negative effect on MS among viral infections. After that, EBV, HHV-6, HSV-2, and VZV, respectively, with 3.33, 2.81, 1.76, and 1.72 odds ratios, had a significantly negative relationship with MS (p < 0.05). Conclusions: Although the theoretical evidence mostly indicates that EBV has the greatest effect on MS, recent epidemiological studies have challenged this conclusion and put forward possibilities that SARS-CoV-2 is the culprit. Hence, it was necessary to investigate the effects of SARS-CoV-2 and EBV on MS.

Keywords: Multiple Sclerosis, Viral Infection, Umbrella Review



# Benign Prostatic Hyperplasia- an Autoimmune Disease with Novel Markers and Therapeutic Consequences

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Background: Lens epithelium-derived growth factor-splice variant of 75kDa (LEDGF/p75) is an au-toantigen overexpressed in solid tumors and acts as a stress-related transcriptional co-activator. Participation of autoimmune responses in the pathophysiology of benign prostatic hyperplasia (PBH) and a corresponding immunosuppressive therapy by TNFalpha antagonists has been recently suggested. Thus, autoAb testing could aid in the diagnosis of BPH patients profiting from such therapy. Methods: We generated CRISPR/Cas9 modified HEp-2 LEDGF knockout (KO) and HEp-2 LEDGF/p75 over-expressing (OE) cells and examined IgG autoantibody reactivity in patients with prostate cancer (PCa, n=89), bladder cancer (BCa, n=116), benign prostatic hyperplasia (BPH, n=103), and blood donors (BD, n=60) by indirect immunofluorescence assay (IFA) and line immunoassay (LIA). Results: We could not detect elevated binding of autoAbs against LEDGF/p75 in cancer patients, but autoAb reactivity to LEDGF/p75 OE cells in about 50% of patients with BPH was unexpectedly significantly increased. Furthermore, a LIA enabling the detection of 18 different autoAbs revealed a significantly increased occurrence of anti-dsDNA autoAbs in 34% of BPH patients in contrast to tumor patients and BD. This finding was confirmed by antimitochondrial (mDNA) autoAb detection with the Crithidia luciliae immunofluorescence test that also showed a significantly higher prevalence (34%) of anti-mDNA autoAbs in BPH. Conclusion: Our study provided further evidence for the occurrence of autoimmune responses in BPH. Furthermore, LEDGF/p75 over-expression renders HEp-2 cells more autoantigenic and an ideal target for autoAb analysis in BPH with a potential therapy consequence.

Keywords: LEDGF/p75, Autoimmunity, CRISPR/Cas9, dsDNA, mDNA



### Investigation of Janus Kinase 2 Gene Promoter Methylation Status in Immune Thrombocytopenia Patients

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Background: Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by decreased platelet count. Aberrant methylation of genes involved in immune regulation has been implicated in ITP pathogenesis. This study investigated the methylation status of the JAK2 (Janus Kinase 2) gene promoter in ITP patients compared to healthy controls. Methods: DNA methylation of the JAK2 promoter was assessed using methylation-specific PCR (MSP) in peripheral blood mononuclear cells (PBMCs) from ITP patients (n=48) and healthy controls (n=48) in Isfahan, Iran, over a one-year period. Clinical data, including platelet count and response to treatment, were collected. Results: ITP patients showed significantly higher JAK2 promoter methylation compared to healthy controls (p<0.05). This suggests a potential association between abnormal methylation patterns in the JAK2 gene and ITP development. Furthermore, the degree of methylation, meaning the extent to which the JAK2 promoter was methylated, displayed a significant correlation with two important clinical parameters. Firstly, a negative correlation was observed with platelet count (p<0.05). This implies that patients with higher levels of JAK2 promoter methylation tended to have lower platelet counts, a hallmark feature of ITP. Secondly, the degree of methylation also correlated with response to treatment (p<0.05). This finding warrants further investigation to determine if JAK2 methylation status could serve as a potential predictor of treatment efficacy in ITP patients. Conclusion: Increased JAK2 promoter methylation is associated with ITP and may serve as a potential biomarker for diagnosis and prognosis. Further studies are needed to elucidate the functional role of JAK2 methylation in ITP development and progression.

Keywords: Immune Thrombocytopenia, JAK2, Methylation, MSP, Biomarker



### Studying the Prevalence of HBsAg, Anti-HCV, and HIV Ab in Hemodialysis Patients of Ahvaz in 1402

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Background: Hemodialysis, the most common treatment method used for kidney failure, involves blood purification via a machine outside the body which then directs it back in. This method requires vascular access. Veno-arterial fistula is the most significant new method that provides this access. Dialysis is used to treat conditions like metabolic acidosis, high calcium, sodium imbalances, uremic syndrome, acute pulmonary edema, pericardial effusion, and drug intoxication. Patients undergoing hemodialysis often have weak immune systems, which increases infection risks. Hemodialysis can transmit various infections including viral infections, such as HIV, HBV, and HCV. This study aims to investigate the prevalence of these viruses in hemodialysis patients in Ahvaz. Methods: Blood samples of 445 hemodialysis patients were sent to Aria laboratory in 1402 from different dialysis centers in Ahvaz city. These samples were tested for antibodies against HIV, HBV, and HCV viruses using the Vidas machine. The patients' information and test results were analyzed using SPSS Statistics 29 (2022) software. Results: Out of 445 patients, 200 were women (44.9%) and 245 were men (55%). Among these people, 5 (1.1%) were positive for anti-HCV and all patients were negative for HBsAg and HIV Ab. Conclusion: Considering the low prevalence of HIV, HBV, and HCV among hemodialysis patients in Ahvaz, it can be concluded that the process of prevention and care of these patients regarding these viruses in dialysis centers is being performed well.

Keywords: Hemodialysis, HBsAg, Anti-HCV, HIV Ab



### **Novel Laboratory Diagnostic Methods of Cardio-Metabolic Disorders**

P50-P52



# Methylation Status of FTO Gene Promoter in Obese Diabetic (Type II) Patients with Hypertension

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Introduction: Increasing the overweight not only causes physiological problems, but also lead to death by increasing the peril of chronic diseases like diabetes type 2, cardiovascular disease, high blood pressure, different kinds of cancers. The reason of creating diabetes type 2 is so complicated and most genetic and environmental factors was role in creating it where the role of genetical factors is very important. Materials and Method: The current study was done on 63 obese women. The control group included 13 obese non-diabetic women with natural blood pressure. The patients was classified in two groups which included 25 obese diabetics with high blood pressure and 25 obese diabetics with natural blood pressure. After sampling, the biochemical tests were done by auto analyzer set and their DNA was extracted by RGDE method; FTO Methylation Promoter Gen was done also by MSP method. Results: Serum levels of fasting blood glucose, two-hour-glucose, the percentage of glycosylated hemoglobin and systolic and diastolic blood pressure in studying individuals were more than the control group. From the methylation point of view, the non-diabetics obese women without blood pressure (control group) had 23% methylation and 77% unmethylated. The obese diabetics women with high blood pressure (patient group 1) had 32% methylated and 68% unmethylated and the obese diabetics women without blood pressure (patient group 2) were 23% methylated and 76% unmethylated. Conclusion: Based on obtained results, it can be concluded that genetic base and epigenetic factors of obesity cause to may changes on FTO methylation promoter gene. Therefore, determining its biological effects need to much studying.

Keywords: Obesity, Diabetes Type 2, Hypertension, Cardiovascular Diseases, FTO gene, Methylation, MSPCR



# Exploring the Relationship between PCSK9, Cardiac Function, and Oxidative Stress: Findings from a Case-Control Study on Coronary Artery Disease

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This study conducted to examined the association between PCSK9, cardiac parameters, and oxidative stress markers in 63 healthy individuals and 63 MI patients with coronary artery blockages above 50%. Assessment of oxidative stress parameters (TAC, MDA, MPO, SOD, CAT, and GPx) and cardiac biomarkers (PCSK9, ox-LDL, hs-cTnI, hs-CRP, and EF%) was performed using various biochemical assays. Results revealed that higher levels of EF%, TAC, GPx, CAT, and SOD activity were associated with decreased risk of significant coronary artery blockages (>50%), while elevated levels of MDA, MPO, hs-CRP, ox-LDL, and hs-cTnI increased this risk. PCSK9 levels did not significantly differ between the groups. Positive relationships were observed between EF% and SOD, and negative relationships with MDA, MPO, ox-LDL, hs-cTnI, and hs-CRP. Hs-cTnI showed positive correlations with ox-LDL, MDA, and MPO, but negative correlations with CAT, GPx, and SOD. Ox-LDL positively correlated with MPO and negatively correlated with TAC, CAT, and GPx. Hs-CRP exhibited a negative association with TAC. Based on ROC and AUC curve analysis, ox-LDL, EF%, and hs-cTnI emerged as the best biomarkers for diagnosing significant coronary artery blockages, with respective AUC values of 83.22, 82.35, and 83.22. In conclusion, while PCSK9's involvement in MI through oxidative stress and inflammation is acknowledged, its primary impact on LDL-C levels must be considered. Ox-LDL, EF%, and hs-cTnI stand out as key biomarkers for diagnosing significant coronary artery blockages.

Keywords: PCSK9, Oxidative Stress, Myocardial Infarction, hs-CTnI, EF%



# Association of PECAM1 Val125Leu Polymorphism with Risk of Coronary Artery Disease in a Lur Population of Iran

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Background: Atherosclerosis is a multifactorial disease influenced by environmental and genetic factors. According to importance of PECAM1 in pathogenesis atherosclerosis, we intend to investigate the Val125Leu polymorphism with risk of atherosclerosis in the Lur population of Iran among the individuals who underwent coronary angiography. Methods: In this case-control study, a total of 300 subjects, including 145 controls and 154 patients were included that atherosclerosis based on the expert opinion of interventional cardiologists. The DNA was extracted, and then the PECAM1 Val125Leu gene polymorphisms were determined by ARMS-PCR methods respectively. Results: Genotype distributions were consistent with Hardy-Weinberg equilibrium (P >0.05). Genotype Leu/Leu showed an association with increased risk of atherosclerosis. However, this association was not statistically significant (odds ratio [OR] =1.86, P =0.066). Allele Leu showed an association with increased risk of atherosclerosis. However, this association was not statistically significant (OR =1.34, P =0.069). Conclusion: Susceptibility to atherosclerosis was not significantly associated with Val125Leu polymorphism of PECAM1 gene among the patients with acute chest pain in Lur population of Iran.

**Keywords**: Atherosclerosis, Adhesion Molecules, PECAM1, Genetics Polymorphisms.



# **POCT: Innovations, Challenges and Opportunities** P53-P61



### The Efects of Remdesivir and Dexamethasone on Renal Sirtuin-1 Expression and Renal Function in Male Rats

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Remdesivir (REM) and dexamethasone (DEX) both have been used to treat coronavirus disease 2019 (COVID-19). The present study aimed to evaluate the Lignifi of REM and DEX on kidney structure and function with particular focus on the probable renal sirtuin-1 (SIRT1) expression alteration in rats. Twenty-four male Wistar rats were divided into four groups, as follows: group A (control) received normal saline (5 mL/kg/day for 10 days); group B (REM) received REM (17 mg/kg/day on the frst day, and 8.5 mg/kg/day on the 2nd days); group C (REM+DEX) received both REM (17 mg/kg/day on the frst day, and 8.5 mg/kg/day on the 2nd L0th days) and DEX (7 mg/kg/day, for 10 days); group D (DEX) received DEX (7 mg/kg/day for 10 days). Renal SIRT1 expression and kidney structure and function-related factors were evaluated by standard methods. The mean levels of urea in the REM+DEX group (60.83±6.77, mg/dL) were Lignificantly higher than in the control (48.33±3.01, mg/dL; p=0.002) and DEX (51.22 $\pm$ 4.99, mg/dL; p=0.018) group s. The mean levels of creatinine in the REM (0.48 $\pm$ 0.08, mg/dL) and REM+DEX (0.50±0.04, mg/dL) groups were higher than in the control group (48.33±3.0 mg/dL) □ ignificantly (p=0.022 and p=0.010, respectively). The renal SIRT1 expression was □ ignificantly (p=0.018) lower in the REM+DEX group (0.36±0.35) than in the control group (1.34±0.48). Tubulointerstitial damage (TID) scores in REM+DEX-treated rats (2.60±0.24) were □ignificantly higher than in the control (0.17±0.17, p=0.001) and DEX (0.50±0.29, p=0.005) groups. The administration of DEX and REM might lead to kidney injury associated with SIRT1 downregulation.

Keywords: COVID-19, Dexamethasone, Nephrotoxicity, Remdesivir, Sirtuin-1



### **Evaluation of the Neutralizing Antibody Serum Level in Infants Whose Mothers Received the Covid-19 Vaccine**

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Introduction and Objective: During the Covid-19 pandemic, pregnant women and infants constitute a vulnerable population. Vaccination of pregnant mothers during pregnancy can cause the transfer of antibodies to the fetus through the placenta and as a result create passive immunity in the fetus. In this regard, this study was designed to determining the amount of SARS-CoV-2 neutralizing antibodies in the serum of infants whose mothers were vaccinated. Materials and methods: In this study, the serum level of the neutralizing antibody of the Covid-19 virus in the serum of 64 infants who visited Dena Yasouj& pathobiology laboratory for bilirubin testing was investigated using the ELISA test. The age of the examined infants was 7 days at most. Data were analyzed in SPSS V.20 statistical software. Results: The mean and standard deviation of neutralizing antibody concentration was 24.1±21.7. Based on the obtained results, the concentration of neutralizing antibody has a direct relationship with the number of vaccination doses, and with the increase in the number of vaccinations, the average concentration of neutralizing antibody in the serum of infants has also increased. Conclusion: Based on the results obtained from this study, it has been observed that maternal vaccination causes passive immunity in infants, and the higher the number of vaccinations, the greater this immunity.

Keywords: Covid-19 Vaccine, Pregnant Women, Infant Serum, Neutralizing Antibody, ELISA



### A Case Report of Intercellular Bridge Antinuclear Antibody Pattern in A 35-Year-Old Women With Multiple Sclerosis Disease in Dena Pathobiology Laboratory of Kohgiloyeh and Boyerahmad

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Background: Multiple sclerosis (MS) is a long-lasting (chronic) disease of the central nervous system. It is thought to be an autoimmune disorder, a condition in which the body attacks itself by mistake. MS is an unpredictable disease that affects people differently. Intercellular bridges (ICBs) are conserved biological structures that arise when a contractile cleavage furrow is arrested before complete abscission and is subsequently stabilized into a noncontractile ring. Staining of the intercellular bridge that connects daughter cells by the end of cell division, but before cell separation. This rare antinuclear antibodies (ANA) pattern is defined as a pattern that occurs in < 1% of patients testing positive on indirect immunofluorescence (IIF). Case Report: The patient was a 35-year-old married woman who referred to the laboratory due to low white blood cell count (2.7×1000/mm3) and a history of MS. Retesting showed the patient's white blood cell count to be low (3.14×1000/mm3). Considering that MS is one of the autoimmune diseases and the patient also had a history of this disease, so the patient's sample was also tested to check the types of autoimmune tests using the IIF method. After performing the ANA test, an intracellular bridge pattern with the number AC-27, which is a rare pattern, was observed.

Keywords: Multiple Sclerosis, Antinuclear Antibodies, Intracellular Bridge Pattern, Indirect Immunofluorescence



# DNA and RNA Stability: A Comparative Study of Four Designed Storage Buffers and a Common Laboratory Buffer

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Background: In our study, we aimed to preserve DNA and RNA integrity for Polymerase Chain Reaction (PCR) testing. We designed four different buffers to improve the stability of these specimens, which are increasingly used in liquid biopsies for cancer detection. Methods: We evaluated the impact of the four buffers on DNA and RNA preservation and their inhibitory effects on the PCR process. The buffers contained a phosphate-buffered saline (PBS) solution with added chelating agent, microbicide, fungicide, and bovine serum albumin. The study was carried out in two phases, 10 nasopharyngeal samples were collected, and the DNA was extracted and preserved at different time intervals (day 0, day 7) per preservative. Results: The Ct values for the samples collected on day zero indicated distinct variations among the buffers. Buffers 1 and 2 displayed relatively higher Ct values, indicating lower amplification efficiency. In contrast, buffers 3 and 4 exhibited superior performance, closely resembling the results obtained from the reference sample (VTM). After a week of storage in the freezer, buffers 1 and 2 failed to produce any measurable Ct values, indicating a significant loss of amplification capability. However, buffers 3 and 4 demonstrated remarkable stability, maintaining consistent Ct values. Conclusions: Our findings suggest that buffers 3 and 4 not only improve PCR efficiency but also exhibit notable temporal stability. These buffers ensure reliable and reproducible results that closely align with the reference sample, thus simplifying the clinical diagnostic workflow.

**Keywords**: Polymerase Chain Reaction, Liquid Biopsy, Nucleic Acids, Buffers



### Study of the Effect of Oleuropein on the Heart Tissue in D-Galactose-Induced Aging in Rat Model

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Background: Many researches have indicated that Oleuropein (OLE) has potential ability to decrease oxidative stress and inflammation. As a result, our current study aimed to examine the protective impact of Oleuropein (OLE) against d-galactose (D-Gal)-induced heart aging in rats model. Methods: In the present study, 40 Wister male adult rats were categorized into 5 groups. The first group was given distilled water and the second group was given D-Gal at a dose of 100 mg / kg/ip. The rats in groups 3 to 5 were orally administered D-Gal (100 mg/kg) once a day. Additionally, these groups were simultaneously subjected to different doses of OLE (20, 40 and 80 mg/kg, respectively) through oral administration. All administrations were done once a day for 8 consecutive weeks. 24 hours after last treatment the rats were sacrificed and serum and heart samples were collected for evaluating biochemical serum markers of heart damage (AST, LDH, cTnI and CK-MB), oxidative stress (MDA, PC, GSH, GPX, CAT and SOD), gene expression (SIRT1 and PGC1) and histopathological observations. Results: The findings indicated that D-Gal significantly reduced the GPx, CAT and SOD activities, GSH level as well as SIRT1 and PGC1 expression in the heart tissue (P<0.05). (P<0.05). Also, D-Gal, significantly increased PC and MDA levels and serum cardiac markers (CK-MB, LDH, AST and cTnI) (P<0.05). Administration of OLE restored all of the above parameters close to control group. Conclusion: The results of the present study showed that OLE dosedependently reduced heart lesions caused by D-Gal. The authors suggest that OLE exerts this protective effect through reducing oxidative damage.

Keywords: Oleuropein, D-Galactose, Oxidative Stress, Heart Tissue



# Conjugation of Fraxinus Excelsior-Synthesized Silver Nanoparticles with Polymyxin and Investigation of its Antibacterial Activity on Resistant Bacteria

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Background: Metal nanoparticles have been studied by researchers due to their application in various scientific and industrial fields. Antibiotic resistance in pathogenic bacteria is one of the most serious global public health threats in this century. Therefore, silver nanoparticles with unique properties of high antimicrobial activity have attracted much interest from scientists. This research aimed to evaluate the synergistic antibacterial activity of the biologically synthesized silver nanoparticles conjugated to polymyxin against polymyxin-resistant bacteria. Methods: synthesized silver nanoparticles using the Fraxinus plant were conjugated to polymyxin-B. The absorbance was measured by Nanodrop in the range of 300 to 700 nm at different times. To measure the size and charge of conjugated nanoparticles DLS and ZETA were used. The antibacterial effects were carried out on several types of polymyxin-B-resistant bacteria such as Pseudomonas aeruginosa, and Acinetobacter baumannii. Results: An absorption peak was observed in the 400-450 nm during a month, which indicated the formation and stability of conjugated silver nanoparticles. The antibacterial assay displayed the highest inhibitory effect of silver nanoparticles in 40 micrograms per microliter concentration for Pseudomonas aeruginosa, and Acinetobacter baumannii. Conclusion: The results of the present study showed using biologically synthesized silver nanoparticles conjugated to polymyxin-B at appropriate concentrations can utilize their antibacterial properties as a suitable alternative to chemical drugs in polymyxin-B-resistant bacteria.

Keywords: Silver nanoparticle, Fraxinus, Polymyxin, Antibacterial



# Utilization of Endophytic Fungi Isolated from the Viburnum Lantana for Vincristine Production: A Novel Approach in Drug Production

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Vincristine is naturally extracted from the medicinal plant Catharanthus roseus, but due to the low amount of this compound in the plant, it is very important to find an alternative way to produce this valuable compound. Vincristine is a powerful anti-cancer drug that works by stopping cells from mitosis. One of the best alternative methods for the production of vincristine on a large and commercial scale is the use of vincristine-producing endophytic fungi. First, plant samples of Arasbaran Viburnum lantana shrub were collected from five areas of Arsbaran. In the next step, leaf and stem explants were separated from the plant sample and after surface disinfection with alcohol and 1.5% sodium hypochlorite, they were cultured in PDA culture medium for one week. After the emergence of endophytic fungi, recultivation of endophytic fungi was carried out in PDA culture medium and finally liquid culture of fungi was done. Among about 20 grown endophytic fungi, a screen was made to detect vincristine-producing endophytic fungi using HPLC method. The results showed that only VO2 fungi has the ability to produce 202 mg/l of vincristine. To identify the endophyte fungal species, both molecular methods and morphological characteristics of the fungi were used. So, in the molecular identification of the fungi, the PCR reaction was used to amplify the ITS fragment. The amplified ITS fragment was sequenced and by BLAST the desired sequence in the NCBI database, the scientific name of the fungal species was determined. SEM electron microscope was also used for morphological identification of the desired fungi. In an experiment on two breast cancer cell lines, MCF-7 and BT-474, it was shown that the fungi extract at concentrations of 400-100 µg/ml has a high impact on breast cancer cells.

Keywords: Endophytic Fungi, Secondary Metabolites, Viburnum Lantana, Vincristine



# Acute Myeloid Leukemia with CNS Involvement Following HBc-Ab Positive Allogeneic Hematopoietic Stem Cell Transplantation

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Background: Acute Myeloid Leukemia (AML) is a heterogeneous disease that can be treated with stem cell transplant (HSCT). CNS involvement, a rare but serious complication of AML, can impact treatment decisions. In this case, we report a case of AML with CNS involvement who underwent HSCT from an HBc-Ab positive donor. Methods: A 17-years-old girl with AML underwent HSCT from an HLA-matched brother with HBc-Ab positive. Despite the donor's positive HBc-Ab status, he was selected for the transplant due to the highest compatibility with the recipient. A series of immunologic tests have been performed for the donor and recipient, with the results showing the recipient to be CMV-Ab (IgG) positive, HBc Ab negative, HBs Ab Titr=38.4 mIU/ml (indicating vaccination for the recipient), HBe Ag and Ab negative, and other immunologic tests negative. For the donor, the results of the immunologic tests include CMV Ab (IgG), CMV Ab (IgM) and Toxoplasma Ab (IgG) positive, Toxoplasma Ab (IgM) negative, total HBc Ab positive, unimmune HBs Ab Titr=0.6 mIU/ml, and other immunologic tests negative. Results: Before transplant, the patient received Cytarabine and Daunorubicin chemotherapy for CNS involvement, followed by broad-spectrum antibiotics and antifungals. Additionally, both patient and donor received daily tenofovir prophylaxis starting one week beforehand. Conclusion: Due to the patient's need for an allogeneic transplant and the availability of a HLA-matched donor, recovery after metastatic malignancy in CNS, and considering the fact that hepatitis is treatable and not considered fatal, we prioritized the transplant for the treatment of AML despite the donor being HBc Ab positive, with the initiation of hepatitis B prophylaxis in the patient.

Keywords: Acute Myeloid Leukemia, HSCT, HBc Ab positive



### Production of Membrane Protein (M1) of Influenza TypeA and Investigationof Its Immunogenicity in a Rabbit Model in Order to be Used in Vaccine Production and Serological Tests

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Background: The spread of the influenza virus is a threat to human societies due to genetic mutations and the creation of respiratory infections. Influenza virus proteins can create immunity, and the antibodies produced against them can have antiviral effects. Matrix protein (M1) is the most abundant protein in influenza, which can be a candidate for the production of influenza vaccine. Methods: In this study, pET21-M1 gene construct was propagated in Top10f host and confirmed by EcoR\(\text{\temp}\) and xho\(\temp{\temp}\) enzymes, then it was transferred to BL21 expression host and it expression was checked by SDS-PAGE technique. The protein was extracted by sonication and it was purified by ion exchange chromatography. After dialysis, the male rabbit was periodically injected three times at intervals of one month from the first injection and 15 days from the second injection with specific amounts, which was checked for the amount of antibodies from the animal's blood serum by ELISA and DOT Blot methods. Results: The results obtained from ELISA and DotBlot show an increase in antibody titer against M1 protein. Conclusion: In this study, M1 antigen and produced antibody were able to be used in serological tests to detect influenza a virus.

Keywords: Polyclonal Antibody, Recombinant Pprotein, Serological Methods



### **Prenatal Screening and Diagnosis of Fetal Abnormalities**

P62-P66



# Effect of Maternal Age on the Rate of Chromosome Abnormality in the Fetus: Presentation of Prenatal Karyotype Result of 8245 Amniotic Fluid Samples in Iranian Women

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Aims: The aim of this study was to assess the prevalence of different chromosomal abnormalities in amniotic fluid samples of Iranian women referred to Sarem Women's hospital. Besides, to identify different indications of referral and the prevalence of abnormalities in each category, and assigning the abnormality rate to mothers' age, of 35 years and above and less than 35. Material and Methods: 8245 amniotic fluid samples of women were referred to Sarem women shospital from March 2006 to March 2022. Afterreceiving genetic counseling, they were referred for cytogenetics investigation. Findings: 4.8% of samples had chromosomal abnormalities of which 70.45% were numerical and 29.55% were structural. The most common numerical abnormality was trisomy 21 accounting for 36.11% of all abnormal cases and 51.25% of numerically abnormal cases. Abnormal Maternal Serum Screening Test (AMSST) was found to be the major indication of referral with 76.5% of all referrals. 46.71 % and 53.29% belonged to the <35 and ≥35 age groups, respectively with trisomy 21 responsible for 45.02% of abnormalities in women of ≥35 age and structural abnormalities of 29.18 % of women <35. Conclusion: This study emphasizes prenatal screening and cytogenetic testing for chromosomal abnormalities. Furthermore, the high level of both numerical and structural chromosomal abnormalities in women of both age groups highlights the significance of cytogenetic testing for all pregnant women regardless of their age.

**Keywords**: Iranian Women, Prenatal Diagnosis, Chromosome Abnormalities, Maternal Age, Maternal Serum Screening Test, Down Syndrome



#### Undiagnosed Gilbert's Syndrome in an Adult Male After 21 Years

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Background: Gilbert's syndrome (GS) is an autosomal recessive condition characterized by a relative lack of glucuronyl transferase, inadequate hepatocyte absorption of unconjugated bilirubin, and recurrent bouts of jaundice. Case Presentation: A 24-year-old male patient was diagnosed with Gilbert's syndrome during a routine checkup. All tests except unconjugated bilirubin were normal. Conclusion: It was the first report from Bushehr. This case was asymptomatic patient which, identified only during routine checkup tests.

Keywords: Diagnosis, Gilbert's Syndrome, Laboratory Test



# Frequency of Alpha Thalassemia Deletional Mutations in the Western Provinces of Iran Majid Arash 1 \*

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Background: Alpha thalassemia is one of the genetic disorders of alpha globin chain production, which is caused by a mutation in the alpha globin chain gene. One of the mutations that cause this disease is deletional mutations. the most common of which include  $\alpha 3.7$  and  $\alpha 4.2$  single gene mutations and  $\Delta$ MED and  $-(\alpha)20.5$  two-gene mutations. The purpose of this study is to investigate Frequency of alpha thalassemia deletional mutations in the western provinces of IranMethods: To write this article, the pubmed website as well as the scientific journals of Iranian universities of medical sciences and searching for alpha thalassemia keywords and the names of the provinces were used. Findings: In this study, the main investigation was carried out on four common deletional mutations, including  $-\alpha 3.7$ ,  $-\alpha 4.2$ ,  $-\alpha 20.5$  and --MED. The findings showed that the most deletion mutations in Hamedan, Kurdistan, Kermanshah and Ilam province is  $-\alpha 3.7$  and other mutations are in the next ranks. Conclusion: Based on the obtained results, it is recommended that couples with suspected alpha thalassemia blood characteristics should be screened so that appropriate and appropriate decisions can be made for their reproduction, so that the condition of the newborns can be controlled in terms of this disease. It is also better to check the beta globin gene that the combination of defects in  $\alpha$  and  $\beta$  chains does not occur

Keywords: Alpha Thalassemia, Mutation, Alpha Globin



# Relationship between Thyroid Stimulating Hormone and Risk Level Screening Tests in the Second Trimester of Pregnancy

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Introduction: The most common thyroid disorder during pregnancy is subclinical hypothyroidism. It is defined as the manifestation of thyroid stimulating hormone concentration (TSH) higher than the specific reference value with normal thyroxine concentration. In this study, we evaluated the relationship between the final risk of screening tests and thyroid function in the second trimester. Method: In current study, 40 pregnant women were enrolled. The ELISA method was performed to evaluate the serum levels of Inhibin-A, Free esteriol. TSH and anti TPO levels and also BhCG, AFP, were done by Electro-chemiluminescent (ECL) method. Results: The average levels of TSH and anti TPO, were significantly higher than control group. The mean levels of beta-hCG and inhibin-A were higher in patients group, but it was not statistically significant. Result showed that, there was no statistical difference between the patients and control groups in terms of free esteriol, and AFP. The final risk of trisomy 21, in the patient group were higher; However, it was not statistically significant. There was no difference between the patients and control groups in terms of the final risk of trisomy 13/18. Conclusion: Considering the effect of thyroid hormones on the body's metabolism, regular control of thyroid hormones in pregnant women should be done carefully and sensitively. It is suggested to identify hypothyroid pregnant womens early and make it mandatory to perform timely fetal health screening tests in pregnancy, with the aim of identifying fetuses at risk of developing chromosomal disorders.

Keywords: TSH, TPO, BhCG



# Lymphocytic Choriomeningitis Virus (LCMV): Current Status and Future Directions for Clinical and Molecular Diagnostic Techniques

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Background: The lymphocytic choriomeningitis virus is an RNA virus that is often overlooked, despite the potential for causing severe illness. It is an important cause of viral meningitis, particularly in certain clinical situations. LCMV is transmitted to humans when they come into contact with the secretions of infected mice, and its strong neurotropism primarily results in neurological symptoms. The most vulnerable populations are fetuses and immunosuppressed individuals. LCMV infection acquired through various means can manifest with a wide range of clinical symptoms, varying from being asymptomatic to severe manifestations. Additionally, in cases where individuals are affected by this viral infection, it can result in fatal central nervous system disorders. Specifically, in pregnant women, intrauterine LCMV infection has been observed to lead to fetal or neonatal mortality. Furthermore, it can cause chorioretinitis and hydrocephalus in infants, which not only causes significant harm but also results in long-term impairments. Main Idea: Timely identification and immediate intervention play a crucial role in improving the prognosis, especially among high-risk groups and in regions where the infection is prevalent. Failure to promptly diagnose the condition can lead to significant mortality rates and leave survivors with long-term neurological complications. Consequently, it is imperative to utilize the most appropriate laboratory diagnostic approach, considering the patient's clinical symptoms, exposure history to the virus, and the prevalence of the pathogen in the area, in order to facilitate accurate clinical detection. Conclusion: This comprehensive review encompasses various diagnostic methodologies employed in the management of LCMV, encompassing clinical manifestations, diagnosis, treatment, and potential complications associated with viral infections affecting the central nervous system.

Keywords: LCMV, CNS, Diagnosis, Chronic Infection



### Role of Resource Management in Effectiveness & **Quality Improvement of Medical Labs**

**P67** 



#### The Results of Urine Culture Analysis and the Necessity of Screening

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As there are few positive urine culture results in most laboratories, employing a primary screening method with a high predictive value seems to be necessary. In this research, 3358 midstream clean-catch urine samples were cultured from April to December in 2023 in Maragheh Health Center Laboratory. The grown bacteria were identified by routine biochemical tests. Out of 3358, 3099 were women and 259 were men. The results were positive in 4.34%, 4.3%, and 4.6% of total, female, and male samples, respectively. Microscopic analysis of the samples indicated that in 93.83% of the positive culture samples, the bacteria were observed at a medium to high level. In 78.76% of the positive culture samples, the >5 WBC were observed in each field of 400X microscopic analysis. The nitrite test was positive in 46.42% of the positive culture samples. Therefore, in general, the infection indicators in the microscopic analysis confirmed the culture results. However, low percentage of the positive cultures can be attributed to the use of antibiotics before sampling, the target population, the laboratory techniques, clinical indications for the test, and non-cultivable bacteria under routine conditions. Therefore, it is emphasized to review and use primary indicators to reduce negative results and waste of resources in such tests.

Keywords: Urine Culture Analysis, Screening Test, Urine Cultures



**Smart Medical Laboratory: the Role of New** Generation Artificial Intelligence in Improving the **Quality and Management of the Medical Laboratories** 

P68-P72



### Deciphering the Role of Artificial Intelligence in Quality Improvement in Clinical Laboratories

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Background: Clinical laboratories play a critical role in healthcare and the quality of laboratory results directly impacts patient diagnosis, treatment, and outcomes. To ensure accurate and reliable results, maintaining high-quality standards is of utmost importance. Artificial Intelligence (AI) has emerged as a powerful tool in improving quality control processes within clinical laboratories. In this article, we will explore the role of AI in quality improvement in clinical laboratories. Methods. This study used a comprehensive literature search in PubMed, Scopus, Web of Science, and Google Scholar databases to identify relevant articles. The search strategy included the following MeSH terms and keywords: clinical laboratory, laboratory medicine, artificial intelligence, and quality improvement. The language of the articles that were reviewed was limited to English and review and original articles were included in this study. Results. The literature suggests that AI provides many services to clinical laboratories, which include 1) data management and analysis; 2) error detection and prevention; 3) automated quality control; 4) equipment monitoring and maintenance; 5) trend analysis and predictive analytics; 6) workflow optimization; and 7) decision support systems. As a result, AI-powered solutions enable proactive maintenance, trend analysis, and data-driven decision-making in laboratory medicine. Ultimately AI can help laboratories provide accurate, reliable, and efficient services. Conclusion. In conclusion, AI is revolutionizing quality improvement in clinical laboratories, ultimately improving patient outcomes. Of note, as technology continues to evolve, the role of AI in quality improvement within clinical laboratories will undoubtedly become even more crucial.

Keywords: Clinical Laboratory, Laboratory Medicine, Artificial Intelligence, Quality Improvement



### The Evolution of ChatGPT in Cancer: A Revolutionary Journey from Inception to Advancement

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Background: Cancer biology is a complex and rapidly evolving field that has witnessed significant advancements, driven mainly by the integration of cutting-edge technologies and artificial intelligence (AI). Among the notable breakthroughs in AI is the development of chat generative pre-trained transformers (ChatGPT), which has emerged as a revolutionary tool in cancer research and analysis. ChatGPT is a language model with tremendous potential in cancer biology. This review article aimed to comprehensively explore the multifaceted role of ChatGPT in cancer biology, tracing its evolutionary journey from its inception to its current state. Method: By leveraging its advanced language generation capabilities, ChatGPT can process vast amounts of cancer-related data and contribute valuable insights to our understanding of the disease. Throughout this review, we presented a comprehensive overview of ChatGPT's contributions to cancer biology. We explored its applications in cancer genomics, immunology, therapeutic development, the limitations and challenges of ChatGPT's utilization in cancer research, validation, and ethical considerations. Results: The results demonstrate the revolutionary impact of ChatGPT in cancer biology, clinical decision-making, and drug discovery. It highlights the potential of ChatGPT in identifying novel biomarkers, facilitating breakthrough discoveries, and accelerating research endeavors in cancer immunogenetics. However, it emphasizes the importance of rigorous experimental validation before incorporating ChatGPT's suggestions into clinical practice. Conclusion: By investigating the current study, we shed light on the potential of ChatGPT as a powerful tool in advancing cancer research and treatment.

Keywords: ChatGPT, Biology, Cancer, Immunogenetics, OpenAI



# Identification of a Novel Pathogenic Variant in the TPP1 Gene Associated Neuronal Ceroid Lipofuscinosis Type CLN2

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Bakground: Neuronal ceroid lipofuscinosis (NCL) is a group of neurodegenerative lysosomal storage disorders characterised by the accumulation of neuronal and extraneuronal ceroid lipopigments. Mutations in the TPP1 gene that encodes the lysosomal enzyme tripeptidyl peptidase 1 (TPP1) are associated with an autosomal recessive disease known as the CLN2 variant. Methods: Whole exome sequencing (WES) was performed on an Iranian 5-year-old girl presented with bilateral Babinski signs, proximal lower limbs atrophy, spasticity, and Mental retardation. Sanger sequencing was used to confirm candidate pathogenic variants. Results: We reported a novel variant in the TPP1 gene that is a frameshift mutation that produces a truncated protein with 46 amino acids. It is a null variant of the TPP1 gene where the loss of function (LoF) is a known mechanism of disease. The 3D structure modelling of the TPP1 protein using SWISS-MODEL shows a truncated protein that is different from the original protein structure. Conclusion: The variant was classified as pathogenic according to the American College of Medical Genetics and Genomics guideline. This study expands the spectrum of TPP1 pathogenic variants in Iran and demonstrates the utility of whole exome sequencing in genetic diagnostics.

Keywords: Neuronal Ceroid Lipofuscinosis, Whole Exome Sequencing, Mutations



### Advancements in AI for Digital Pathology: Enhancing Diagnostic Accuracy and Healthcare Availability

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Background: Artificial intelligence (AI) is a simulation of the human mind in a computer system trained to imitate actions like problem-solving. AI system assists clinicians by interpreting diagnostic and prognostic disorders associated with decreased errors in laboratory and clinical diagnosis to provide suitable economic and social costs. Classification of the main advantages of AI's role in the development of clinical laboratory methods is the aim of this study. Methods: Artificial intelligence, diagnosis, and digital pathology keywords have been searched in Google Scholar, PubMed, and Scopus for the last 5 years. The retrieved titles and abstracts are screened to find the suitable full text. Results: Application of AI technical approaches affected histopathology finding and analyzing, medical imaging, and disease biomarkers via signal processing, text mining, imaging, and data processing. The digital images and signals are evaluated in detail to present complete wives of pathological events in patients. The large sets of possible biomarkers are analyzed to determine the initiation or development of diseases. Development of the three highlighted fields via the application of AI can lead to quick and careful detection of early stages of diseases. Conclusion: Since access to complete information of single tissue slides is a vital process of proper and efficient diagnostic methods, AI is a suitable tool to solve the problem of missing data in single tissue slides which contain a huge amount of information. This significant event increases both the accuracy and availability of high-quality health care, so the process of diagnosis and treatment of diseases is accelerated.

Keywords: Artificial Intelligence, Diagnosis, Digital Pathology



# **Exploring Current and Future Trends: Machine Learning's Application in Leukemia Diagnosis**

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Background: Leukemia is a major hematological malignancy that has a high prevalence worldwide and causes many deaths and complications at different ages. Leukemia diagnosis is challenged by various factors, including lack of access to health care, and misclassification due to lack of trained personnel, making accurate identification difficult. Advances in artificial intelligence (AI) techniques, especially machine learning (ML), allow us to use it to diagnose leukemias faster and more accurately. Methods: We searched PubMed, Scopus, and Google Scholar for Applications of machine learning for leukemia diagnosis, published up to February 13, 2024. Results: Nowadays, the use of ML in the diagnosis of leukemias has become prevalent. Studies show that various features are used in ML to help diagnose leukemias more easily and quickly. Among the most important features, studies mention the examination of patients' demographic characteristics, evaluation of genetic data, examination of peripheral blood and bone marrow slides, and examination of flow cytometry results. However, the use of ML in diagnosing leukemia can go further. Among the things that can be used for the diagnosis of leukemias in the future are increasing the number of people examined, increasing the features used, using the data of patients in different diagnostic centers, and most importantly, using the combination of the above-mentioned items, for faster and better diagnosis of patients because ML is a powerful tool in understanding and overcoming the disease. Conclusion: Finally, despite the increasing use of AI in the diagnosis of cancers, this field still has the potential to improve, and by collecting more data from patients, the accuracy of machine learning in diagnosis will increase. With AI, we can perform initial diagnosis, estimate prognosis and predict treatment complications as quickly as possible, to monitor relapse in hematological malignancies, on par with specialists.

Keywords: Diagnosis, Machine Learning, Leukemia



### The Role of the Microbiology Laboratory in an Era of **Increasing Antibiotic Resistance**

P73-P80



# Biosynthesis of silver nanoparticles using Fraxinus Extract and investigation of its Antibacterial Activity

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Background: Increasing bacterial resistance in human pathogenic bacteria to antibiotics led to research and investigation for new biocompatible antibacterial agents and strategies to combat antimicrobial resistance. Silver nanoparticles have shown excellent antibacterial properties against a wide range of microorganisms. The main goal of this study was the synthesis of silver nanoparticles using Fraxinus extract and the investigation of its antibacterial activity. Methods: An herbal extract was prepared biologically using the Fraxinus plant, and synthesized silver nanoparticles by this extract were used. The absorbance was measured by Nanodrop in the range of 300 to 700 nm at different time intervals. DLS and ZETA were performed to measure the size and charge of nanoparticles. The antibacterial effects were carried out on several types of Gram-positive and Gram-negative bacteria, including Staphylococcus aureus, and Escherichia coli. Results: An absorption peak was observed in the 400-450 nm from the first day to one month, which indicated the formation and stability of silver nanoparticles. ZETA potential analyzer confirmed the negative charge of nanoparticles. Nanoparticles were found to be spherical by the DLS technique. The antibacterial test showed the highest inhibitory effect of silver nanoparticles in 40 micrograms per microliter concentration for Escherichia coli and in the case of Staphylococcus aureus a concentration of 10 micrograms per microliter was obtained. Conclusion: The results of the present study showed using biologically synthesized silver nanoparticles at appropriate concentrations can utilize their antibacterial properties as a suitable alternative to chemical drugs.

Keywords: Silver Nanoparticle, Biosynthesis, Fraxinus, Antibacterial



#### Drug Resistance Pattern of Mycobacterium Tuberculosis in Guilan Province, Iran

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Background: Mycobacterium tuberculosis (MTB) is causative agent of tuberculosis (TB), which still remains one of the most common infectious diseases in developing countries. In the recent years, emergence and spread of multidrug-resistant (MDR) TB pointed as public health problem worldwide. This study aimed to determine the rate of drug resistance to first-line anti-TB drugs in Guilan province. Methods: MTB isolates were collected from March 2016 to July 2018. Drug susceptibility testing to rifampicin, isoniazid, ethambutol, and streptomycin was performed on L; wenstein-Jensen medium using proportion method. Results: A total of 138 MTB isolates were included to this study. The mean age of patients was 47.41, ranged from 17-84 years and 104 (84.1%) patients were male. A set of 128 (92.8%, 95% CI = 87.2%-96%) isolates were pan-susceptible and 10 (7.2%, 95% CI = 4%-12.8%) were resistant to at least one drug. Five isolates (3.6%, 95% CI = 1.6%-8.2%) were resistant to streptomycin, 6 isolates (4.3%, 95% CI = 2%-9.2%) were resistant to isoniazid, 3 isolates (2.2%, 95% CI = 0.7%-6.2%) were resistant to rifampicin, one isolate (0.7%, 95% CI = 0.1%-4%) was resistant to ethambutol. In this study three isolates (2.2%, 95% CI = 0.7%-6.2%) showed resistance to rifampicin and isoniazid then identified as MDR. Conclusions: The prevalence of drug resistant isolates in this study area point to the necessity for further enforcement of TB treatment and disease control management. Drug susceptibility testing for all TB cases and continuous monitoring of drug resistance are recommended to prevention and control of drug-resistant TB.

Keywords: Mycobacterium Tuberculosis, Tuberculosis, Multidrug Resistant



# The Effect of Chlorhexidine Gluconate Foley Care on Bacteriuria and UTI in CVA elderly Female Inpatients Using Indwelling Urinary Catheters

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Introduction: One of the most common NI is urinary tract infection (UTI) which is more commonly occurs in patients with urinary catheters, especially female inpatients with indwelling-urinary-catheters (IUC). Aim of this survey was to determine and compare the effect of daily foley-care (periurethral cleaning) using chlorhexidinegluconate0.2% (CG) versus normal-saline0.9% (NS) on indwelling catheter-associated bacteriuria/UTI on CVA elderly female. Patients and Methods: This clinical trial survey performed at four months of 2023 in Bou Ali Sina Hospital, Sari in 1500 CVA female inpatients using IUC without history of UTI. Patients were randomly divided into two groups, CG and NS, for once/day foley-care. All organisms isolated from a positive urine/blood culture, the antibiotic susceptibility/resistance pattern was screened via Kirby-Bauer DD according to CLSI instructions. Data was analyzed using SPSS V19 (P<0.05). Ethics approval has been obtained of MAZUMS. Results: The average-age of the patients was 46-83 years (51.28±14.12). There was no baseline difference between groups in mean age, presence of underlying disease, use of antibiotics, intake of fluids, and urinary output. The frequency of bacteriuria was 22(2.94%), and 2(0.27%) in the NS and CG groups, respectively (P<0.001). In the CG group, the only isolates detected were Staphylococcus saprophyticus and Enterobacter of Gram-positive-cocci. In NS group Gram-negativebacilli (72.7%) were predominant isolates The predominant organisms isolated were E. coli (59%), followed by Staphylococcus epidermis, Staphylococcus saprophyticus, Klebsiella pneumoniae and Pseudomonas aeruginosa. Conclusion: Findings showed a significant reduction in the incidence of catheter associated asymptomatic bacteriuria/UTI in the perineal-care of CG group and no detection of BSI during throughout the study. Due to the lower side effects, the CG solution could be used in the short term as a simple, inexpensive and safe antiseptic in the above-mentioned patients with once/day foley-care in short-term. This could be a potential prevention strategy for patients, as significant reductions in a variety of microorganisms can have a significant impact on reducing NI, mortality and healthcare-related costs

Keywords: Chlorhexidine Gluconate, Foley care, Indwelling Urinary Catheters, Nosocomial Infection



The Rate of Nosocomial Infection and Antimicrobial Resistance in Male Disease in COVID-19 Pre-Pandemic and Pandemic Era: Coronavirus an Opportunity or a Challenge?

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Introduction: Nosocomial infections represent a global health problem. The causes are responsible for significant morbidity and mortality, particularly in developing country. Hospitals are a conducive environment for the spread of infections and a serious challenge for healthcare professionals worldwide during the coronavirus era.

Materials and methods: The descriptive cross-sectional study was conducted during a of two years of the prepandemic and in the two years of the pandemic periods at Bou Ali Sina Hospital. All male inpatients at the teaching hospital who were suspected of having symptoms of NI were assessed. The antibiotics sensitivity/resistant pattern was screened using Kirby-Bauer disc-diffusion method according to clinical and laboratory standard institute(CLSI) instructions. Data was analyzed using SPSS V19 (P<0.05). The research was approved by the Ethics Committee of MAZUMS.Results: Of all 458 identified cases of NIs, 153 cases(33.4%) were related to pre-Corona and 305(66.6%) to Corona era. In both the pre-pandemic and pandemic eras, the most common cases were Urinary tract infections, Respiratory tract infections, Surgical site infections, and Bloodstream infections, respectively. Also mainly isolated were Gram-negative bacteria.

The Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter aerogenes and Acinetobacter baumannii were the most common cause in both groups. There was a significant decrease(\( \S00\)) in extended-spectrum beta-lactamase(\( \SBL \))-producing samples in the pandemic(5.6%) compared to the pre-pandemic era(12.4%). While the vancomycin-resistant isolates with 3.3% of pre-pandemic versus 7.2% of pandemic era shown a significant increase(\( \S00\)). Conclusion: Although the increase in health protocols during the Corona crisis was expected to be accompanied by a decrease in NI, this could not always lead to a decrease in all hospital-acquired infections. This will further restrict treatment choices and jeopardize global public health.

Keywords: COVID-19, Pandemic, Pre-Pandemic, Nosocomial Infection



# Investigating the Antibiotic Resistance Pattern and Broad-Spectrum β-Lactamase Genes in Enterobacter Species Isolated from Infants with Sepsis from Ahvaz, Southwest Iran

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Background: The global challenge of neonatal sepsis caused by antibiotic resistant Gram negative bacteria is a significant concern, primarily due to the high mortality rates and increased hospital costs that accompany it. The elevated resistance rate can be attributed to the existence of extended-spectrum beta-lactamases (ESBLs) within Enterobacteriaceae family. The antibiotic resistance patterns of Gram negative bacteria that lead to neonatal sepsis can vary depending on the hospital setting and the timeframe. This study aimed to investigate the antibiotic resistance pattern and ESBL genes in Enterobacter isolates collected from infants with sepsis from Ahvaz, southwest Iran. Methods: In this study, Enterobacter isolates were collected from blood samples of infants with sepsis admitted in Imam Khomeini and Abuzar teaching hospitals located in Ahvaz city. The identification of isolates was performed with standard bacteriology tests. Disc diffusion test was performed to evaluate the antibiotic resistance rate. Polymerase chain reaction (PCR) was performed to investigate the presence of ESBL genes. Results: Among 850 neonates suspected of sepsis, a total of 41 (4.8%) Enterobacter isolates were collected. In this study, the highest and the lowest resistance rates were observed to ceftazidime and cefotaxime antibiotics (100%) and imipenem (70.7%), respectively. The PCR results showed the frequency rates of 9.8% (n = 4/41), 24.4% (n = 10/41), 31.7% (n = 13/41), and 58.5% (n = 24/41) for blaTEM, blaSHV, blaCTX-M14, and blaCTX-M15, respectively. Conclusion: Considering the high rate of antibiotic resistance observed, it is suggested to adopt strict monitoring policies to prevent the increase of this trend and further spread of ESBL genes in neonatal care centers.

Keywords: Antibiotic Resistance, ESBLs, Klebsiella Pneumoniae, Sepsis



# **Evaluation of Antibiotic Resistance in Klebsiella Pneumoniae Isolated from ICU Patients** with Pneumonia: A Case Study

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Background and Aim: This study aimed to investigate antibiotic resistance patterns in Klebsiella pneumoniae strains isolated from ICU patients with pneumonia. A total of 30 isolates were collected and subjected to antibiotic susceptibility testing using the disc diffusion method. The study also included molecular analysis to identify resistance genes. Methodology: The Klebsiella pneumoniae isolates were obtained from patients admitted to the ICU with pneumonia. Antibiotic susceptibility testing was performed using the disc diffusion method following CLSI guidelines. Molecular analysis was conducted to detect resistance genes, such as blaTEM and blaCTX-M, using PCR techniques. Results: The results revealed that 62% of the Klebsiella pneumoniae isolates resisted multiple antibiotics, including third-generation cephalosporins and carbapenems. The most common resistance genes detected were blaTEM and blaCTX-M, indicating the presence of extended-spectrum beta-lactamases (ESBLs) in the isolates. Conclusion: The study highlights the concerning levels of antibiotic resistance in Klebsiella pneumoniae strains isolated from ICU patients with pneumonia. The presence of ESBL genes underscores the need for vigilant monitoring and implementation of infection control measures to prevent the spread of multidrugresistant bacteria in healthcare settings. Further research is warranted to explore alternative treatment options and strategies to combat antibiotic resistance in ICU-acquired pneumonia caused by Klebsiella pneumoniae.

Keywords: Antibiotic Resistance, Klebsiella Pneumoniae, ICU-Acquired Pneumonia



# Trends in Carbapeneme-Resistant Klebsiella Pneumoniae in Iran (2013-2023): A Systematic Review and Meta-Analysis

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Background and Aim: The alarming rise of Carbapenem-resistant K. pneumoniae (CRKP) has sounded the alarm due to its limited treatment options. This review illuminates the evolving landscape of carbapenem-resistant K. pneumoniae in the Iranian population, shedding light on recent trends and distribution of microbial resistance genes. Methods: A comprehensive systematic search was performed on PubMed, Scopus, Embase, and Web of Science from 2013 until 28 December 2023. The pooled prevalence of CRKP was calculated by using a proportional metaanalysis with a random-effects model. The heterogeneity of included studies was assessed by forest plot in terms of 12 statistic. All estimations were reported on a 95% confidence interval (CI) and p<0.05 was fixed as statistically significant. Results: Totally, of 26 eligible studies published between 2013 and 2023. The pooled prevalence rate of CRKP was 34% (95% CI 0.24-0.44). The frequency of the resistance genes for blaKPC, blaVIM, blaIMP, blaNDM, and blaOXA-48-like were 16% (95% CI 0.06-0.26), 12% (95% CI 0.02-0.24), 7% (95% CI 0.01-0.1) and 6% (95% CI -0.01-0.13) respectively. Importantly, subgroup analyses indicated that an increase in resistance rates during the periods (2016-2020) was recognized for CRKP 45% (95% CI 0.14-0.44). Crucially, subgroup analyses revealed a concerning surge in CRKP resistance rates from 2016 to 2020, with a 45% increase (95% CI 0.14-0.44). Conclusion: The alarmingly high prevalence of CRKP especially OXA-48-like and NDM carbapenemases, and their worrisome co-existence in clinical isolates, paints a grim picture of the future: potentially unstoppable superbug outbreaks. With limited options remaining in our antibiotic arsenal, the discovery of new drugs or inhibitors targeting NDM/VIM-positive bacteria becomes not just urgent, but a matter of public health survival. Furthermore, the combination of rapid diagnostic tools, early detection, and targeted screening can be an effective strategy for preventing the spread of carbapenemase-producing bacteria to the community.

Keywords: Klebsiella Pneumoniae, Carbapenem-Resistant, Prevalence, Iran



#### Candida auris: A Globally Emerging and Worrisome Pathogen

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Background: Emerging cases of Candida auris have been globally recognized as a serious health threat significantly among immunocompromised population. This species shows multi-drug-resistant capacity at an alarming rate due to its extensive innate and acquired resistance to the standard antifungal treatments, the ability of forming biofilms, spread at an alarming rate across healthcare settings, and misidentification with other related pathogens. Our aim was to review the literature available on C. auris infection to highlight this species as a rising problem worldwide due to the increasing incidence of cases since 2011. Methods: A google scholar search was performed for all English language cases concerning C. auris published during 2000 through March 2024.Results: A growing trend of infection due to C. auris has been described by various countries during 2011-2024. Among reported 40 cases with C. auris, mixed infections with other species of Candida (e.g., C. albicans, C. tropicalis, and C. haemulonii) and bacterial species (e.g., K. pneumonia, S. aureus, E. coli, P. aeruginosa, P. jirovecii, M. morganii, and A. Baumanni) were in 16.2% (6/37) and 35.1% (13/37), respectively. Likewise, co-infection of C. auris with viral infections (e.g., Covid-19 and CMV) was found in 5.4%. and 2.7%, respectively. The age of the patients ranged from < 1 to 81 years, of whom 50.3% were males, 23.1% were females, 21.3% were newborns, and 5.3% were infants. Although it remains an uncommon pathogen, its resistance to one or multiple types of antifungals represents a major clinical challenge to clinicians and microbiologists across the globe. Of reported C. auris cases, nearly 51% of C. auris isolates were resistant to fluconazole or voriconazole, amphotericin B, and echinocandins. Conclusion: Our findings highlight the need to increase focus on C. auris in order to promote health system preparedness and to properly address the emergence and the spread of this antifungal-resistant pathogen.

Keywords: Candida Auris, Mixed Infections, Multi-Drug-Resistant



### **Platelets in Thrombosis and Hemostasis**

P81-P87



# Evaluation of the Diagnostic Value of Platelet to Lymphocyte (PLR) and Neutrophil to Lymphocyte Ratio (NLR) Indices in the Development of Immune Thrombocytopenic Purpura (ITP)

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Background: Immune thrombocytopenic purpura (ITP) is a hematological disorder that affects a wide range of people, but its prevalence is higher in children and the elderly. Although the exact pathophysiology of ITP is still not well understood, dysregulation of the immune system has been implicated in the occurrence of ITP due to various causes such as autoimmune conditions, infections, inflammations, and genetics. Lymphocyte-to-neutrophil ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are cheap, quick and readily available inflammatory indices. Our aim of this study was to investigate the inflammatory parameters including NLR, PLR in patients with ITP compared to the control group. Methods: In this case-control study, the files of 200 patients with a definite diagnosis of ITP were examined, and the control group was also examined among the individuals not suffering from ITP and without risk factors. The results were analyzed using t-test, SPSS and ROC curve. Results: The values of NLR, PLR in ITP patients were significantly different from the control group. NLR increased significantly in ITP patients compared to the control group, while PLR decreased significantly in ITP patients. Among the clinical symptoms, petechiae had a statistically significant relationship with PLR, NLR and was associated with their reduction. On the other hand, there was no significant relationship between the inflammatory parameters of NLR, PLR and the duration of hospitalization. Conclusion: The diagnostic power of the test is excellent for PLR, but the diagnostic power is poor for NLR. In general, NLR and PLR were identified as valuable markers for better identification of ITP patients.

Keywords: Immune Thrombocytopenic Purpura, Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio



#### Common Flow Cytometry Pitfalls in Diagnostic Inherited Platelet Disorders

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Background: Inherited platelet disorders encompass various conditions characterized by abnormalities in platelet structure, function, or production. Accurate diagnosis is crucial for guiding clinical management, and flow cytometry has emerged as a powerful tool for single-cell analysis of platelet parameters. Methods: The data of this study extract from electronic databases such as: Pub med, google scholar and Scopus. Results: Here are some common pitfalls and challenges: 1 Sample Preparation: Proper sample preparation is crucial for accurate flow cytometry analysis. Issues such as clumping of platelets, inappropriate anticoagulants, or delays in sample processing can all impact the quality of the data. 2. Data Interpretation: Flow cytometry generates complex multidimensional data. Correct interpretation requires an understanding of platelet biology and the specific markers relevant to the inherited disorder being investigated. 3. Instrument Variation: Differences between flow cytometers can lead to variations in data, so standardization and calibration are critical. 4. Background Noise and Non-Specific Binding: Non-specific binding of antibodies and background noise can obscure the detection of true events. Proper controls and gating strategies must be employed to distinguish specific signals from noise. 5. Rare Cell Populations: In some inherited platelet disorders, the population of abnormal cells may be rare. This can make their detection challenging and may require specialized gating strategies or enrichment techniques. 6. Antibody Selection: The choice of antibodies is critical. Inherited platelet disorders often involve subtle changes in specific surface markers, and using the wrong antibodies may lead to inaccurate results. 7. Rare Platelet Disorders: In some rare inherited platelet disorders, specific diagnostic markers may not be well characterized, making it difficult to develop reliable flow cytometry assays. Conclusion: To address these challenges, it's important to ensure that the laboratory performing the flow cytometry analysis is experienced in platelet disorders, employs rigorous quality control measures, and uses appropriate controls.

Keywords: Inherited Platelet Disorders, Flow Cytometry, Pitfalls



# Thromboelastography as a Tool for Personalized Medicine in Hematology: Unveiling Insights

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Background: This study explores the intricate role of thromboelastography (TEG) as a potent tool for advancing personalized medicine in hematology. Unraveling TEG's potential to personalize hematological interventions requires a comprehensive understanding of its applications, limitations, and clinical significance. With its real-time assessment of clotting dynamics, TEG stands as a transformative force in shaping individualized approaches to hematological interventions. Methods: A thorough review of the existing literature and studies was undertaken to evaluate TEG's efficacy in guiding personalized hematological care. Special attention was given to diverse clinical scenarios, including trauma-induced coagulopathy, major trauma, and cardiac surgery, shedding light on TEG's predictive capabilities for transfusion outcomes and bleeding reduction. The review highlighted TEG's ability to offer unique insights into hemostatic profiles, thereby guiding personalized therapeutic strategies. Results: TEG emerges as a versatile instrument with promising applications in tailoring hematological interventions to individual patient needs. Research findings include its superior predictive accuracy in major trauma and cardiac surgery, indicating its potential for precision medicine. By providing detailed and immediate analyses of clot formation and strength, TEG facilitates a nuanced understanding of individual coagulation responses. This personalized insight proves particularly valuable for patients with complex coagulation disorders or those undergoing anticoagulant therapies. Conclusion: The integration of TEG into personalized medicine strategies holds immense potential for optimizing hematological care.

Keywords: Thromboelastography, Personalized Medicine, Hematological Interventions



# **Evaluation of the Frequency of Thrombophilia-Predisposing Gene Polymorphisms in Patients with Thrombophilia in South Iran**

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Background: Venous thromboembolism (VTE) is a multifactorial disorder, which can result from either genetic or acquired factors. Genetic factors include a change in coagulation factors such as proteins S, C, and antithrombin that can be inherited. However, some VTE cases are not associated with any of these known genetic factors. Therefore, in this study, other genetic variations are being explored to determine their prevalence and possible association with this disease. Recent research has identified three polymorphisms, namely Protein Z (rs3024731), FV (rs1800595), and FGA (rs6050), that could potentially be risk factors for VTE. Method: The current study was conducted with 118 patients with clinical symptoms of VTE and 118 healthy individuals with no personal or family history of thromboembolic disorders. Peripheral blood samples were collected from patients for DNA extraction. The genotyping was done using the amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) technique. The results were validated through DNA sequencing. Finally, the data was analyzed using the SPSS 27 software. Result: There were significant differences in the genotypic and allelic frequencies of the rs1800595 polymorphism between the control and case group, as confirmed by the chi-square test. According to the genotyping model, individuals with the AG genotype are 2.22 times more likely to experience thrombophilia events (OR=2.229, P=0.039, CI=95%). Similarly, the G allele increases the risk of thrombophilia events by 2.103 times (OR=2.103, P=0.047, CI=95%). There was no correlation found between VTE and the rs3024731 and rs6050 polymorphisms. Conclusion: The rs1800595 polymorphism in the FV gene may increase the risk of thrombophilia.

Keywords: Polymorphism, Southern Iran, Thrombophilia, Thrombosis



#### Thrombocytopenia in COVID-19: A Potential Marker of Disease Severity

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Background: The seventh human coronavirus, called SARS-CoV-2, was discovered in Wuhan, China, during a pneumonia outbreak in January 2020. A significant relationship exists between the severity and mortality rates in patients with COVID-19 and factors such as thrombocytopenia, oxygen saturation (SaO2), age, gender, and presence of thrombosis. However, there have been some reports of contradictory results. In this study, we explored the aforementioned parameters in addition to other parameters among patients diagnosed with COVID-19 to ascertain the implications on Iranian patients and assess if our findings contradict prior research or align with their conclusions. Methods: In this prospective study, comprehensive data, encompassing age, gender, clinical presentations, SaO2, bleeding indications, thrombosis, and other pertinent factors was acquired from the medical records. The assessments of platelet levels were prospectively performed by Sysmex analyzers (kx 21, Kobe, Japan) at admission and discharge or expiration. Results: Following the inclusion and exclusion criteria, 264 individuals (150 females and 114 males) were included. Based on statistical analysis, death or recovery from the disease had a significant association with the presence or absence of thrombocytopenia, SaO2 percentage, age, gender, and the presence or absence of thrombosis, but did not have a significant association with the presence or absence of hemorrhage. Conclusion: The findings obtained from this study, not only enhance insight into COVID-19 outcomes but may contribute to the better management of coronavirus infections.

Keywords: COVID-19, Mortality, Severity, Clinical Manifestation, Thrombocytopenia



### Translating Mechanisms in to Therapeutic Strategies for Immune Thrombocytopenia (ITP): Lessons from Clinical Trials

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Immune thrombocytopenia (ITP) is an autoimmune disorder that causes a significant reduction in peripheral blood platelet count. Fortunately, due to an increased understanding of ITP, there have been significant improvements in the diagnosis and treatment of these patients. Over the past decade, there have been a variety of proven therapeutic options available for ITP patients, including intravenous immunoglobulins (IVIG), Rituximab, corticosteroids, and thrombopoietin receptor agonists (TPO-RAs). Although the effectiveness of current therapies in treating more than two-thirds of patients, still some patients do not respond well to conventional therapies or fail to achieve long-term remission. Recently, a significant advancement has been made in identifying various mechanisms involved in the pathogenesis of ITP, leading to the development of novel treatments targeting these pathways. It seems that new agents that target plasma cells, Bruton tyrosine kinase, FcRn, platelet desialylation, splenic tyrosine kinase, and classical complement pathways are opening new ways to treat ITP. In this study, we reviewed the pathophysiology of ITP and summarized updates in this population's management and treatment options. We also took a closer look at the 315 ongoing trials to investigate their progress status and compare the effectiveness of interventions. May our comprehensive view of ongoing clinical trials serve as a guiding beacon, illuminating the path toward future trials of different drugs in the treatment of ITP patients.

Keywords: Immune Thrombocytopenia, ITP, Thrombopoietin Receptor Agonist, TPO-RAs, Clinical Trials



#### Clot Waveform Analysis as an Advance in Coagulation Laboratory

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background: Clot waveform analysis (CWA) is a technique that monitors changes in light transmission, absorption, or scattering within a plasma sample during clotting processes, such as activated partial thromboplastin time (APTT), prothrombin time (PT), or thrombin time (TT). It offers insights into the entire process of hemostasis beyond traditional clotting tests like APTT, PT, and TT, which primarily indicate clotting initiation. Methods: Using specific keywords, an electronic search of scientific papers was conducted in the entire PubMed, Web of Science, and Google Scholar databases within the last few years. The papers were identified as suitable to the keywords included in this study. Results: CWA differs from traditional clotting tests in several key ways: Traditional clotting tests, such as APTT, PT, and TT, indicate the time required for clot formation under specific conditions. CWA goes further by offering a comprehensive view of the entire clotting process by evaluating waveform patterns and quantifiable parameters. Moreover, traditional clotting tests only report numerical values, whereas CWA generates visual representations of clot formation, allowing for easier identification of abnormalities and trends. Additionally, CWA enables the detection of subtle differences in clotting dynamics, providing additional information about the underlying causes of hemostatic disturbances and allowing for the calculation of quantitative parameters, including the first and second derivatives, which describe the speed and acceleration of clot formation, respectively. Unlike traditional clotting tests, CWA measures clot formation continuously over time, enabling real-time observations of dynamic events occurring during coagulation. Further, CWA often complements traditional clotting tests, helping clinicians make informed decisions regarding patient care. Conclusion: CWA encompasses various aspects of clot development rather than focusing solely on clotting times like APTT, PT, or TT. Automated coagulometers equipped with dedicated software allow for the computation of these parameters, simplifying their implementation in routine laboratory settings.

Keywords: Clot Wave Analysis, Hemostasis, Trombosis, Coagulometers



**Young Scientists** 

P88-P114



#### Human Umbilical Cord Mesenchymal Stem Cell-Derived Microvesicles Could Induce Apoptosis and Autophagy in Acute Myeloid Leukemia

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Background: Microvesicles have been identified as candidate biomarkers for treating AML. This study investigated the effects of hUCMSC-derived MVs on apoptosis and autophagy in the KG-1 leukemic cell line. Methods: The hUCMSCs were cultured and characterized by flow cytometry. MVs were isolated by ultracentrifugation, and the concentration was determined using the Bradford method. The characteristics of MVs were confirmed using TEM, flow cytometry, and DLS methods. KG-1 cells were treated with the desired concentrations of MVs for 24 h. The apoptosis induction and ROS production were evaluated using flow cytometry. RT-PCR was performed to evaluate apoptosis- and autophagy-related genes expression. Results: Following tretment of KG-1 cells with 25, 50, and 100 μg/ml concentrations of MVs, the apoptosis rates were 47.85%, 47.15%, and 51.35% (p < 0.0001), and the autophagy-induced ROS levels were 73.9% (p <0.0002), 84.8% (p < 0.0001), and 85.4% (p < 0.0001), respectively. BAX and ATG7 gene expression increased significantly at all concentrations compared to the control, and this level was higher at 50 μg/ml than that of the other concentrations. In addition, LC3 and Beclin 1 expression increased significantly in a concentration dependen manner. Conversely, BCL2 expression decreased compared to the control. Conclusion: Our findings indicate that hUCMSC-MVs could induce cell death pathways of autophagy and apoptosis in the KG-1 cell lines and exert potent antiproliferative and proapoptotic effects on KG-1 cells in vitro. Therefore, hUCMSC-MVs may be a potential approach for cancer therapy as a novel cellto-cell communication strategy.

Keywords: Acute Myeloblastic Leukemia, Apoptosis, Autophagy, Mesenchymal Stem Cells



### The Effect of rs950826802 SNP on Expression of MMP1 in Signaling by ALK Fusions as a Gastric Cancer Factor

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Background: Gastric cancer remains one of the leading cancers in the world and an important global healthcare problem due to its overall high prevalence and high mortality rate (1). ALK is activated in a range of cancers as a result of amplification or overexpression, fusion event or activating point mutations, resulting, in general, in constitutive activation of intracellular signaling. In this study we have tried to identify some biomarkers for the treatment of gastric cancer using bioinformatics analysis. Methods: First, the appropriate GSE (GSE151633) was downloaded from NCBI. After sorting the data, a suitable gene (|logFC|>6, P.Value < 0.05) was selected. The significance of the selected gene was confirmed by GEPIA2 and ENCORI databases. Using the Reactome, the signaling pathway associated with the selected gene was determined. To determine the effective factors in expression of the selected gene, we identified a SNP effective in the expression of the selected gene using the miRNASNP database. Results: We figured out that MMP1 presents in Signaling by ALK fusions and activated point mutants. According to the data obtained from the miRNASNP database, rs950826802 SNP reduces the binding affinity of hsa-miR-132-3p to mRNAs, which can increase the expression of the MMP1 gene which can be one of the factors causing gastric cancer. Conclusion: According to the aforementioned, this study suggests the correlation between rs950826802, hsa-miR-132-3p, and MMP1 which might increase the possibly of gastric cancer by affecting the ALK pathway. Consequently, these findings can help to provide therapy for gastric cancer patients.

**Keywords**: Gastric, Cancer, Database, ALK, MMP1



#### Evaluation of Effective Features in the Diagnosis of Covid-19 Infection from Routine Blood Tests with Multilayer Perceptron Neural Network: A Cross-Sectional Study

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Background and Aim: Coronavirus is an infectious disease that is now known as an epidemic, early and accurate diagnosis helps the patient receive more care. The aim of this study is to investigate Covid-19 using blood tests and multilayer perceptron neural network and affective factors in improving and preventing Covid-19. Methods: This cross-sectional study was performed on 200 patients referred to Sina Hospital, Tehran, Iran, who were confirmed cases of Covid-19 by computerized tomography-scan analysis between 2 March 2020 to 5 April 2020. After verification of lung involvement, blood sampling was done to separate the sera for C-reactive protein (CRP), magnesium (Mg), lymphocyte percentage, and vitamin D analysis in healthy and unhealthy people. Blood samples from healthy and sick people were applied to the multilayer perceptron network for 70% of the data for training and 30% for testing. Result: By examining the features, it was found that in patients with Covid-19, there was a significant relationship between increased CRP and decreased lymphocyte levels, and increased Mg (p < 0.01). In these patients, the amount of CRP and Mg in women and the number of lymphocytes and vitamin D in men were significantly higher (p < 0.01). Conclusion: The important advantage of using a multilayer perceptron neural network is to speed up the diagnosis and treatment.

Keywords: Blood Test, Coronavirus, Covid-19, Multilayer Perceptron Network, Neural Network



# Identification of a Novel Start-Loss Mutation in the SLC29A3 Gene by Whole Exome Sequencing in an Iranian Family with H Syndrome

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Introduction: The SLC29A3 gene encodes a nucleoside transporter protein. Mutations in this gene are associated with H syndrome, characterized by hyperpigmentation, hypertrichosis, hepatosplenomegaly, and cardiac abnormalities. The aim of this study was to report two Iranian patients with H syndrome and describe a novel mutation in the SLC29A3 gene. Methods: In this study, whole exome sequencing (WES) was used as a method to identify the genetic change causing H syndrome in a 16-year-old girl and her 8-year-old brother from an Iranian consanguineous family. In silico tools were used to evaluate the pathogenicity of the identified variant. Additionally, we performed segregation analysis and confirmed the presence of this variant in the affected patients' parents through Sanger sequencing. Results: We identified a novel start-loss mutation (c.2T>A, p.Met1Lys) in the SLC29A3 gene in both patients. Segregation analysis through Sanger sequencing confirmed that this variant was inherited from the parents. Various databases were utilized to evaluate the pathogenicity of the identified variant. Furthermore, bioinformatics tools were used to predict the three-dimensional structure of the mutant SLC29A3 protein. Discussion and Conclusion: Our study contributes to expanding the evidence supporting the association between mutations in the SLC29A3 gene and H syndrome. Molecular analysis of SLC29A3-related disorders is crucial for understanding the range of variability and increasing awareness of H syndrome, with the ultimate goal of facilitating early diagnosis and appropriate treatment.

Keywords: H Syndrome, SLC29A3 Gene, Novel Mutation, Whole Exome Sequencing, Iran



#### Non-Invasive Diagnosis of Acute Myeloid Leukemia Using Cell-Free DNA

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Background: Acute Myeloid Leukemia (AML) is a clonal disorder of hematopoietic progenitor cells and the most common type of leukemia in adults. Although tumor cells are the most reliable source of tumor DNA in AML patients, biopsy of the tumor is an invasive procedure and samples may not represent all malignant clones due to tumor heterogeneity. This study evaluates the potential of cell-free DNA (cfDNA) as an excellent diagnostic marker, as it reflects the disease in more detail than existing biomarkers and allows for noninvasive peripheral blood sampling. Methods: In this review, articles were collected from PubMed, Scopus and Google Scholar databases that were published between 2017 and 2023. These databases were searched using the keywords of cell-free DNA, acute myeloid leukemia, and non-invasive diagnosis. Results: Investigations showed that screening and quantification of tumor-specific mutations (such as FLT3 and NPM1) in cfDNA by next-generation sequencing (NGS), quantitative real-time PCR (qPCR) and droplet digital PCR (ddPCR) analysis could facilitate accurate and early diagnosis of AML, early assessment of therapy response and Minimal Residual Disease (MRD) monitoring. CfDNA also has the potential to capture intratumor heterogeneity that maybe missed by tissue biopsy, as it's gathered from all tumor sites into circulation. Conclusion: The results showed that the cell-free DNA assay is more sensitive and less invasive than the current clinical methods that allows periodic multiple tests over time and provides real-time data on tumor dynamics and evolution. Therefore, cfDNA analysis may complement existing genetic tools for diagnosis and disease monitoring in AML.

Keywords: Cell-free DNA, Acute Myeloid Leukemia, Non-Invasive Diagnosis



#### Non-Invasive Prenatal Diagnosis of Thalassemia

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Background: Thalassemia is a group of monogenic hereditary blood disorders that significantly affect the production hemoglobin. The invasive prenatal diagnostic technique is the main method of thalassemia screening that has the risk of fetal abortion. The discovery of cell-free fetal DNA that present in the blood of pregnant women during the first trimester allows for a non-invasive test that can be used to determine fetal abnormalities. This study evaluates noninvasive prenatal testing (NIPT) for fetal thalassemia using cell free fetal DNA (cff-DNA). Methods: We conducted a review of published articles were collected from PubMed and Google Scholar databases, published between 2018 and 2023, that evaluated the use of Non-invasive prenatal diagnosis (NIPD) for the early detection of prenatal inherited mutation of thalassemia in maternal plasma. Results: NIPT of thalassemia was developed base on extract cffDNA, polymerase chain reaction (PCR), highly sensitive DNA quantification techniques and molecular haplotyping. Studies have also shown that the diagnosis of the father's hereditary mutation can be done on cell-free fetal DNA(cff-DNA) with high sensitivity and specificity, and with high accuracy, hereditary mutations in  $\alpha$ -(-SEA) or  $\beta$ - (CD 41/42-TCTT, CD17A>T, IVS1-1G>T and CD26G>A) globin genes can be detected using cell-free fetal DAN analysis. Conclusion: Due to the high accuracy and precision of thalassemia NIPD (using cffDNA), this test is available for the detection of single nucleotide polymorphism (SNP) related to the globin locus and the definitive diagnosis of fetal disease and is recommended for high-risk families.

Keywords: Thalassemia, Cell-Free Fetal DNA (cffDNA), Noninvasive Prenatal Diagnosis (NIPD)



#### Clear Cell Renal Cell Carcinoma

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Background: Clear cell renal carcinoma(ccRCC), is the most common subtype of kidney tumors and characterised by the highest mortality rates among the genitourinary cancers. The currently used models for predicting patient outcome, are based on clinicopathological features only. Method: Microarrary analysis was performed on GSE168845 in the field of clear cell renal carcinoma from the GEO database. AQP2 gene was selected as a gene with significant expression reduction after checking with ENCORI and GEPIA2 databases. The signaling pathways in which the AQP2 gene was active were checked by KEGG and Reactome databases. After analyzing the SNPs related to the said gene through the SIFT,miRNASNP and dbSNP databases,after analyzing SNPs related to the mentioned gene through SIFT,miRNASNP and dbSNP databases.A SNP in 3'UTR namedrs1467864547was selected and a SNP in coding sequence were selected and their effects on the target gene were analyzed with the Hope database. The protein-protein interaction of the gene was analyzed by STRING database. The interaction between the desired gene and its related miRNAs was checked by miRWalk database. Result: The deleterious SNP obtained from the SIFT database named rs28931580 after checking by the Hope database showed that it had a change in the 57th amino acid position and this change was from glutamine to proline. The post-mulation state of this amino acid is smaller than the normal state and also the mutant residue is more hydrophobic than the wild-type residue. After analyzing the desired gene with its related miRNAs,hsa-mir-1224-3p was selected as the miRNA affecting the 3UTR region.KCNQ10T1 IncRNA was selected in the IncRResearch database as the IncRNA associated with the AQP2 gene. Finally, the interaction between the selected lncRNA and its related miRNAs was studied. Conclusion: After microarray analysis on AQP2 gene, the result of this study was that the said gene has a significant decrease in expression on clear cell renal carcinoma and can be a biomarker in this cancer.

Keywords: Clear Cell Renal Cell Carcinoma, Microarray, Data Analysis, Protein Structure



# Exploring Trifolium Pratense Extract: A Novel Approach to Inducing Apoptosis and Autophagy in B-Acute Lymphoblastic Leukemia Cells

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Background: Acute lymphoblastic leukemia (ALL), a prevalent malignancy, particularly in the pediatric population, necessitates innovative approaches to combat its progression. The exploration of natural compounds derived from plants has gained prominence for their ability to impede cancer cell growth. Trifolium pratense extract has garnered attention owing to its multifaceted anti-cancer properties identified in various studies. This pioneering study aims to assess the potential of Trifolium pratense extract in triggering apoptosis and autophagy in NALM-6 cells. Methods: In this experimental investigation, NALM-6 cells underwent treatment with Trifolium pratense extract. Metabolic activity and apoptosis rates were assessed using MTT and flow cytometry, respectively. Additionally, the impact of Trifolium pratense extract on the expression of pivotal genes in the autophagy pathway was scrutinized through Real-time PCR. Results: Determination of the half-maximum inhibitory concentration (IC50) through MTT assays revealed the optimal treatment concentration of Trifolium pratense extract as 231 µg/ml (in a dose- and timedependent manner, p<0.0001). Flow cytometry analysis demonstrated a significant induction of apoptosis by Trifolium pratense extract. Moreover, the extract exhibited the capacity to induce autophagy, evidenced by the upregulation of LC3 and Beclin-1 genes in NALM-6 cells. Conclusion: The study's outcomes underscore the anticancer efficacy of Trifolium pratense extract, positioning it as a promising strategy with favorable side effect profiles when integrated with existing treatments. While these findings highlight its potential, further research is imperative to validate its clinical applicability.

**Keywords**: B-Acute Lymphoblastic Leukemia, NALM-6 Cell Line, Autophagy, Apoptosis, Trifolium Pratense Extract



# Combination of Curcumin and Etoposide Enhances Apoptosis in Breast Cancer Cells: A Potential Therapeutic Strategy

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Background: Common chemotherapeutic drugs encounter significant challenges, including reduced efficacy due to chemoresistance and negative impacts on various body organs. Consequently, the combination of natural compounds has emerged as a potential strategy to combat cancer. Curcumin, a natural polyphenol, exhibits various anti-cancer properties, such as inducing apoptosis and arresting cell cycle progression. The present investigation aimed to examine the impact of curcumin and etoposide, both independently and in conjunction, on the initiation of apoptosis in cell lines of breast cancer. Methods: Curcumin and etoposide-treated cell proliferation was assessed using MTT viability assays. The drugs' influence on cancer cell apoptosis was evaluated using Annexin V flow cytometry and caspase-3 and 9 activity assays. Quantitative real-time PCR (qRT-PCR) was utilized for assessing the gene expression of Bax and Bcl-2. The western blotting technique was employed to determine the quantity of p53 protein. Results: A non-significantly effective dose of etoposide was chosen through the MTT assay and used in combination with 75 µM of curcumin. Curcumin enhanced the effects of etoposide on cancer cell apoptosis by increasing caspase activities. Additionally, the combination of curcumin and etoposide exhibited a more significant reduction in the expression of the Bcl-2 gene and the concomitant upregulation of Bax expression. Furthermore, the protein levels of the tumor suppressor p53 were elevated upon treatment with the curcumin and etoposide combination compared to etoposide and curcumin alone. Conclusion: Curcumin has the potential to enhance the apoptotic impact of etoposide on breast cancer cells. Therefore, we propose the aforementioned combination as a potential treatment for breast cancer.

Keywords: Breast Cancer, Combination, Curcumin, Etoposide, Apoptosis



#### Combination of Quercetin and Gemcitabine Enhances Apoptosis in U87 Glioblastoma Cells: A Potential Therapeutic Strategy

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Bakground: Glioblastoma is the most malignant primary brain cancer. There is currently no effective treatment for glioblastoma. Chemotherapy agents used, including gemcitabine, are toxic to surrounding brain cells, and drug resistance develops quickly. Gemcitabine resistance is an important issue for clinicians and researchers, and ways to overcome it should be identified. Quercetin synergistically enhances the anti-glioblastoma effects of chemotherapy drugs. Therefore, the overall goal of this project is to increase the effectiveness of gemcitabine in low doses of this drug and reduce drug resistance in U87 glioblastoma cells using non-toxic concentrations of the quercetin. Method: In this study, U87 cells were used, the effects of gemcitabine and Quercetin on cell viability and proliferation were measured by MTT method, and the combined index was determined with Compusan software. Apoptosis by flow cytometry method and the expression level of genes involved in apoptosis (Bax, bcl2) It was evaluated by Real-Time PCR. Results: Quercetin in amounts (IC50: 200 µM) can produce cytotoxic effects on the cell line U87 resistant to gemcitabine. The results show that gemcitabine/quercetin combined treatment compared to gemcitabine and quercetin alone has a significant increase in the induction of apoptosis as well as the expression of proapoptotic genes (Bax). Conclusion: Combined treatment with gemcitabine and quercetin increases apoptosis induction and decreases cell viability. Therefore, this combination therapy may be an effective strategy to overcome gemcitabine resistance and increase the effectiveness of this drug in glioblastoma patients.

Keywords: Gemcitabine, Quercetin, Gemcitabine Resistance, Glioblastoma



# Evaluation of the Effect of Exosomes Extracted from Human Umbilical Cord Wharton Jelly Mesenchymal Stem Cells in HSC-T6 Cell Line Treated with PDGF-BB

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Background: liver fibrosis is a wound healing reaction which characterized by accumulation of extracellular matrix (ECM). Platelet derived growth factor (PDGF) is an important pathway in liver fibrosis. Increased PDGF ligands and receptors in liver fibrosis led to activation of human satellite cells (HSCs). One of the important therapeutic goals in liver fibrosis is to block of PDGF signaling. Mesenchymal stem cells (MSCs) such as Wharton's jelly-MScs repair tissue damage through paracrine mediators such as exosomes. The aim of this study was to investigate the effects of exosomes derived from Wharton's jelly of mesenchymal stem cells (WJ-MSCs) on the factors involved in the progression of liver fibrosis in HSC-T6 cell line Methods: WJ-MSCs was isolated and after performing differentiation and flowcytometry methods, exosome was extracted. PDGF-BB with a concentration of 10 ng/ml was used to induce HSC-T6 cells. Then, the exosomes were used with two concentrations of 25 and 50  $\mu$ g/ml and the expression of  $\alpha$ -SMA, COL1 $\alpha$ 1 and E-cadherin genes was investigated with Real-Time PCR. Results: The size of exosomes was confirmed with a nanosizer and its morphology was confirmed with scanning electron microscopy (SEM). PDGF-BB increases the expression of  $\alpha$ -SMA and COL1 $\alpha$ 1 and decreases the expression of E-cadherin. Exosomes with a concentration of 50  $\mu$ g/ml significantly decrease the expression  $\alpha$ -SMA and COL1 $\alpha$ 1 genes and E-cadherin gene expression increase. Conclusion: The results of this study showed that the exosome therapy can be a suitable solution in improving liver fibrosis by reducing the expression of ECM genes.

Keywords: WJ-MSCs, PDGF-BB, HSC, Liver Fibrosis, Exosomes



#### The Effect of Static Magnetic Field on Survival of K562 Cells

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Background: The regulation of the pathways that control cell death is crucial in the management of cancer therapy. Over the years, there has been considerable focus on the influence of static magnetic fields on living organisms. It was shown that static magnetic fields can reduce the growth of cancer cells and change the cell cycle. This study assessed the potential influence of static magnetic fields on cancer cells. Methods: The impact of static magnetic field on viability and cell death of the K562 cell line in 24h was evaluated by MTT assay and flow cytometric methods, respectively. Also flow cytometric analysis was used to measure cell cycle in the presence of a static magnetic field. Results: Exposure K562 cell line to static magnetic fields shows an increase in cell death as well as alters the cell population in cell cycle phases after 24 hours of treatment. Conclusion: The static magnetic field could modify cellular metabolism, thereby causing a change in the rate of apoptosis and cell cycle. Our data point to that static magnetic field can decrease the viability of cells, enhance apoptosis, and cell cycle alteration in cancer cells, but additional research is necessary to identify the exact associated mechanisms.

Keywords: Static Magnetic Field, Apoptosis, K562



#### Cell Viability Reduction in Nalm6 Cell Line by Metformin and Sorafenib Combination Therapy

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Background: Acute lymphoblastic leukemia (ALL) with high mortality among hematological malignancy demands more effective drugs. Recent studies, investigate sorafenib as a potential chemotherapy drug in ALL, however there are some serious problems. Since it is demonstrated that metformin has anti-tumor properties this study aims to assess the effect of metformin combined sorafenib on cell viability in the NALM-6 cell line. Methods: Sorafenib and metformine was administered alone and together with a dose of 10 uMand 5 mM, respectively. MTT assay was used to evaluate cell survival during a 24-hour treatment period. Results: The findings demonstrated that the sorafenib treated cells exhibited a cellular viability rate of 53%. Conversely, the metformin group displayed a lower cellular viability rate of 28%. Notably, the simultaneous administration resulted in a statistically significant MTT test outcome of 33%. Survival experiments corroborated these results, revealing a substantial reduction in the survival rate of ALL cells, emphasizing the presence of a synergistic effect. Conclusion: Combining metformin with sorafenib exhibited a synergistic reduction of malignant cell viability in vitro. These findings provide a basis for further clinical investigations. In an era where combinatorial therapy and precision medicine are advancing to optimize outcomes in ALL patients, our research adds to the knowledge. Keywords: NALM-6; Metformin; Sorafenib

Keywords: NALM-6, Metformin, Sorafenib



# Prevalence of JC Polyomavirus among Rheumatoid Arthritis and Systemic Lupus Erythematosus Patients and its Correlation with Vitamin D Levels

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Background: Progressive multifocal leukoencephalopathy (PML) caused by JC polyomavirus (JCPyV) is a life-threatening disease among compromised immune individuals. The majority of therapeutic approaches for rheumatologic diseases involve immunosuppressive agents, which can potentially contribute to the development of PML. The role of vitamin D deficiency in viral infection associated with autoimmune diseases is well documented. This study assessed the prevalence of JCPyV in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), in Ahvaz, Iran. Materials and methods: Serum and urine samples collected from 50 patients with RA and SLE. DNA was extracted and subjected to PCR test. Positive PCR products were sequenced, phylogenetic tree constructed to determine the JCPyV genotype. The level of vitamin D was evaluated. Results: Of 50 patients, 19 (38%) diagnosed RA, and 31 (62%) diagnosed SLE. JCPyV DNA was identified in 2 (4%) serum samples and 17 (34%) urine samples. 5 patients with RA (26.3%) and 12 patients with SLE (38.7%) had positive JCPyV DNA in urine samples. JCPyV genotype 3A was dominant, while only one JCPyV genotype 1. RA and SLE patients positive JCPyV had lowered vitamin D than negative JCPyV patients (P<0.002) Conclusion: Given the high rate of JCPyV DNA detection and susceptibility of patients for PML development, it is recommended that detection of JCPyV DNA and vitamin D levels should be implemented for patients with RA/SLE prior to treatment.

**Keywords**: JC polyomavirus, Progressive Multifocal Leukoencephalopathy (PML), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Vitamin D Levels



# **Evaluation of Laboratory Results in Patients Hospitalized with Coronavirus Disease within the Recovery Process**

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Background: Coronavirus disease 2019 (COVID-19) is a form of respiratory and systemic disease caused by a virus related to the coronaviridae family. It first appeared in the city of Wuhan, China, and is still spreading around the world. Although the medical laboratory results of COVID-19 have been broadly studied, a comprehensive study of the laboratory results that refers to the recovery process in patients with COVID-2019 has not yet been performed. In this study, we have attempted to present a plan for the relationship between blood parameters and the recovery process through statistical analysis of the medical laboratory results of 205 patients who recovered from COVID-19 disease. Methods: We collected and analyzed laboratory results within 3 weeks after hospitalizing 205 improved patients with laboratory-confirmed COVID-19. The results were analyzed by SPSS statistical software, T-test, and ANOVA statistical tests. Results: The results indicate that the mean normalization of results occurs within the second week, except for the Ferritin, D-Dimer, and Procalcitonin tests, which return to the normal range within the third week. Conclusion: In this innovative study, we attempted to provide an overview of the recovery process of patients with COVID-19 by focusing on laboratory results during the recovery process, unlike previous studies of others that focused on patients — mortality. By considering these results, it helps to shorten the hospital stay of these patients.

Keywords: Coronavirus Disease, Coronavirus, Laboratory Results, Recovery Process, Patients Hospitalized



## Biofilms Formation in the Different Phenotypes of Cryptococcus Neoformans

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Background: Cryptococcus neoformans guarantees its survival by phenotype switching in response to some specific signals (temperature shocks, hypoxia, low or high pH, low iron, low glucose, and the host's immune system. Since biofilm formation is a trick of C. neoformans to resist environmental stress, its increase or decrease can affect the course of infection and its mortality rate. Due to limited information about the effect of the switch on biofilm formation and severity, we described the effect of switches on biofilm formation Methods: One hundred and six phenotypes including mucoid smooth, non-mucoid smooth, granular, wrinkle, and serrated of C. neoformans var. grubii (identified by phenotypic and PCR methods) was tested to detect the rate of biofilm formation on 96-well microtiter plates. The intensity of the biofilm formation in different phenotypes was compared using Student's t-test, version 16 of SPSS. Results: There was a significant difference between the biofilm mass-produced by different phenotypes. The non-mucoid smooth phenotype formed a stronger biofilm mass than the other non-mucoid and mucoid phenotypes (P < 0.05). However, no significant difference between other non-mucoid and mucoid phenotypes. Conclusion: Our data showed that the switch could affect the biofilm formation of Cryptococcus so that the smooth phenotype of C. neoformans showed the highest degree of biofilm formation compared to other phenotypes. Since Cryptococcus changes its biochemical and biophysical structures to adapt to environmental signals, the size, and polysaccharide composition of the capsule, this point can be considered a key point in creating different degrees of biofilm formation.

Keywords: Cryptococcus Neoformans, Biofilms, Phenotype Switching



# The Association between Maternal HbA1c in Gestational Diabetes Mellitus and Fetal Left Ventricular Hypertrophy

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Background Adequate management of blood sugar levels in pregnant women with gestational diabetes mellitus (GDM) can help prevent fetal cardiac complications. The objective of this study was to examine the correlation between maternal HbA1c levels in GDM and the occurrence of fetal left ventricular hypertrophy. Methods This cross-sectional study included women with GDM and gestational age 17-19 weeks. Key data points such as maternal age, insulin usage, gestational age, and fetal gender were carefully recorded Maternal HbA1c was measured in random blood samples with levels ≥6.5% regarded as abnormal. All participants underwent fetal echocardiography, during which measurements of left ventricular (LV) wall diameter were taken both during systole and diastole. Data were analyzed with SPSS software. Results Of the 90 mothers with a mean HbA1c of 5.79±0.99%, four (4.4%) had received insulin therapy. Of the 90 fetuses, three (3.3%) had abnormal LV wall diameter both during systole and diastole. Maternal HbA1c was significantly higher in fetuses with abnormal LV wall diameter than those with normal diameter (7.67±0.58% vs. 5.72±0.94%, P=0.002). Also, fetuses with abnormal LV wall diameter were from significantly older mothers (30.33±11.59 vs. 27.36±5.98 years, P=0.0 02). Moreover, all fetuses with abnormal LV wall diameter were from mothers with abnormal HbA1c (100% vs. 66.7%, P=0.010). Mothers insulin therapy and fetal gender were not different between fetuses with and without abnormal LV wall diameter (P=1.000). Conclusions Poor glycemic control of mothers with GDM together with their older age appears to be associated with fetal LV hypertrophy irrespective of maternal insulin therapy and fetal gender.

**Keywords**: Gestational Diabetes Mellitus, HbA1c, Ventricular Hypertrophy



## Vitamin D and Zinc Deficiency in Children with Congenital Heart Defects

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Background: one of the most prevalent birth disorders is Congenital heart defects (CHDs) worldwide. Research on humans has yielded inconsistent results about the effects of zinc on these groups. In children with CHD has been seen hyperparathyroidism and vitamin D deficiency. This study aims to evaluate the serum vitamin D and zinc levels in children with CHD and compare them with a control group. Methods: This case-control study included children with CHD (N=53) admitted to Bandar Abbas Children si Hospitalfrom June 22 to December 21, 2018. The inclusion criteria of the study were the age between One-month-olds to 14 years, and echocardiography-confirmed CHD. A group of children without CHD were also evaluated as controls (n=53). After recording the demographic information of participants, 4cc blood samples were collected from children to measure vitamin D and zinc levels in the serum. Results: In the current study, there wasn't a significant difference between groups in serum vitamin D levels (P=0.242). In contrast, the mean serum level of zinc was lower in CHD patients than in controls and the result was significantly differences and showed a medium effect (SMD=-0.67, 95% confidence interval [CI] -1.06; -0.28). On the other hand, both groups were comparable regarding the frequency of deficit and insufficiency of serum vitamin D (P=1.000 and P=0.767, respectively). However, the odds of zinc deficiency were 4.31 times greater in CHD children compared to the control group (OR=4.31, 95% CI 1.52; 13.31). Also, simultaneous insufficiency of zinc and vitamin D levels was only observed in CHD children (P=0.006). Conclusion: Zinc deficiency was observed in children with CHD in this study, while there was no difference regarding the deficit and insufficiency of the serum vitamin D or between CHD children and the control group. Future longitudinal studies are required to confirm these findings.

Keywords: Congenital Heart Disease, Vitamin D, Zinc



# The Effect of Moderate Strength-Static Magnetic Field (MS-SMF) on the Survival of Lymphoblastic Nalm-6 Cell Line

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Introduction: Acute lymphoblastic leukemia (ALL), which most often affects children, is a rare malignancy. Using alternative therapies such as static magnetic fields (SMF) can be a method for the inhibition of cancer cells. The purpose of this research was to provide a useful treatment in ALL by SMF to have greater results and fewer side effects in the patients. Methods: The viability and metabolic activity of Nalm-6 cells were assessed using Trypan blue and MTT assay. Apoptosis and reactive oxygen species (ROS) were performed by flow cytometric analysis. Additionally, qRT-PCR was used to evaluate desired gene expression in Nalm-6 cells. Results: The Trypan blue and MTT assay revealed decreased NALM-6 cell viability and metabolic activity due to SMF. Flow cytometry demonstrates that SMF-induced elevation in apoptosis rates and increased ROS production in Nalm-6 cells. Gene expression analysis shows that SMF-induced apoptosis through the ER stress and intrinsic pathway by an increase in expression of BAX, BAD, BIM, BID, and CHOP, and a decrease in BCL-2 and BCL-XL genes. Furthermore, SMF upregulated ROS-associated gene expression like Sirt-1, FOXO3a, and FOXO4 (p ≤ .05). Interestingly, SMF had no cytotoxic effect on PBMC and NAML-6 as normal cells. Conclusion: In summary, SMF induces ROS production, causing apoptosis, and inhibition of proliferation in Nalm-6 cells. Furthermore, SMF can decrease viability and metabolic activity in NALM-6 cells but has no significant effect on normal cells.

Keywords: Static Magnetic Field, Acute Lymphoblastic Leukemia, ROS, Apoptosis



# The Comprehensive Study of the Prevalence of Hyperphenylalaninemia in Iran by National Biochemistry Reference Laboratory from 2010-2021

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Background: Hyperphenylalaninemia (HPA) is an autosomal recessive disorder which if diagnosed at birth, is a treat-able and prevent-able disease. In order to prevention and reduce of disorders caused by HPA, newborn screening program were implemented in most countries of the world. This study is to present the first report of the prevalence of HPA in Iran by National Biochemistry Reference Laboratory (as the only reference center in Iran) from 2010 to 2021. Methods: Selective tests that were done for all newborns with HPA included blood Phe measurement and urinary neopterin and biopterin analyses and the DHPR activity test. Results: From 2010 to 2021, a total of 3338 patients with HPA from all over Iran referred to NBRL of the Pasteur Institute of Iran which 52.7% were male and 47.3% were female and 59.2% of them resulting from consanguineous marriage. In 3338 patient with HPA, consanguineous marriage existed in 1975 (59.2%) families that significant difference was observed between patients resulting from consanguineous marriage with patients without consanguineous marriage (P = 0.005). Among the Iranian ethnic groups, there is the highest percentage of HPA(42.8%) among the Fars, followed by the Turk (27.7%). Then the Lur(11.4%), Kurd(9.6%) and Arab(3%) ethnic groups have the highest number of HPA. My data shows the number of HPA its types in different ethnic groups of Iran including Fars, Turk, Lur, Kurd, Arab and others. The screening results of HPA patients referred to the NBRL from 2010 to 2021 shows that HPA prevalence rate is approximately 1 per 5050 neonates. Conclusions: The result of our study shows which Iran is among the countries with high prevalence of HPA. The most important reason for the high incidence of HPA in Iran related to the high degree of consanguineous marriages.

Keywords: Prevalence, Hyperphenylalaninemia, Iran, Newborn Screening Program



# Cytokine-Induced Memory-Like NK Cells: Emerging Strategy for AML Immunotherapy

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Background. Acute myeloid leukemia (AML) is a heterogeneous disease developed from the malignant expansion of myeloid precursor cells. Although intensive chemotherapy and hematopoietic stem cell transplantation (HSCT) have improved outcomes in AML patients, relapse, and suboptimal outcomes, require exploring new therapeutic strategies. In this regard, natural killer (NK) cell-based immunotherapy has attracted clinical interest due to their critical role in immunosurveillance. Although NK cells are well-known as short-lived innate immune cells with nonspecific responses that have limited their clinical applications, the discovery of cytokine-induced memory-like (CIML) NK cells could overcome these challenges. NK cells pre-activated with the cytokine combination IL-12/15/18 achieved a long-term life span with adaptive immunity characteristics, termed CIML-NK cells. The CIML-NK cells have revolutionized NK cell-based immunotherapy. This review highlights the current application, challenges, and opportunities of CIML-NK cell-based therapy in AML. Methods. This study used a comprehensive literature search in Web of Science, PubMed, Scopus, and Google Scholar databases to find eligible articles. Articles were identified using the following MeSH terms and keywords: Acute myeloid leukemia, Natural killer cells, Cytokine-induced memory-like NK cells, and Immunotherapy. The review and original articles were included in this study. Results. This literature review demonstrated that CIML-NK cells-based therapy in AML patients not only is a safe strategy but also resulting promising clinical outcomes such as elevation complete remission (CR) and overall response rate. Further investigation in this field clarifies the combination of CIML-NK cells with other approaches including immune checkpoint blockade, chimeric antigen receptors (CARs) structure, bispecific antibody, and nanotechnology potentially intensifying their killing activity. Conclusion. Taken together, CIML-NK cells are valuable candidates for AML immunotherapy, but further research is needed to investigate their full range of biological functions and explore new strategies incorporating all the anti-cancer aspects of CIML-NK cells.

**Keywords**: Acute Myeloid Leukemia, Natural Killer Cells, Cytokine-Induced Memory-Like NK Cells, Immunotherapy



## Harnessing Natural Killer Cell for Non-Hodgkin Lymphoma Immunotherapy

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Background: Non-Hodgkin lymphoma (NHL) encompasses a diverse group of diseases and is the most commonly diagnosed hematological malignancy worldwide. NHL is usually treated with a combination of chemotherapy drugs. While the standard treatments work well for most patients, some experience drug resistance and disease recurrence, resulting in poor outcomes. Therefore, investigating novel therapeutic approaches is required. In this line, Natural killer (NK) cells and NK engineered with chimeric antigen receptors (CAR) cellular therapy provide numerous benefits for patients with lymphoma. In addition, the utilization of NK/CAR-NK cell-based immunotherapy shows significant potential for patients with B-NHL. This comprehensive review delves into the diverse applications of NK/CAR-NK-based immunotherapy in individuals diagnosed with NHL, shedding light on its promising implications for patient care. Methods. Eligible studies were identified from several databases including PubMed, Web of Science, Scopus, and Google Scholar. We searched by using a combination of the following MeSH terms and keywords: Non-Hodgkin lymphoma, Natural killer (NK) cell, CAR-NK cell, and Immunotherapy. The review and original articles in the English language were included in this study. Results. This literature suggested that NK cells display functional defects and cancerous cells escape from NK cells' mediated cytotoxicity within the tumor microenvironment of NHLs. Additionally, preclinical studies results outline that NK/CAR-NK cells represent more killing activity, reduce reduction in tumor burden, and increase mouse model survival. Then, the application of NK/CAR-NK cells in clinical trials accompanied by a high response rate to treatment especially in refractory/ relapsed patients as well as effectively suppresses tumor growth. Interestingly NK/CAR-NK cells are not linked to significant cytokine release syndrome (CRS) or neurotoxicity. Conclusion. In conclusion, NK/CAR-NK cell-based immunotherapy in NHLs yields highly favorable clinical outcomes. In addition, evaluating the safety and efficacy of this approach indicated it is a safe strategy to whiteout significant side effects.

Keywords: Non-Hodgkin Lymphoma, Natural Killer (NK) Cell, CAR-NK Cell, Immunotherapy



# Generating and Assessing a Polyclonal Antibody Targeting the Conserved Matrix 2 Protein of Influenza a Virus for Scientific and Diagnostic Applications

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Background: This investigation aimed to synthesize and refine a polyclonal antibody (pAb) targeting the Matrix protein 2 (M2), a highly conserved ion channel protein of the Influenza A virus. The generated pAb against M2 holds potential utility in vaccine development, passive immunotherapy, and various analytical assays. Methods: We engineered the recombinant M2 protein expression in Escherichia coli. Subsequent to purification, the protein, adjuvanted with Freund's Complete and Incomplete solutions, was a dministered to two male New Zealand White rabbits. The resultant polyclonal sera were subjected to radial immunodiffusion (RID), Western blotting, and enzyme-linked immunosorbent assay (ELISA) evaluations. Further, IgG purification was accomplished via diethylaminoethyl (DEAE)-cellulose column chromatography, followed by the assessment of the purified IgG's characteristics through SDS-PAGE and ELISA. Results: ID and Western blot analyses confirmed the anti-M2 antibody's capability to identify epitopes of the recombinant M2 protein. ELISA quantification revealed that the anti-M2 pAb achieved appreciable titers post three immunizations. The purified IgG exhibited adequate concentration and, upon ELISA examination, demonstrated antigen reactivity at dilutions up to 1:32,000. Conclusion: The outcomes indicate that the recombinant M2 protein effectively elicited an immune response, culminating in the production of antibodies at levels deemed satisfactory for research and diagnostic purposes.

Keywords: ELISA, Influenza A Virus, M2 Protein, Polyclonal Antibody, Radial Immunodiffusion (RID)



# Prognostic Biomarkers for Long-term Survival after Autologous Hematopoietic Stem Cell Transplantation: Preliminary Results from a Single-Center Cohort

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Background: Autologous hematopoietic stem cell transplantation (ASCT) remains a pivotal therapeutic intervention for various hematological disorders. However, the factors influencing post-transplantation survival outcomes are multifaceted and warrant comprehensive analysis. This study sought to determine potential prognostic factors affecting 5-year survival rates among patients undergoing ASCT at the Kermanshah Bone Marrow Transplantation Center, Methods: A retrospective cohort study reviewed 40 patient records of those who underwent ASCT between 2013 and 2018. Pre-hospitalization test results and radiological examinations were extracted and analyzed. Kaplan-Meier and univariate Log-rank tests facilitated the initial analysis. Results: The cohort exhibited an average survival time of 91.73 months (95% confidence interval [CI]: 79.56-110.56 months), with a 7-year overall survival rate of 82.5% (95% CI: 66.77%-91.25%). Patients who underwent AHSCT after disease recurrence had significantly lower survival (p=0.0390,  $\chi$ 2=4.26). Our preliminary analysis identified several biomarkers with significant correlations to 7-year survival rates post-ASCT. Positive varicella zoster antibody (VZV-IgM) was significantly associated with lower 7-year survival (p=0.0163,  $\chi$ 2=5.77). Additionally, high purified protein derivative (PPD) levels (p=0.0265,  $\chi$ 2=4.92) and elevated ferritin levels (p=0.0370,  $\chi$ 2=4.35) were associated with decreased survival. In the Kaplan-Meier analysis, the neutrophil-to-lymphocyte ratio and triglyceride-to-HDL ratio showed potential associations with 7-year survival. However, the log-rank test could have been more significant, possibly due to the small sample size. Conclusion: The study underscores the critical role of specific biomarkers in predicting 7-year survival following ASCT. The findings highlight the need for extensive research with larger cohorts to validate these preliminary observations. The ongoing expansion of the cohort is anticipated to furnish more conclusive evidence on the prognostic value of these and potentially other biomarkers in the context of ASCT outcomes.

Keywords: Autologous Hematopoietic Stem Cell Transplantation, Survival, Varicella Zoster Virus, Ferritin, Purified Protein Derivative



# The Number of the Small Bowel Intraepithelial T-Lymphocytes in the Patients with Celiac in Isfahan City: The First Report

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Background: Increased number of intestinal intraepithelial lymphocytes (IELs) is a key histological finding in the diagnosis of celiac disease (CD; however, the number of IELs in celiac patients and healthy subjects may vary from one region to another. This study aimed to determine the number of the CD3+ and CD8+ IELs T-lymphocytes in the celiac patients and healthy subjects (controls) in Isfahan city. Methods: The duodenal biopsies were obtained from the celiac patients (n=15) and the controls (n=19). The total number of IELs/100 epithelial cells (ECs) were counted using the hematoxylin-eosin (H&E) staining method, and that of CD3+ and CD8+ IELs/100 ECs were counted using the immunohistochemistry (IHC) staining method. Results: This study defined the upper normal limit for each variable as mean + 2SD. Accordingly, the upper normal limits of the total IELs, CD3+ IELs, and CD8+ IELs/100 ECs were calculated as 37 (95% confidence intervals, CI: 33-41), 22 (95% CI: 19-25) and 12 (95% CI: 10-14), respectively. In 3 clinically CD diagnoses, the total IELs counts/100 ECs were below the upper normal limit, and the histopathological and serologic assays were negative. Interestingly, these patients responded to a gluten-free diet (GFD). Conclusions: In the clinically diagnosed celiac disease, IELs count/100 ECs below the upper normal limit as well as negative histopathological and serologic assays and the cell density counts of the CD8+ IELs T-cells/100 ECs could be a useful parameter for CD diagnosis and make a decision to put them on a GFD.

Keywords: Celiac Disease, Diagnosis, Gut, Intraepithelial Lymphocytes



# Production of Polyclonal Antibody against the Recombinant Neuraminidase Glycoprotein in Order to Develop Serological Assays for the Diagnosis of Influenza Virus

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Background: The neuraminidase (NA) protein's structure and function, as well as its immunogenicity, have led researchers to investigate it as a primary target in influenza vaccines. Because the virus causes acute respiratory infections, it poses a threat to human health and necessitates effective detection methods. Polyclonal antibodies have been developed to aid in the diagnosis of influenza disease and the development of passive immunity, which inhibits the virus. Methods: The gene construct pET28-NA was propagated in the TOP10 F' host and then confirmed by two methods (using Xho\infty and Xba\infty enzymes) and (sequencing). The gene construct was chemically transferred to the BL21 host for expression and its expression was checked by SDS-PAGE and western blotting techniques. Then the protein was extracted by sonication and purified using Ni-NTA column chromatography. Finally, the resulting protein was injected with Freund's adjuvant into male New Zealand rabbits at regular intervals. The amount of antibodies created in rabbit blood serum was evaluated using ELISA and dot blot methods. Results: The SDS-PAGE and western blot results showed that there is a dense band of the purified NA protein. The ELISA results showed that the NA antibody titer raised within 3 months of the injections. In this study, it was shown that NA recombinant protein can stimulate the immune system and lead to raising antibodies in an animal model. Conclusion: The results showed that the recombinant NA protein can stimulate the immune response to produce antibodies at the desired level to be used in serological assays to identify the influenza a virus.

Keywords: Neuraminidase, Polyclonal Antibody, Recombinant Protein, Influenza Virus, Serology



# Therapeutic Potential of Dimethyl Fumarate During Pregnancy as an Alternative to **Current Treatments For Gestational Diabetes Mellitus**

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Background and Aim: Gestational diabetes mellitus (GDM) is defined as hyperglycemia with the first onset during pregnancy. The purpose of this study is to evaluate whether maternal DMF supplementation (120 mg/kg per day) in the third week of pregnancy can reduce maternal glycemia and protect offspring from metabolic and cardiovascular disorders. METHODS: A rat model of GDM was created using a high-fat and sucrose (HFS) diet, while a control group received a low-fat diet. In pregnancy, maternal hyperglycemia was diagnosed, and the HFS diet was supplemented with DMF. The offspring of GDM mothers were randomly assigned to either diet until 15 weeks of age. Blood samples and liver tissue were taken, and glucose levels, insulin, TGF-β1, MDA levels, and the levels of metabolic regulation genes were evaluated. RESULTS: The study found that GDM in rats caused glucose intolerance in the mother. DMF supplementation significantly improved these disorders. At 15 weeks of age, the offspring of GDM-HFS mothers were more obese. They also showed glucose intolerance, insulin resistance, hepatic steatosis, and increased oxidative stress. The activity of cardiac damage markers decreased by 25-40% in GDM+DMF-HFS offspring compared to GDM-HFS mothers. Additionally, the livers of GDM+DMF-HFS offspring showed restored dysregulated regulation of metabolic genes. Conclusions: Consumption of DMF in the third trimester of pregnancy has shown positive results for the mother and her offspring. Therefore, DMF could be a good option for current GDM treatments.



# Workshops



# **PQR Rules in Clinical Microbiology**

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Selection of proper site of infection, proper sampling, proper transport, Proper culture and diagnosis-rapid.

Keywords: PQR Rules in Clinical Microbiology



## **Between-Laboratory Harmonization: Determination of Bias**

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The main problem in inter-laboratory harmonization of different end-user measuring procedures of a given analyte in order to produce equivalent results and using the same reference interval, is the bias between these procedures. Harmonization can be achieved through metrologically traceable calibration to a certified reference material (CRM) and/or a reference measurement procedure (RMP). However in many cases, there is no available CRM and/or RMP. In this cases, equivalent results can be produced by harmonization of measuring procedures through bias determination between them and its correction by modifying the calibration settings of one measurement procedure to match another measurement procedure,s results, or by mathematical conversion the results one MP to another MP. Bias determination is very challenging, itself. Bias is a term for expression of trueness which is defined as the closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value. These challenges includes: (1) Inaccessibility to true value and/or reference value, and impossibility to determine absolute bias; (2) Necessity to use expected target value which itself may have bias, so only relative bias can be estimated; and (3) determination of expected target value and observed target value, and therefore determination of relative bias has uncertainty which should be considers in interpretation of the results. There are different approaches to bias estimation which will be discussed in the workshop.

Keywords: Harmonization, Bias, CRM, RMP



# **Analysis of Bioligical Fluids**

#### Yoosef Poorkhoshbakht 1 \*

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Presentation and discussion of all body fluids urine analysis - serosal fluids - CSF - gastric Juice semen - sweat test-synovial.



# Challenges of A1C Interpretation in Patients with Thalassemia and Hemoglobinopathies

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Diabetes is one of the most common diseases worldwide with significant morbidity and mortality. HbA1c is one of the most important methods of disease diagnosis and monitoring. Since HbA1c is a reflection of glucose bound to red blood cells, factors affecting hemoglobin and the half-life of red blood cells can affect the measurement of HbA1c. Hemoglobinopathies are the most common monogenic genetic disorders in the world. According to the World Health Organization, about 5.2% of the world's population and more than 7% of pregnant women are carriers of this disease. Sickle cell trait or hemoglobin S, which is the heterozygous state for the sickle hemoglobin gene, is carried by 100 million people worldwide. Thalassemia is a diverse group of inherited autosomal disorders of the alpha or beta chains that affect hemoglobin. Hemoglobinopathies often cause altered HbA1c concentrations. For example, in people with prediabetes, the presence of hemoglobin S type is associated with higher HbA1c concentration. As a result, the challenges related to such diseases are of particular importance when interpreting HbA1c values and it is necessary to be considered by technical officials and related experts.



# Standardization and Harmonization of the Insertion of Measurement Units and How to Write Reference Intervals in the Medical Laboratory

#### Majid Mossalaei 1 \*

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As we all know, about 70% of each patient s medical records make up the results of laboratory tests tha actually represented in the form of the test report. Due to the numerous and varied laboratory tests and methods of conducting and the use of different kits and brands in laboratories, it is necessary that each laboratory in its report tab will include the method used and the measurement unit, as well as the reference intervals used in the correct and formal and standard manner. Unfortunately, we see that not only between different centers but also in one center between different tests and even sometimes when transferring from one kit or brand to another, there is a huge difference between how the units of measurement or how to write reference ranges, and this sometimes causes confusion of doctors and users of laboratory services and since in many cases the patient uses the services of doctors abroad to get advice, it seems that compliance with the standards accepted in international references is more important, in many cases the laboratories even in writing the full name or abbreviation of tests on the test tabs, which damage doctors uslidity of the test tab. In this workshop, we try to provide suggestions on standardization and synchronization of these concepts using international authorities.



#### **Futurism in Clinical Laboratories**

#### Hossein Dargahi 1 \*, Monireh Rahimkhani, Shaban Alizadeh, Ali Mohammad Mosadegh Rad

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1- Acquaintance of the Participants in the workshop with all types of Pessimistic, Possible, optimistic and desired scenarios in the field of futurism in Clinical laboratories. 2- Presentation of documents, Procedures, trend analysis, Scenario making in the scope of forecasting and freighting of clinical laboratories in Iran. 3. Identification of realistic review study for finding of internal and external propellants using six blocks structure including management and leadership, financial guarantee, human resources, laboratory technology, instrument, material, and supply. Laboratory information System (LIS) and laboratory information management System (LIMS), and using STEEP model. 4. Purposeful and snowball interview with workshop participants about future of clinical laboratories in Iran for Presentation of Participants' attitudes, experiences, and viewpoints. 5. Determination of primary codes, study of items and sub items and thematic analysis of interviews. 6. Scenario making by using documents found in scoping review and interviews in the field of preanalytical, analytical, Postanalytical of clinical laboratories. 7. Accreditation of presented scenarios and solutions for attaining the desired scenario from the viewpoints of participants as the elites of laboratory system.



## An Interpretive and Different Look at Blood Bank Tests

#### Nader Vazifeh Shiran 1 \*

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Definition of warm and cold antibodies, sugar and protein antigens, determining the affinity and avidity of antisera and lectins used in the blood bank, ABO subgroups, determining blood type using cell typing and back typing and interpreting discrepancies between them, blood groups Du, Dw, Dv, Rh-null, and D--, preparation of check cells, direct and indirect Coombs test, crossmatching, antibody screening, and antibody identification.



# **Comment Writing and Interpretation in Hematology Tests**

Nader Vazifeh Shiran 1 \*

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The necessity of comment writing in hematology tests, the role of comments and notes in hematology tests, comment writing in CBC tests, comment writing in hemoglobin electrophoresis tests, comment writing in immunofixation tests, comment writing in hematology tests, and comment writing in supplementary tests.



## **Introduction of Risk Management in Clinical Laboratory**

Hossein Babaki \*, Alireza Lotfikian 1

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Definition of risk, Steps of risk management, The executive benefits of risk management, How to identify the risk in the laboratory, Introducing several risk identification methods, Laboratory brand risk.



## **Data-Driven Management in Clinical Laboratories**

#### Roshanak Tahmasian \*

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According to the report of the Economist magazine in 2017, the most valuable resource in the world is no longer oil, but data. After the publication of this report, many business experts discussed the importance of "data" and "data-based decision making". Gradually, many companies and organizations began to use the power of data, and in this way, the phenomenon of "data-driven organization" was born. Today, the best decisions are made by data. This issue can bring many benefits for an organization. Because the data-based strategy follows facts and real data instead of instinct and feelings, in today's competitive world, laboratories as a business entity are not exempt from this rule, and considering the importance of quality in the work of medical diagnostic laboratories and error prevention, the role of data in analysis and decision-making is doubled. But the important challenge that business organizations and especially clinical labs are facing is that despite the data design, especially in the data quality management system, they are not converted into information or remain only as information and prevents effective productivity Considering the upcoming future of laboratories and artificial intelligence, the workshop has been decided to review the methods of real data design, its analysis and its role in decision-making in order to improve data culture and literacy in laboratories, and as a result, increase quality and reduce costs in laboratories.



## How to Resolve ABO Discrepancy Using Blood Bank Toolbox

#### Mostafa Moghadam 1 \*

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The recognition and resolution of ABO discrepancies are challenging aspects of problem solving in the blood banks. ABO typing discrepancy results, when red cell testing does not agree with the results of expected serum testing. The source of discrepancies can be either technical or sample related problems. Technical problems could include, identification and documentation errors, reagent and equipment problems and also standard operating procedure errors. Sample related problems can be related to ABO red cell testing and those that affect the ABO serum testing. During the Workshop causes of ABO discrepancies like mixed field reactions, contaminations in reagent anti-sera, unexpected antibodies in test sera will be discussed using real patient cases and specific serologic procedures used in the resolution of problems that can be adopted and performed by the hospital blood bank technologist will be discussed and worked on with the help of and participation of workshop attendees.



# Current Developments and Comparison between 3 Blood Bank Techniques Manual, Gel and Solid Phase (PROS & CONS)

Mostafa Moghadam 1 \*

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Current developments in three methods available in the transfusion services, Tube conventional method, Gel and Solid phase techniques are discussed and their advantages and disadvantages in terms of equipment, procedures, test reactions, sensitivity, specificity, stabilities, endpoint reproducibility, and quality control will be compared and shared with attendees at the workshop.



# **Advancing Medical Laboratory Quality Through AI Integration**

#### Omid Pournik 1 \*

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The integration of AI in medical laboratories introduces a paradigm shift, offering innovative solutions to streamline processes, minimize errors, and elevate the overall efficiency of laboratory services. This workshop aims to bridge the gap between traditional laboratory practices and cutting-edge AI technologies, empowering professionals to navigate this transformative journey and embrace AI as a powerful ally in the pursuit of enhanced quality promotion.



# HPV Sampling from Different Human Body Specimens in Women and Men

Seyyed Mohammad Jazayeri 1 \*

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Proper genitourinary sampling for HPV diagnosis is of paramount importance. Besides of females, HPV identification in male has been considered in recent medical services worldwide. One of great challenges is suboptimal sampling especially from men which results in false-negative reporting due to inadequate cell yielding. The aim of this workshop is to deliver to the audiences the key determiants of proper sampling, how to do the sampling, how difficult it is, and how can mitigate those problems.



## Laboratory diagnosis of Malaria and Diseases Transmitted from Vectors

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Malaria is a potential medical emergency and must be diagnosed and treated immediately. Delay in diagnosis and treatment of this disease leads to the death of patients in many countries. Given that the diagnosis of malaria in areas of the country where this disease is not endemic can cause It will be difficult because neither doctors are aware of the symptoms of a feverish patient as malaria, nor are laboratory colleagues able to diagnose this disease due to insufficient experience. In this workshop, the basics of diagnosing Plasmodium species will be examined. Also, due to the proliferation of the Aedes mosquito in the northern and southern regions of the country, the diseases caused by the vectors of dengue fever, chikungunya & Zika will be investigated in this workshop.



#### **POCT** in the Medical Laboratory: the Future of Laboratory Diagnosis

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Point-of-Care Testing (POCT) is clinical laboratory testing conducted close to the site of patient care where care or treatment is provided. POCT provides rapid turnaround of test results with the potential to generate a result quickly so that appropriate treatment can be implemented. One of the most widely used POCT tests in diagnostic kits is based on fluorescent lateral flow immunoassay technology, which are usually used in clinical and pathology laboratories. Lateral flow-based assays, also known as immunochromatographic assays or strip assays, are antibody-based that are used to detect the presence or amount of analyte in a sample. These assays are based on the use of antibodies that are attached to colored detectors such as gold or fluorescent nanoparticles. Despite the presence of a wide range of color detectors in these types of kits, many manufacturers prefer fluorescent labels such as fluorescent dyes, fluorescent proteins or europium particles. Fluorescence systems have higher sensitivity than observation systems due to the dark and uniform background that is achieved by the efficient blocking of the excitation light. Two main components are necessary to measure an immunofluorescence reaction. The first component consists of a fluorescent nanoparticle that is conjugated to two different antibodies through covalent bonds. The first antibody is the test line antibody that specifically binds to the desired analyte, and the second antibody is the control line antibody. The second component is a strip that includes nitrocellulose, sample pad, absorption pad and conjugate pad. After binding the antibody to the nanoparticle, if it is adjacent to the desired analyte, a signal is formed on the test line, which is directly related to the amount of the desired analyte.



# How to identify and Prevent Complications from Blood Transfusions

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Several cases of blood transfusion complications will be presented during the workshop. Participants will be divided into groups to learn about diagnosis methods and laboratory procedures, followed by the instructor's analysis of each case and necessary explanations. Two blood samples will be provided to participants for determining blood groups with the instructor and learning how to diagnose them.



## **Handeling and Resulting Spurrous CBC Samyhes**

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Reporting accurate results in Problematic and abnormal Samples in the Hematology department is very important. Factors and issues Causing Spurious CBC result Should be Considered. In this Workshop different tricky results of RBC, WBC and platelet; methods of handling related Samples will be discussed.



## **Laboratory Workup of Viral Hepatitis**

#### Morteza Izadyar 1 \*

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Liver is the largest and the most complex organ of gastrointestinal tract. Infectious hepatitis can be considered as the most common disease of this important organ, and in most cases is the cause of long-lasting and important liver complications. In actuality, viruses are the cause of 80% to 90% of acute and chronic hepatitis. Although a wide range of viruses, such as EBV, CMV, VZV, HSV, human herpesvirus 6, HIV and adenovirus are capable of infecting liver transiently, but mainly five hepatitis viruses A, B, C, D and E is recognized as hepatitis viruses. Among them HBV and HCV can cause acute and chronic liver infection and long-lasting consequences like cirrhosis and hepatocellular carcinoma (HCC). To this list, we should add recently recognized hepatitis G virus, which only induces a mild liver damage. Due to clinical similarity between different kinds of hepatitis with variable etiology, serological diagnosis based on detection of specific antibodies or viral antigens and nucleic acids amplification methods, can diagnose diseases, even before the onset of clinical findings. These methods are also helpful in monitoring of treatment efficacy. In addition, liver function tests also provide valuable information about the extent of liver damage and its regeneration after treatment. In current workshop, we try to discuss the most common challenges, which medical laboratories encountered during.



# MRD (Measurable Residual Disease) Assessment in B-Cell Acute Lymphoblastic Leukemia: Methods and Perspectives

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B-cell acute lymphoblastic leukemia/lymphoma (B-ALL/LBL) is a lymphoproliferative disorder of immature B-cells with blastic morphology and specific phenotype. Age at diagnosis, certain chromosomal changes, immunophenotype, and persistence of leukemia after induction therapy comprise other important prognostic parameters. The most common cause of treatment failure in pediatric ALL is relapse, occurring in 15%-20% of patients. The detection of MRD in childhood and adult ALL is an independent risk parameter in both de novo and relapsed ALL and in patients undergoing stem cell transplantation. In childhood ALL, MRD is an independent prognostic factor allowing for risk stratification. Early elimination of leukemic cells is a favorable prognostic indicator. The absence of MRD at the end of induction therapy is considered the main favorable outcome predictor. The most widely applied MRD assays in ALL are flow cytometric identification of leukemia immunophenotypes and PCR analysis of immunoglobulin gene rearrangement or fusion transcripts. The prerequisite for analysis of immunoglobulin gene rearrangement is the molecular characterization of leukemia-specific immunoglobulin gene rearrangement for each individual patient. Among fusion transcript as targets for MRD detection in ALL, BCR-ABL1 and MLL have the broadest clinical use. FC analysis has broad applicability, since most of ALL blasts have identifiable leukemia-associated immunophenotype (LAIP) at diagnosis. LAIP can be identified in ~95% of B-ALL cases. The major advantages of FC analysis of MRD in B-ALL are the speed of obtaining results, wide availability of FC analysis, and relative simplicity. The limitations include inadequate number of cells for analysis, difficulties in separating leukemic cells from normal marrow precursors and change of antigenic profile of leukemic cells after therapy. MRD assessment by FC has many advantages including high sensitivity, fast turnaround time, and lower cost. The proposed FC panels to analyze MRD in ALL include variable combination of the following antibodies: CD10, CD13, CD19, CD20, cCD22, CD24, CD33, CD34, CD38, CD45, CD58, CD66c, CD73, CD304, cCD79a, CD81, CD123, and TdT.



# Identification and Prevention of Common Sources of Error in Medical Laboratories

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The laboratory has an important role in the health of society and more than 70% of medical diagnoses are based on laboratory results. Laboratory errors can be defined as any defects in various steps that lead to a deviation of the reported value from the actual (accepted) value. Errors include random or systematic errors and are classified into three categories including pre-analytical, analytical, and post-analytical, depending on whether they were happened before, during, or after the analysis. Some errors in the pre- analytical phase include misidentification of the patient, misinterpretation of the physician's order, incorrect preparation of the patient, use of the wrong container, wrong labeling of the sample container, wrong mixing of the sample, collection of the sample at the wrong time and wrong in the condition or time of sample shipment. Some errors in the analytical phase include inappropriate test methods, inappropriate or uncalibrated equipment, inappropriate materials, reagents, and kits, inexperienced or inadequately trained personnel, and inappropriate environmental conditions. Some errors in the post- analytical phase include incorrect result, incorrect matching of the result, ambiguity in the report, wrongly attributing the result to another patient, and sending the report to the wrong person. Naturally, identifying the exact source of variation or error in any particular laboratory requires a thorough review of processes, technologies, and staff skills. Reducing error in a clinical laboratory increases confidence in laboratory results and ultimately helps clinicians to provide a higher level of care to the patients.



### Direct and Indirect Laboratory Reference Interval Calculations: A Review of the Latest Statistical Methodology

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Laboratory reference intervals, crucial for accurate diagnosis and monitoring of medical conditions, are traditionally established through statistical methodologies. This abstract explores the calculation of reference intervals employing both direct and indirect statistical approaches. Direct methods involve the collection of samples from a healthy population, and statistical parameters such as mean and standard deviation are computed to define the interval. While direct methods are straightforward, they may be affected by demographic variations and limited sample size. In contrast, indirect methods utilize existing data, often transforming observed values to fit a specific statistical distribution. This approach proves useful when direct sampling is impractical or costly. Various techniques, such as parametric and non-parametric methods, contribute to the indirect methodology, ensuring robust and versatile reference interval determination.



#### Practical Bacteriology (Detection of Common Gram Positive and Negative Bacteriin the Bacteriology Laboratory

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This workshop is held with the aim of acquiring skills in the diagnosis of common clinical bacteria by differential tests and diagnostic tables. In this training cours, you will be taught how to read differential test, how to work with diagnostic tables and flow charts, and how to recognize bacteria whose differential tests are very similar.



## Practical Bacteriology (Evaluation of Applied Methods and Error Sources in Key and Widely Used Bacteriological Diagnostic)

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The workshop is aimed at how to perform the diagnostic tests of common and frequent pathogenic bacteria. In this training course in addition to practical techniques, in identifying and identifyin bacteria, we will address the challenges in the tests in the case of cases of interventional factors will change the results of diagnostic tests in the microbiology sector. for example, most microbiology experts ore familiar with how to perform diagnostic test, but what may change the results of this test may be ignored as a result, they are mistaken in the final diagnosis of bacteria.



#### Validation of ELISA

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The enzyme-linked immunosorbent assay (ELISA) is an analytical immunochemistry assay based on the specific bond between the antigen and the antibody. The application of this test has significantly changed the practice of medical laboratories in which it is used for the detection and quantification of molecules such as hormones, peptides, antibodies, and proteins. Validated analytical methods such as ELISA for quantification of biomarkers, drugs, biological products, and their metabolites in a given biological matrix (e.g. blood, plasma, serum, or urine) are critical for the successful conduct of nonclinical and clinical studies. Validating the analytical method ensures that the data are reliable. Validated methods provide critical data to support the safety and effectiveness of drugs and biological products. In this workshop, first, an introduction to optimization, standardization and validation will be provided, and then different ELISA validation methods are explained.



#### Covid-19 and the Progress of Artificial Intelligence in the Medical Diagnosis Laboratory

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Machine learning (ML) is defined as a discipline of artificial intelligence (AI) that provides machines the ability to automatically learn from data and past experiences to identify patterns and make predictions with minimal human intervention. The COVID-19 pandemic has galvanized the machine learning community to create new solutions that can help in the fight against the virus. The body of literature related to applications of machine learning and artificial intelligence to COVID-19 is constantly growing



#### Sclerosis Laboratory Progress in the Diagnosis of Multiple

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There are no laboratory tests that are completely specific for MS, but several are helpful in diagnosing or excluding this disease as the cause of signs and symptoms. The most useful tests look for evidence of immunoglobulin G (IgG) production within the central nervous system. Oligoclonal test is one of the most specific tests and is performed by electrophoresis.



#### **Accreditation for Medical Laboratories**

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- CLSI document EP26-A.: User Evaluation of Between-Reagent Lot Variation; Approved Guideline
- Metrological Traceability of Measurement Results ILAC-P10:07/2020 & IACLD-P10



#### A Comprehensive Review of Prenatal Screening Tests (Troubleshooting and Pitfall)

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Fetal screening tests to investigate neural tube defects and syndromes of trisomy chromosome 21 (Down), trisomy chromosome 18 (Edwards), trisomy chromosome 13 (Pato) in the form of double, triple, quad, integrated or sequential tests by measuring the thickness of the back of the neck of the fetus (NT) in sonography, the biochemical biomarkers of the mother's serum such as PAPP-A, Free βHCG, Alphafetoprotein (AFP), unconjugated estriol and Inhibin A are calculated. MoM index (Multiple of Median) is the ratio between the concentration of each substance in the patient's blood to the median of the same substance in the normal population with the same fetal age, which is influenced by clinical variables such as maternal age, maternal weight, diabetes, IVF, parity, gravida. One of the disadvantages of these screening tests is their false positive rate of 1%, which is caused by pregnancy risk calculation software, biochemical markers, the number of previously screened patients, the number of software updates and corrections. Possible errors are the age distribution of the screened population. The NIPT or Cell-free DNA test is a non-invasive screening test that detects chromosomal abnormalities from the 10th week of pregnancy with a specificity and sensitivity of over 99%. In this workshop, the conditions and time of performing the NIPT test and the interpretation of its results will be discussed with an emphasis on factors affecting screening by presenting case report, how to determine MOM and factors affecting false positive screening and comparing these methods with the NIPT test.



#### **Method Validation of Basic Indicators in Medical Laboratories**

#### Mozafar Jabari \*

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Method Validation is an important and fundamental part of quality assurance, which evaluates the implementation instructions and test procedures and finally shows the assurance of the quality, effectiveness and reliability of the test. Method validation is basically the process of defining an analytical requirement and verifying whether the capabilities of the method are consistent with its applications or not. Purpose of method validation

- Identify potential error sources and quantify them.
- Determining whether the test method is appropriate for the intended use or not?
- Proving that a method can be used for decision making.
- Fulfilling the requirements of accreditation and legal authorities, such as the qualification approval system, standards department, Ministry of Health, etc.
- To prove that what we claim is true.
- To increase the value of test results.
- To justify the trust of patients and doctors.

The purpose of the quality assurance program is to build the trust of the laboratory staff, patients and doctors in the laboratory results and thus increase the confidence in the laboratory achievements.

Therefore, the main goal is to achieve acceptable accuracy at the same time as the accuracy of the results. Implementation steps of the validation process

There are many implementation steps of authentication, but in this discussion, the following items are evaluated in order of priority:

- Precision
- Accuracy
- Linearity or Reporting Range
- Determine or Validate the Reference Range
- Verified the Reference Range
- Recovery
- Interference
- Comparison of Methods
- Determining the lower limits of measurement including: LOB / Iimit of blank, LOD / limit of detection and LOQ / limit of quantification.

No matter how appropriate the practical criteria are, if the scientific criteria are not acceptable, the answers obtained from the method used will not be reliable.



#### Step-by-Step Implementation of Quality Control and Charts Interpretation

#### Mozafar Jabari \*

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When making a decision to treat a disease, doctors need accurate answers from the laboratory and other paraclinical services. And taking any wrong decision in this direction may end up endangering the patient's life. Therefore, it is necessary for the laboratory to play its main role in this field by relying on the power of tools, materials and the efficiency of all those involved in the laboratory.

Purpose of quality control:

- Providing accurate information in order to diagnose and help the doctor.
- Identifying errors with the aim of improving methods, reducing errors and gaining awareness and knowledge to fix them.
- Communication and belief of the doctor and the patient in presenting the results and performance of the laboratory.
- Increasing scientific ability and more awareness, and as a result, complying with the above.
- Identifying and correcting those errors that are the responsibility of the laboratory

The purpose of the quality assurance program is to build the trust of the laboratory staff, patients and doctors in the laboratory results and thus increase the confidence in the laboratory achievements.

Therefore, the main goal is to achieve acceptable accuracy at the same time as the accuracy of the results. Quality is something that:

Everyone claims to know it and everyone is looking for it, and if they do not reach it, it is someone else's fault

Scientific criteria: includes the closeness between the results, the closeness of the results with the real value Accuracy / Inaccuracy

Accuracy / Inaccuracy

The correctness or authenticity of the results

Practical criteria include the issues that must be followed in setting up and performing each experiment Speed, price, required expert force, required devices and safety

No matter how appropriate the practical criteria are, if the scientific criteria are not acceptable, the answers obtained from the method used will not be reliable.



#### The ICSH Practical Guide for Internal Quality Control of Hematology Analyzers

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Quality control is carried out in the medical laboratory in order to ensure the validity of the laboratory data. Two factors guaranteeing laboratory data are accuracy and precision. In hematology analyzers, the accuracy (reproducibility) can be checked by using cell controls (internal quality control or IQC), and the accuracy of the responses of these devices by participating in external quality assessment programs designed by national or region organizations. Quality control materials play a very important role in the validity of laboratory results. IQC methods for blood cell counting have evolved from the days when IQC materials were prepared and tested within the laboratory itself.

Even in remote areas of the world, laboratories use commercial QC materials produced by cell counter manufacturers or third-party suppliers. The International Committee for Standardization in Hematology (ICSH) review of QC practices in 191 laboratories showed that there is great variation in QC practices in laboratories worldwide and even within countries. The ICSH guidelines suggest a coordinated and targeted approach in this regard; Among other things, it identifies issues facing diagnostic laboratories, provides guidance to manufacturers on the information they should provide to purchasers of cell counters, and proposes a policy for IQC procedures that diagnostic laboratories should adopt. In this presentation, we will describe IQC methods based on ICSH guidelines.

Keywords: Cell Counter, Hematology, Cell Control, IQC



#### The Role of Artificial Intelligence in the Future of Medical Laboratories

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An important part of the future of medical laboratories will definitely be in the center of artificial intelligence, so the intellectual investment and special attention of the research and development unit of modern laboratory centers in the world to the subject of artificial intelligence is inevitable. The role of artificial intelligence in the survival of laboratories and increasing financial productivity and special acceleration in managerial and technical decision-making in the laboratory is very key, and many professional laboratory centers in the world have started investing and team building in this axis with a forward-looking view. have done The main specialized application of artificial intelligence in the field of medical laboratories is mainly in the field of cyto-hematology, cyto-screening and pathology, and in the fields of human resource management, customer Customer Relationship Management management, and equipment management, there have been tremendous advances and analytical analysis is suitable for optimizing decision-making. It has been presented to senior decision-making managers. In the current situation, the biggest challenge of deploying artificial intelligence in medical laboratories is the need to collect a lot of data with high quality and accuracy, and to remove incomplete and incorrect information in the process of data collection.



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