



International Tehran Hepatitis Conference

Held by



Iran Hepatitis Network

Iran Hepatitis Network www.Hep.ir



Kowsar Corporation



Baqiyatallah Research Center for Gastroenterology and Liver Diseases

Conference Venues

Main Part: 6-8 September 2017, Razi Convention Center, Iran University of Medical Sciences, Tehran, Iran.

Additional Day (Satellite Meetings):

I. 10 September 2017, Eghbal-Lahoori Hall, Nemazee Hospital, Shiraz University of Medical Science, Shiraz, Iran.

II. 10 September 2017, Shahid Rahimi Hall, Birjand University of Medical Science, Birjand, Iran.

THC7 Secretariat

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Table of Contents 6-8 September 2017, Tehran 10 September 2017, Shiraz & Birjand

Welcome Messages	4
About Tehran	10
About Shiraz	12
About Birjand	12
THC7 Boards and Committees	13
THC7 Internationally Invited Speakers	15
International KOWSAR Award	16
Yas Young Investigator Award	18
NINA Prize	22
THC7 Program at a Glance	25
Scientific Program - Hall A	30
Scientific Program - Hall B	35
THC7 Workshops	40
Scientific Program - Satellite Meeting (Birjand)	43
Scientific Program - Satellite Meeting (Shiraz)	44
Paper and Electronic Poster Presentations	45
Abstracts-Invited Speakers	55
Congress Online	101
Drawing & Illustration Book	103

Welcome Message

Dear colleagues,



As the director of Iran Hepatitis Network and Global Hepatitis Community, I would like to mention that viral hepatitis is one of our priority in healthcare system now. The burden of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in the region mandates us to work more in this issue. We made a link between epidemiologists, clinicians, pathologists, virologists, specialists in transfusion medicine as well as research and laboratory centers from Iran and the world. We would like to facilitate scientific

communication between researchers who are working in the field of viral hepatitis and other liver diseases. One of our activity is Tehran Hepatitis Conference which has been held for 6 times yet in Tehran, Iran.

I would like to take great pleasure in inviting you to participate in the 7th International Tehran Hepatitis Conference (THC7) hosted by Iran Hepatitis Network which will take place in Iran, September 2017. In THC6 in Tehran around 2000 scientists participated and we had distinguished speakers from USA, Canada, UK, Germany, France, Italy, Netherlands, Austria, Belgium, Sweden, Cyprus, Turkey, Australia, and the region as well. I invite all universities, research centers and other scientific professions in hepatology and liver diseases to join us.

Kind Regards, Seyed-Moayed Alavian, M.D. THC7 Chairman Professor of Gastroenterology and Hepatology Director of Iran Hepatitis Network Tel/Fax: +98 21 8126 2072 Tehran, I.R. Iran editor@hepatmon.com / alavian@thc.ir

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International Tehran Hepatitis Conference

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أعزاءي الزملاء

5

7th Tehran Hepatitis Conference, September 2017

رساله تحبه

نود أن ندعو كم الى المشار كة في مؤتمر طهران الدولى السابع للهباتيت، الذي تقيمه شبكة الهباتيت في إيران والمزمع عقده في إيران، في العام ٢٠١٧

في هذه الموتمرالعالمي الذي في طهران حوالي ٢٠٠٠ مشترك في البلدان الاخرى من امريكا، كانادا، المملكة المتحدة، المانيا، فرانسا، إيطاليا، هلندا، استراليا، قبرص، تركيه و البلدان المجاورة

بإمكانكم إرسال خلاصة مقالاتكم الى المؤتمر عبر الموقع التالى .www.thcv ir. سيقوم فريق اللجنة العلمية فى التدقيق فى الخلاصات المرسلة، ليتم من بعد ذلك الإعلان عن الخلاصات التى تم الموافقة عليها لتقديم عرض شفهى أو ملصق نموذجى للمقالة

نحن نتطلع إلى الاستمتاع معكم بالبرنامج العلمى القوى والجذاب، الذى سيتضمن كل جوانب وجميع التطورات الأخيرة في جميع تخصصات التهاب الكبد الفيروسي. البرامج العلمية التمهيدية متاحة على الموقع الرسمى لمؤتمر طهران الدولى السابع للهباتيت

> مع أطيب الأمنيات الدكتور سيد مؤيد علويان المدير العلمي لمؤتمر طهران الدولي السادس للهباتيت مدير شبكة الهباتيت في إيران



karsilama Mesaji

Sevgili meslektaşlarım,

İran Hepatit Ağı ev sahipliğinde 2017 yılında İran'da gerçekleşecek olan 7. Uluslararası Tahran Hepatit konferansında sizleri de aramızda görmekten büyük mutluluk duyacağız.

Tahran'daki THC6'da 2000'e yakın bilim adamını ve ABD, Kanada, İngiltere, Almanya, Fransa, İtalya, Hollanda, Avusturya, Belçika, İsveç, Kıbrıs, Türkiye, Avustralya ile bölgemizden seçkin konuşmacıları ağırlamıştık.

Bildiri özetlerinizi konferans web sitesi www.thc7.ir üzerinden sunmanızı rica ediyoruz. Bildiri özetleriniz bilimsel kurulda meslektaşlarınız tarafından gözden geçirilecek olup verilen karara göre ya sözlü sunum ya da bir tanıtıcı duvar ilanı olarak onaylanacaktır.

Viral hepatit ve karaciğer hastalığının tüm disiplinlerindeki en yeni gelişmeleri içeren bu yaman ve çekici bilimsel programda bizlerle birlikte olmanızdan büyük onur duyacağız. Bilimsel program tanıtımına şu adresten ulaşabilirsiniz: THC7 resmi İnternet sitesi.

Saygılarımla,

Dr. Seyed-Moayed Alavian

THC7 Yönetim Kurulu Başkanı – İran Hepatit Ağı Direktörü



– Message from EILF Chairman -

Dear Colleagues, dear Friends,



I wish to convey both greetings and gratitude of the Board of the EASL International Liver Foundation together with my personal thanks for being invited to present at this prestigious meeting.

Let me remind you that the scope of the Foundation is networking with non-profit institutions, exactly like the Iranian Society of Hepatology, with the vision of promoting and delivering science, education and care in the field of liver disease, globally.

I am therefore delighted to be attending the 7th International Tehran Hepatitis Conference where the presence of numerous European KOLs embedded in the Best of EASL workshop offers the opportunity for the Foundation to partner with renown experts of the Iranian Society of Hepatology in promoting awareness and management of liver diseases in such a vast and historically rich geographical area, where your community live and is operating.

Mixing the expertise of European hepatologists with the Iranian colleagues, we wish also to further enhance the attractiveness of EASL that annually hosts more than 10,000 physicians from every continent, who convene at the International Liver Conference, an event that, in 2018, will take place in Paris.

Throughout my career as physician and professor of medicine focusing on liver diseases, I have had the rare privilege to experience the completion of the whole scientific cycle starting from the discovery and characterization of a highly prevalent disease such as viral hepatitis (here we enjoy the presence of the discoverer of hepatitis delta), while I had the opportunity to scientifically and socially interact with most scientists whose amazing discoveries paved the way for the development of effective therapies for a number of fatal liver diseases.

Regrettably, the benefits of scientific progress have so far been enjoyed by a very small fraction of those in need, and this is true not only in the area of viral hepatitis, currently estimated at a global tool of more than 300 million by WHO, but other increasingly prevalent diseases, such as liver cancer and fatty liver disease.

In an effort to increase educational impact, our Foundation has begun an extensive round of consultations with colleagues from Middle East, Africa and the East Mediterranean region, a process which has already led to the identification of a great demand for both science and health care delivery. In particular, the Foundation looks at Iran as a gatekeeper hoping to run joint programs with a view of targeting physicians from the neighbouring regions including Azerbaijan, Afghanistan, Pakistan and Turkmenistan. I cordially wish all the attendees a fruitful meeting!

Massimo Colombo

Chair EASL International Liver foundation

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International Tehran Hepatitis Conference

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A Message from Scientific Manager

Good day to you,



Viral hepatitis and liver diseases have significant health and economic burden in the world. The burden in the countries with high prevalence of viral hepatitis becomes a health problem should be considered in a timely manner. The middle eastern countries mostly have high prevalence of HBV and HCV which neglected by the governments. Here, in 7th Tehran Hepatitis Conference (THC7), we all come together to overcome the health-related burden of

liver diseases in our countries. We have the goal of our region without viral hepatitis which needs the efforts of all colleagues. The scientific program of THC7 would focus on all aspects of liver diseases with concentration on viral hepatitis. We have provided interesting scientific sessions and discussions for all participants.

In a close collaboration between Iran Hepatitis Network (IHN) and European Association for the Study of the Liver (EASL) International Liver Foundation (EILF), the first day of the 7th Tehran Hepatitis Conference (THC7) will be dedicated to the lectures of scientific leaders of hepatology from Europe and Iran. The EILF Educational Program at THC7 will take place on 6th September, 2017 with an interesting and comprehensive scientific program concentrated on viral hepatitis and other liver diseases. The guests from EILF will present the new findings in hepatology and the Iranian distinguished speakers will present their experience on management of liver diseases in Iran. We take great pleasure to invite you to participate in the EILF Educational Program at THC7 which intends to promote the knowledge of hepatology in Iran and the region.

Looking forward to seeing you in THC7.

Kindest Regards,

Heidar Sharafi, PhDc. Scientific Manager, 7th Tehran Hepatitis Conference & EILF Educational Program in Tehran h.sharafi@meldcenter.com

International Tehran Hepatitis Conference

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A Massage from Executive Manager



We are honored to gather together again for the 7th International Tehran Hepatitis Conference and celebrate this great scientific festival in a great city of Tehran. The main objective of the Conference is to present the most interesting topics in the field of viral hepatitis and liver diseases to a wide range of audiences such as physicians, professionals, researchers, and students. Moreover, the conference focuses on activists in the field of liver disease. In THC7 which is the second international collaboration between European Association for the study

9

7th Tehran Hepatitis Conference, September 2017

of Liver Disease (EASL) in the format of International Liver Foundation (EILF) and Iran hepatitis Network, in addition to prominent Iranian specialists and researchers who are invited, we are pleased to host many invited speakers from all over the world, such as United States, Canada, Australia, Austria, Germany, Italy, France, Cyprus, Turkey, England and Georgia. In addition to the invited speakers, we are going to witness the presence of other scholars and enthusiasts from the countries including, Iran, Afghanistan, Pakistan, Iraq, Turkey, Bangladesh, Republic of Sierra Leone, Malaysia, Uzbekistan, Philippine, Netherland, Poland, Canada, Switzerland and Belgium. Last but not least, for the first time in the history of THC, enthusiasts can enjoy scientific conferences using the webinar system.

I need to thank and appreciate my dear fellows' strenuous efforts in Iran Hepatitis Network and all across the country. It's my pleasure to extend a cheerful welcome to you all and I hope you enjoy super academic programs of this conference.

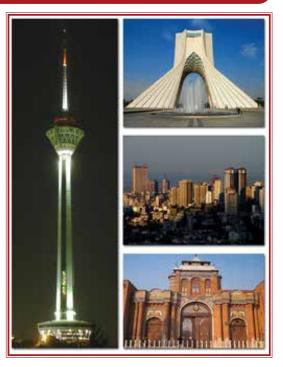
Best regards,

Khashayar Hesamizadeh, Executive Manager, 7th Tehran Hepatitis Conference & EILF Educational Program in Tehran



About Tehran

Tehran is the capital and largest city of I.R. Iran. and the administrative center of Tehran Province. Tehran is a sprawling city at the foot of the Tochal mountain range with an immense network of highways unparalleled in Western Asia. The city is famous for its numerous resorts on the Alborz slopes, large museums, art centers, and palace complexes. Tehran is the largest city in the Middle East and is the 16th most populated city in the world with a population of around 7,800,000 people. Most Iranian industries are headquartered in Tehran, including the manufacturing of automobiles, electrical equipment, military weaponry, textiles, sugar, cement, and chemical products. Tehran is also a lead-



ing center for the sale of carpets and furniture. There is an oil refinery located south of the city. In the 20th century, Tehran faced a large migration of people from all around I.R. Iran. Today, the city contains various religious minorities, and has many historic mosques, churches, synagogues and Zoroastrian fire temples. Contemporary Tehran is a modern and expensive city featuring many skyscrapers, of which the Azadi Tower and the Milad Tower have come to be symbols of Tehran itself.

History



The origin of the name Tehran is unknown. Excavations place the existence of settlements in Tehran as far back as 6000 BC. Tehran was well known as a village in the 9th century, but was less well-known than the city of Rhages (Ray) which was flourishing nearby in the early era. In the 13th century, following the destruction of Ray by Mongols, many of its inhabitants escaped to Tehran. In some sources

of the early era, the city is mentioned as "Rhages's Tehran". The city is later mentioned in Hamdollah Mostowfi's Nuz'hat al-Qulub (written in 1340) as a famous village. Don Ruy Gonzáles de Clavijo, a Castilian ambassador, was probably the first European to visit Tehran, stopping in July 1404, while on a journey to Samarkand (now in Uzbekistan) and the Mongol capital at the time. At this time, the city of Tehran was unwalled. Tehran became a residence of the Safavid rulers in the 17th century. Tahmasp I built a bazaaar and a wall around the city, but it somewhat fell out of favor after Abbas I turned sick when he was passing the city to go to a war with the Uzbeks. In the early of 18th century, Karim Khan Zand ordered a palace, a harem, and a government office to be built in Tehran, possibly to declare the city his capital, but later moved his government to Shiraz. Tehran finally became the capital of I.R. Iran in 1795, when the Qajar king Agha Mohammad Khan was crowned in the city. It remains the capital to this day

Climate



Tehran's climate is largely defined by its geographic location, with the towering Alborz Mountains to its North and the central desert to the South. It can be generally described as mild in the spring, hot and dry in the summer, pleasant in the autumn, and cold in the winter. As a large city with a significant differ-

ences in elevation among various districts, the weather is often cooler in the hilly north as compared to the flat southern part of Tehran. Summer is usually hot and dry with very little rain, but relative humidity is generally low and the nights are cool. The majority of the light annual precipitation occurs from late-autumn to mid-spring, but no one month is particularly wet. The hottest month is July (mean minimum temperature 23°C, mean maximum temperature 36°C) and the coldest is January (mean minimum temperature -1°C, mean maximum temperature 8°C). Although compared with other parts of the country Tehran enjoys a moderate climate, weather conditions can sometimes be unpredictably harsh. The record high temperature is 48°C and the record low is -20°C.

About Shiraz



Shiraz is the sixth most populous city of Iran and the capital of Fars Province. In the 13th century, Shiraz became a leading center of the arts and letters, due to the encouragement of its ruler and the presence of many Persian scholars and artists. Shiraz is known as the city of poets, literature, wine and flowers. It is also considered by many Iranians to be the city of gardens, due to the many gardens and fruit trees that can be

seen in the city, for example Eram Garden. Shiraz's climate has distinct seasons, and is overall classed as a hot semi-arid climate, though it is only a little short of a hot-summer Mediterranean climate (Csa).Summers are hot, with a July average high of 38.8 °C (101.8 °F). With more than 25 malls and 10 bazaars, Shiraz is known as the easiest place for shopping in Iran and the Middle East. The Vakil Bazaar, one of the oldest bazaars in the world, is located in the old city center of Shiraz. Featuring beautiful courtyards, caravanserais, and bath houses, its shops are deemed among the best places in Shiraz to buy all kinds of Persian rugs, spices, copper handicrafts and antiques. Shiraz has had major Jewish and Christian communities. The crafts of Shiraz consist of inlaid mosaic work of triangular design; silver-ware; pile carpetweaving and weaving of kilim, called gilim and jajim in the villages and among the tribes

About Birjand



Birjand is the east Iranian provincial capital of South Khorasan, ranks among the most important historical cities of Iran and also it is known for its saffron, barberry, rug and handmade carpet exports. Being close to the Afghanistan border, Birjand is located on the «Silk Road»of opium smuggled from Afghanistan on the way to Europe. Birjand also boasts of being the frst city in Iran to

have a modern water distribution system. The economy of Birjand is agrobased and the city has also been recognized as the science and education hub in the east of Iran for its large numbers of universities and education centers. Global registration of Akbarieh Garden on the UNESCO World Heritage List has contributed to the increase in the arrivals of tourists to the city. However, many attractions of the city including Hosseinieh Navvab, Mir Hassan Khan Mansion, Shokatieh School and Chaharderakht Mosque are still out of bounds for tourists. The city also lacks adequate hotels and guesthouses to accommodate tourists. The city has a dry climate with signifcant difference between day and night temperatures. It is a fast-growing city, thus becoming one of the major centers in the East of Iran.

THC7 Boards and Committees

Held by:

Iran Hepatitis Network Kowsar Corporation Baqiyatallah Research Center for Gastroenterology and Liver Disease

THC7 Governing Board:



Prof. Seyed-Moayed Alavian, MD, Director of Iran Hepatitis Network, Tehran, IR Iran



Prof. Kamran Bagheri-Lankarani, MD, Shiraz University of Medical Sciences, Shiraz, IR Iran

13

7th Tehran Hepatitis Conference, September 2017



Prof. Massimo Colombo, MD, University of Milan, Milan, Italy



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Scientific Manager:



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THC7 Internationally Invited Speakers



Bijan Eghtesad, USA



Behzad Yeganeh, Canada



Robert Gish, USA



Hadi Karimzadeh, Germany



Pascal Pineau, France



Thomas Michalak, Canada



Jean Dubuisson, France



Mario Mondelli, Italy



Mario Rizzetto, Italy



Massimo Colombo, Italy



Peter Ferenci, Austria



Homie Razavi, USA



Cihan Yurdaydin, Turkey



Peter Karayiannis, Cyprus



Behzad Hajarizadeh, Australia



Saeid Ghavami, Canada



Amiran Gamkrelidze, Georgia



Laurent Castera, France



Siamak Seddigh-Tonekaboni, UK



International KOWSAR Award

The International Kowsar Award in Hepatology is an international scientific award, which for the first time in history is going to be presented to top researchers with lifelong experience in the field of hepatology, who have extended our knowledge and understanding of the epidemiological aspects, the pathobiological mechanisms, new therapeutics and the molecular basis for the diagnosis and treatment of liver diseases, particularly viral hepatitis, up until the present time, or to those researchers who are likely to do so, in our estimation, in the future. This award was established by Prof. Seyed-Moayed Alavian, Professor of Gastroenterology and Liver Diseases and Editor-in-Chief of the Hepatitis Monthly journal, the only specialized journal pertaining to liver diseases in the Middle East and central Asia, and with the cooperation of Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL).



The Kowsar Award 2009

The Kowsar award 2009 was conferred on Prof. Mario Rizzetto, Professor of Gastroenterology and Liver Diseases at the University of Torino, Italy, who was the discoverer of the delta antigen and antibody in carriers of the hepatitis B surface antigen.



The Kowsar Award 2010

The Winner of the Kowsar International Hepatology Award 2010 was Prof. Dr. Med. Michael Roggendorf, Professor of Hepatology at the University of Essen, Germany.



The Kowsar Award 2011

The Winner of the Kowsar International Hepatology Award 2011 was Prof. Howard Thomas, UK.



The Kowsar Award 2013

The Winner of The Kowsar Award 2013 was Prof. Daniel Lavanchy, Honrary Member at Viral Hepatitis Prevention Board (VHPB), Geneva Area, Switzerland.



The Kowsar Award 2015

The winner of the Fifth Kowsar Award was Prof. Peter Karayiannis, Professor of Microbiology/Molecular Virology from UK.



Kowsar Award 2017

In the Name of Allah

The Compassionate, the Merciful Islamic Republic of Iran Baqiyatallah University of Medical Sciences

Dear Professor Massimo Colombo,

In recognition of your outstanding achievements in the scientific world, your contribution to human health and prosperity, and a life- time efforts in medical sciences, I am in the privileged position to present to you on behalf of Baqiyatallah Research Center for Gastroenterology and Liver Diseases and Iran Hepatitis Network, the

"International Kowsar Award, 2017 in THC7 in Tehran".

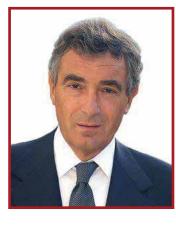
Your prominent studies in the field of hepatology, particularly diagnosis, natural history and treatment of viral hepatitis, hepatocellular carcinoma and liver transplantation are highly commendable. Moreover, you have authored more than 480 original manuscripts in peer-reviewed journals. It is precious that you were appointed Chairman of EASL International Liver Foundation in September 2016 as well.

Furthermore, your activities as the Editor-in-Chief of the Journal of Hepatology for many years and also as the editorial board of many hepatology journals globally have greatly added to our understanding of these fields and have helped scientists and clinicians all over the world. It is an honor for Iranian scientific community to recognize your exceptional endeavors and accomplishments. We pray for continued success in your services to humanity, and wish you a prosperous and healthy life.

Professor Seyed Moayed Alavian,

Chairman of 7th International Tehran Hepatitis Conference, September, 6-8, 2017 Tehran, IR Iran

Biography of KOWSAR Award Winner



Professor Massimo Colombo, MD, is professor of gastroenterology and hepatology, at university of Milan. In the past 15 years, he has been chairman of department of liver, kidney, lung and bone marrow units and organ transplant, IRCCS Maggiore hospital Milan, university of Milan.

Professor Colombo gained his medical degree from the University of Milan, before completing a residency in gastroenterology at IRCCS Maggiore Hospital. Subsequently he undertook an international fellowship in liver diseases at Mount Sinai Hospital in New

York, USA (1974-1975), before returning to IRCCS Maggiore Hospital. He has also been a Professor of Medicine and Gastroenterology at the University of Milan for more than 25 years.

Professor Massimo Colombo is Director of the Center for Translational Research in Liver Disease at Humanitas Research Hospital, Rozzano in Italy.

Professor Colombo's research interests include the diagnosis and treatment of viral hepatitis and liver cancer. A member of many professional societies including EASL, AASLD and several Italian societies, he is the recipient of numerous awards including the 2010 European Association for the Study of Liver (EASL) Recognition Award for outstanding medical and scientific contributions, the Italian Association for the Study of the Liver (AISF) Distinguished Service Award, the Than Hauser Medal Award of the German Society of Gastroenterology and the Nelson Fausto Award of the International Liver Cancer Association(ILCA).

Professor Colombo was Editor-in-Chief of the Journal of Hepatology from 2005-2009 and currently sits of the editorial boards of many hepatology journals and in September 2016 he was appointed Chairman of EASL.

Yas Young Investigator Award



As the important impact of young people in the science, we should encourage them to be more active in this field. We had six Tehran Hepatitis Conferences (THCs) yet and many participants from Iran, the region and other parts of the world. Many of them were young investigators. We would like to attract the young people to participate actively in the conference and research activities in field of hepatology.

The "Yas Young Investigator Award" in Hepatology is a scientific award, which for the first time in history is going to be presented to top young researchers with novel experiences in the field of hepatology, who designed an integrated a new modality for diagnosis and treatment of liver diseases, publishing original

articles with high impact factor, sharing the experiences with others, and to be more active in social support of patients. This award was founded in 2015 by Prof. Seyed-Moayed Alavian, Professor of Gastroenterology and liver disease and editor-in-chief of the Hepatitis Monthly Journal, the only specialized journal pertaining to liver disease in the Middle East and central Asia.



The Yas Young Investigator Award 2015

The winner of the first Yas Award was:

Dr. Christine Hartoonian, Pharm.D. and Ph.D. in Pharmaceutical Biotechnology.

Yas Award 2017

In the Name of Allah

The Compassionate, the Merciful Islamic Republic of IRAN Baqiyatallah University of Medical Sciences

Dear Dr. Forough Golsaz Shirazi

As the important impact of young people in the science, they should be encouraged to be more active in this field. Six Tehran Hepatitis Conferences (THCs) have been held with the presence of many participants from Iran, the region and other parts of the world. Many of them were young investigators. I am in the privileged position to present to you on behalf of Bagiyatallah Research Center for Gastroenterology and Liver Diseases the

"Yas Young Investigator Award, 2017 in THC7 in Tehran"

in Hepatology is a scientific award, which for the second time in history is going to be presented to the top young researcher with novel experiences in the field of hepatology, who designed integrated and new modalities for diagnosis and treatment of liver diseases, publishing high impact original articles, and sharing the experiences with others. This award was founded in 2015 by Prof. Seyed-Moayed Alavian, Professor of Gastroenterology and liver disease.

I pray for more success in your service to humanity and wish you a prosperous and healthy life.

Professor Seyed Moayed Alavian

Conference Chairman The 7th International Tehran Hepatitis Conference 6-8 September, 2017 Tehran, IR IRAN

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Biography of YAS Award Winner



Forough Golsaz-Shirazi holds Ph.D of Immunology and has been graduated from Department of Pathobiology, Public Health School, Tehran University of Medical Sciences.

She was born on 05.April.1980 in Ahwaz in a well-educated family. She received her bachelors' degree in Microbiology in 2002 and received her Master degree in Immunology from Mashhad University of Medical Sciences, School of Medicine in 2005. Developing a lively interest for Immunology, she was able to produce monoclonal antibody against saffron pollen Profilin under supervision of Professor Abdol-Reza

Varasteh during her Master study. During this time she was recognized and encouraged as the chosen student of Mashhad University of Medical Sciences.

In 2006, she ranked the third in PhD entrance exam of Medical Immunology. She then earned her PhD degree in Immunology at Tehran University of Medical Sciences, Public Health School in 2013. Following her interest in Immunology, she was introduced to viral hepatitis in Professor Fazel Shokri' laboratory in Public Health School, Tehran University of Medical Sciences. During her Ph.D study under the supervision of Professor Fazel Shokri, she was able to produce murine and mouse-human chimeric anti-HBs monoclonal antibodies for prophylaxis of HBV infection. During her Ph.D study, she was able to attend a sabbatical course in Technical University of Munich/Helmholtz Zentrum München, Germany under supervision of Professor Ulrike Protzer. During this course, she evaluated the neutralization effect of anti-HBs monoclonal antibodies in HepaRG cells. This Sabbatical course in Germany was very beneficial for her and provided many experience in the field of viral hepatitis. She still has kept this collaboration with Professor Ulrike Protzer.

In 2014, she was awarded for the "Excellent oral presentation" in the "12th international congress of immunology and allergy in Tehran". Forough Golsaz-Shirazi is very diligent and determined and after graduation she joined Immunology Department, School of Public Health, Tehran University of Medical Sciences as a faculty member. Encouraged by Professor Shokri, she pursued her dream and decided to challenge her abilities and enthusiasm in Immunology and viral hepatitis. As a faculty member, she pursued her studies regarding the effect of neutralizing anti-HBs monoclonal antibodies on control of HBV infection, molecular details of HBV life cycle, and the interaction of HBV with the innate immunity in hepatocyte. She is trying and hope to establish new and innovative methods for treatment of chronic hepatitis B infection.

Considering the difficulties of research in a developing country especially under sanction, she never stopped trying and also believed in collaborating with well-known and successful researchers in this field worldwide. She believes in an old saying about the beauty of teamwork "Coming together is a beginning, keeping together is progress, working together is success". She is always grateful to her mentor and colleagues, Dr. Fazel Shokri, Dr. Ulrike Protzer, Dr. Mahmoud Jeddi-Tehrani, and Dr. Mohammad Mehdi Amiri.

Motivation of Novelty in NOhep Activities (NINA) Prize

NOhep as a global movement which follows the elimination of viral hepatitis by 2030 tries to unite those activities in the field of hepatitis around the world. According to NOhep's request from individuals and organizations across the world to sign-up to be part of the next greatest achievement, the elimination of viral hepatitis, Iran Hepatitis Network did its best to pledge of support for this aim.

Therefore, as the important impact that creative and compassionate people have in raising public awareness about viral hepatitis, we should encourage them to be more active in this field. It is noteworthy that we have had six Tehran Hepatitis Conferences (THCs) in which many specialists (or scientists in different specialties) from Iran, the region and other parts of the world have taken part. Therefore, we would



like to attract inventive people to participate actively in the plan of viral hepatitis elimination and appreciate their valuable efforts in the seventh THC. Hence, the "Novelty in NOhep Activity Prize" (NINA Prize) was elected to be presented to the top creative active people with novel experiences in the field of educating people or treating patients. This award belongs to those designing a new activity along with NOhep's ideals. Therefore, activists and enthusiasts from all areas of the art and science are invited to participate in this competition. This prize was founded in 2017 by Prof. Seyed-Moayed Alavian, professor of gastroenterology and liver diseases and editor-in-chief of the Hepatitis Monthly Journal.

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The Awardees of NINA Prize



Novelty in NOhep Activity (NINA) prize in recognition of outstanding efforts in order to eliminate Hepatitis C in Hemophilia and Thalassemia patients in South Khorasan Province and also the idea of iconic gravestone of Hepatitis C was proudly presented to **Dr. Masoud Ziaee.**



Novelty in NOhep Activity (NINA) prize in recognition of outstanding efforts in creating a NOhep Media in order to eliminate Viral Hepatitis in country was proudly presented to **Mr. Mohammad Ehsan Kharamid.**



Novelty in NOhep Activity (NINA) prize in recognition of your outstanding efforts in designing NOhep scarf in order to unify student activities in national campaigns for elimination of Viral Hepatitis was proudly presented to **Ms. Sara Rezaee.**

Certificate of Appreciation



Dr. Hosein Poustchi: I was born on March 30th 1969 in Qom, Iran, where I spent most of my childhood years and primary and secondary education. I received my high school diploma from Sadoughi High School in Qom, then attended Tehran University of Medical Sciences, in Tehran. After acquiring my MD, I received a scholarship in Clinical Epidemiology from Sidney University, where besides my PhD, I also completed a fellowship

in Advanced Liver Training at the Storr Liver Unit (Westmead Hospital).

Ever since my return to Iran, I have been working at the Digestive Diseases Research Institute (DDRI), Tehran University of Medical Sciences, as an assistant professor of Clinical Epidemiology, where I am heavily involved in research. I am the Deputy of Education at DDRI, and the Deputy of Research at the Liver and Pancreatobiliary Research Center, one of the three major research centers within DDRI.

I have been privileged to be involved in and manage many important, large-scale research studies. I am the executive director of the Prospective Epidemiological Research Studies in Iran, a cohort of 500,000 individuals in Iran investigating noncommunicable diseases, as well as the 40,000 individual cohort of Hepatitis B and Hepatitis C Screening in Khouzestan province. I also manage the follow-up phase of the Golestan Cohort Study, and am starting another project evaluating the efficacy of point of care Hepatitis C treatment in prisoners in Iran.

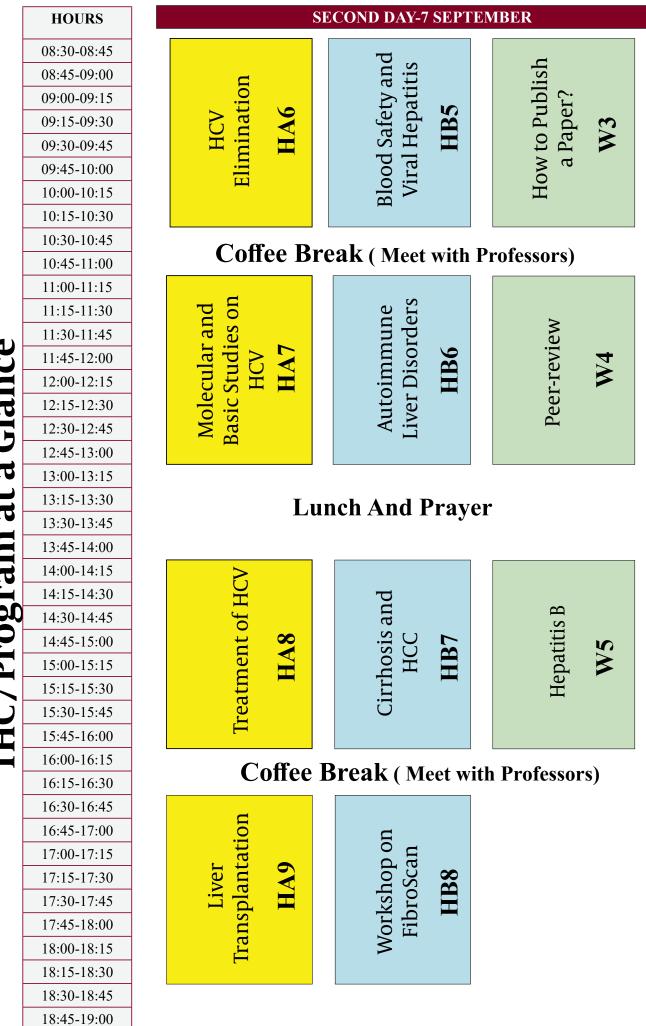
I am very eager to attend conferences around the world to stay up do date in this field, and also share important findings of research conducted at DDRI. In doing so, receiving the Young Investigator Award (2006) and the Poster of Distinction (2013) from the Asia Pacific Association for the Study of the Liver (APASL) has been a great honor. I was also chosen as a Distinguished Researcher by the Iranian Association for Gastroenterology and Hepatology in 2014.

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	18:30-18:43					
	10.45-19.00]				

Hall D

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Hall A



Hall D

Hall B

Hall A

THC7 Program at a Glance

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THC7 Program at a Glance

Hall A Hall B

Hall D

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HOURS	Additional Day, 10 th September, 2017, Shiraz Hepatitis Conference
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Shiraz

First Day, 6th September, 2017

HA1 Management of Hepatitis **B-Educational Program of EASL International Liver Foundation**

08:45-10:30

Titles and Speakers:

• Management of HBsAg Inactive Carriers Mohamadreza Zali (Iran), 15 min

• Prevention and Treatment of Hepatitis B Reactivation during Immune Suppressing and Chemotherapy

Nasser Ebrahimi Daryani (Iran), 15 min

• T Cell Therapy for Management of Chronic Hepatitis B Infection and Related Diseases Hadi Karimzadeh (Germany), 10 min

• Treatment of HBV with NA: Updated EASL Recommendations Massimo Colombo (Italy), 20 min

• Treatment of Hepatitis B with Pegylated-IFN based Regimens Cihan Yurdaydin (Turkey), 20 min

• New Treatments for HBV: What is the Pathway for Drug Development? Robert Gish (USA), 20 min

Discussion, 5 min

Moderator:

Mohamadreza Zali

Members:

Nasser Ebrahimi Daryani Hadi Karimzadeh Massimo Colombo Cihan Yurdaydin Robert Gish Farhad Zamani

HA2 General Session/Keynote Talk

11:00-12:30

Kowsar and Yas Award Ceremony:

Introduction of Kowsar and Yas Awardees

Keynote Talk:

Systematic Strategies towards HCV Elimination Massimo Colombo (Italy), 30 min

HA3 Epidemiology and Burden of **Hepatitis B-Educational Program** of EASL International Liver Foundation

13:30-15:00

Titles and Speakers:

- Global Burden of Hepatitis B Homie Razavi (USA), 20 min
- Non-invasive Diagnosis: from Viral Hepatitis to NAFLD Laurent Castera (France), 25 min

 HBV and Burden of HCC Mohamad Amin Pourhoseingholi (Iran), 20 min

• O19 Estimating the Prevalence of Hepatitis B Virus Infection and Exposure among General Population in Iran Behzad Hajarizadeh (Australia), 15 min

• Discussion, 10 min

Moderator:

Homie Razavi

Members:

Laurent Castera Mohamad Amin Pourhoseingholi Behzad Hajarizadeh Mohamad Javad Zahedi Akram Pourshams

HA4 Occult Hepatitis B-Educational Program of EASL International Liver Foundation

15:00-17:00

Titles and Speakers:

- Is OBI the Fifth Phase in HBV Natural History? Peter Karayiannis (Cyprus), 25 min
- Experimental OBI in the Woodchuck HBV Infection Model Thomas Michalak (Canada), 25 min

• Vertical OBI, Myth or Truth? Seyed Mohammad Jazayeri (Iran), 15 min

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• Anti-HBC (+) Tests: Getting to the Core of the Issue Robert Gish (USA), 25 min

• OBI in Iranian Blood Donors Sedighe Amin-Kafiabad (Iran), 15 min

• Discussion, 15 min

Moderator:

Seyed Mohammad Jazayeri

Members:

Peter Karayiannis Thomas Michalak Robert Gish Sedighe Amin-Kafiabad Farah Bokharaei-salim Ali Akbar Shayesteh

HA5 Hepatitis D-Educational Program of EASL International Liver Foundation

17:30-19:00

Titles and Speakers:

• An Update on the Virology and Molecular Biology of Hepatitis D Virus Peter Karayiannis (Cyprus), 20 min

- HDV Classification and Immunobiology Hadi Karimzadeh (Germany), 20 min
- Interferon Therapy of Chronic Hepatitis D Mario Rizzetto (Italy), 20 min
- The Upcoming Treatments of Hepatitis D Cihan Yurdaydin (Turkey), 20 min

• Discussion, 10 min

Moderator:

Hadi Karimzadeh

Members:

Peter Karayiannis Mario Rizzetto Cihan Yurdaydin Abdosamad Gharavi

Second Day, 7th September, 2017

HA6 HCV Elimination: Opportunities and Challenges

08:30-10:30

Titles and Speakers:

• HCV Cascade of Care and the Requirement to Achieve the Elimination Targets in Different Regions *Homie Razavi (USA), 25 min*

• Hepatitis C Elimination Program in Georgia Amiran Gamkrelidze (Georgia), 25 min

• HCV Elimination in Iran: Next Step after Generic DAA Behzad Hajarizadeh (Australia), 25 min

• Simplified HCV Diagnosis Siamak Tonekaboni (UK), 25 min

• Discussion, 20 min

Moderator: Behzad Hajarizadeh

Members:

Homie Razavi Amiran Gamkrelidze Siamak Tonekaboni Hossein Keyvani Mehrdad Haghazali

HA7 Remaining Challenges and Open Questions for Molecular Studies and Basic Research on HCV in Post-DAAs Era

11:00-13:00

Titles and Speakers:

• Updates on HCV Vaccines Farzin Roohvand (Iran), 15 min

• HCV Viral Particle and Life Cycle Jean Dubuisson (France), 20 min

• Innate Immunity to HCV: the Role of NK Cells Mario Mondelli (Italy), 20 min

• Immune Cell Reservoirs of Persisting HCV and Related Pathogenic Consequences *Thomas I. Michalak (Canada), 20 min*

• Epigenomic Changes and Non-coding Genome Segments involved in HCV-associated HCC *Pascal Pineau (France), 20 min*

• O92 Repression of Hepatitis C Virus Replication

by an Engineered PUF Protein Seyed Jalal Kiani (Iran), 15 min

• Discussion, 10 min

Moderator: Farzin Roohvand

Members:

Jean Dubuisson Mario Mondelli Thomas I. Michalak Pascal Pineau Katayoun Samimi-Rad

HA8 Treatment of Hepatitis C; an Update

14:00-16:00

Titles and Speakers:

• Treatment of Patients with HCV Genotype 1 or 4 Infection *Mario Mondelli (Italy), 25 min*

• Treatment of Patients with HCV Genotype 2 or 3 Infection *Peter Ferenci (Austria), 25 min*

• Retreatment of Patients with Failure to Treatment with DAAs *Shahin Merat (Iran), 20 min*

• Treatment of HCV Infection with Generic DAAs in Iran; an Update on Iranian Consensus for Treatment of Hepatitis C Seyed Moayed Alavian (Iran), 20 min

• Treatment of HCV/HIV Coinfection with DAAs *Minoo Mohraz (Iran), 20 min*

• Discussion, 10 min

Moderator:

Seyed Moayed Alavian

Members:

Mario Mondelli Peter Ferenci Shahin Merat Minoo Mohraz Shahram Agah

HA9 Liver Transplantation

16:30-18:30

Titles and Speakers:

• Liver Transplantation for Autoimmune Hepatitis in Iran (Management and Outcomes) *Kamran Bagheri Lankarani (Iran), 20 min*

•Management of Hepatitis B in Liver-transplanted Patients *Mario Rizzetto (Italy), 25 min*

• Liver Transplantation in Pediatric Age Group. Iranian Experience *Ali Bahador (Iran), 20 min*

• Expanded Criteria Donors in the Era of Organ Shortage. Is There a Role in Possible Expansion of Iranian Donor Pool for Liver Transplantation? *Bijan Eghtesad (USA), 20 min*

• O27 Shortcomings of Organ Procurement, Challenges of MELD Score Kamran Bagheri Lankarani (Iran), 15 min

• Discussion, 20 min

Moderator: Bijan Eghtesad

Members: Kamran Bagheri Lankarani Mario Rizzetto Ali Bahador Seyed Mahmoud Es'hagh Hoseini

Third Day, 8th September, 2017

HA10 A Practical Approach to NA-FLD Diagnosis and Treatment

08:30-10:00

Titles and Speakers:

• Introducing a Case with Elevated Liver Enzyme Raika Jamali (Iran), 20 min

• Pathogenesis of NAFLD – An Update Peter Ferenci (Austria), 20 min

• The Role of Elastography in NAFLD Hossein Poustchi (Iran), 15 min

• The Treatment Strategies for NAFLD Bahram Seifi Zarei (Iran), 15 min

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• O21 Serum Homocysteine Levels as an Important Non-Invasive Diagnostic Biomarker in Patients with Different Stages of Non-Alcoholic Fatty Liver Disease

Ankit Kumar Chakraborty (India), 10 min

• Discussion, 10 min

Moderator:

Raika Jamali

Members:

Peter Ferenci Hossein Poustchi Bahram Seifi Zarei Mohamad Jafar Farahvash

HA11 Virus-Host Cell Interactions and Pathogenesis of Viral Hepatitis

10:30-12:00

Titles and Speakers:

• Impact of Autophagy and Apoptosis on Viral Hepatitis

Behzad Yeganeh (Canada), 15 min

• Immunopathology and Molecular Pathogenesis of Viral Hepatitis Thomas I. Michalak (Canada), 20 min

• Genotype F of Hepatitis B Virus: Benign Commensal or Stealth Destroyer? Pascal Pineau (France), 20 min

• O162 Protective Effect of Opuntia Extracts against Menadione-Induced Oxidative Stress and Apoptosis in Cultured HepG2 Cells Sajedeh Sadat Mirshahvalad (Iran), 10 min

• O30 Protective Role of Specific Pathogen Free Microbiota in Bile Duct Ligated and CCL4 Treated Mice Sheiad Moghadamrad (Switzerland), 10 min

• O159 Oxidative DNA Damage in Association with HBsAg in Chronic Hepatitis B Patients Ashraf Mohamadkhani (Iran), 10 min

• Discussion, 5 min

Moderator: Behzad Yeganeh

Members:

Thomas I. Michalak Pascal Pineau Mohamad Reza Aghasadeghi Seyed Reza Mohebbi Esmaeil Sanei-moghadam

HA12 Liver Fibrosis and End-stage **Liver Diseases**

13:00-14:30

Titles and Speakers:

• Effect of End-stage Liver Disease on Drugs Pharmacokinetic and Pharmacodynamic Simin Dashti (Iran), 15 min

• Coagulopathies in Patients with End-stage Liver Disease

Mohsen Nassiri-Toosi (Iran), 15 min

• Imaging Findings and Interpretation in Patients with End-stage Liver Disease Niloofar Ayoobi Yazdi (Iran), 15 min

• Selection of Patients with End-stage Liver Disease for Liver Transplantation Mohsen Nassiri-Toosi (Iran), 15 min

• Liver Fibrosis in HBV or HCV Infected Patients: Role of Autophagy and Unfolded Protein Response Saeid Ghavami (Canada), 15 min

• O22 "Normal" Liver Stiffness Measure (LSM) Values are Higher in Both Lean and Obese Individuals: A Population Based Study from a Developing Country

Ritwick Mondal (India), 10 min

• Discussion, 5 min

Moderator:

Mohsen Nassiri-Toosi

Members:

Simin Dashti Niloofar Ayoobi Yazdi Saeid Ghavami

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HA13 Viral Hepatitis: a Global Health Challenge

14:30-16:00

Titles and Speakers:

• O32 Hepatitis C Virus Genotype Distribution and Relationship with Serum Alanine Aminotransferase and Quantitative Serum HCV RNA Values in Province of Afyonkarahisar, Turkey *Recep Kesli (Turkey), 10 min*

• O142 High Rates of Hepatitis C (HCV) Coinfection and Advanced Liver Fibrosis among HIV Cohorts in Medecins Sans Frontieres Programmes in Myanmar

Theingi Aye (Myanmar), 10 min

• O147 Missed Opportunities for Diagnosing Viral Hepatitis C in Poland. Results from the Routine HCV Testing Based on Risk Factors at the Emergency Department (ED) in the Hospital of Infectious Diseases in Warsaw

Karolina Pyziak-Kowalska (Poland), 10 min

• O211 Hepatitis C and Hepatitis B Dual Infection: Change in Prevalence and Pattern over a Decade in Pakistan

Nayab Batool Rizvi (Pakistan), 10 min

• O219 Screening of Hepatitis C in Different High Risk and Low Risk Population Groups in Rawalpindi and Islamabad Cities of Pakistan *Yasir Waheed (Pakistan), 10 min*

• Panel: Viral Hepatitis B and C: a Public Health Issue Moderator and Members, 40 min

Discussion,

Moderator:

Mehdi Saberifiroozi Afsaneh Sharifian **Members:** Davood Yadegarynia Mohamad Hosein Antikchi

First Day, 6th September, 2017

HB1 Viral Hepatitis for Nurses

08:45-10:30

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Titles and Speakers:

•Hepatitis C in Hemodialysis Centers, Separation or not Separation? Mostafa Alavi-Moghadam (Iran), 20 min

• Prevention of Hepatitis B in Nurses Mitra Zandi (Iran), 20 min

• Strategy of Ministry of Health in Education of Nurses Maryam Mohammadi Nasrabadi (Iran), 20 min

• Management of Hepatitis B: for Nurses Mitra Ranjbar (Iran), 20 min

•Management of Hepatitis C: for Nurses Bita Behnava (Iran), 20 min

•Discussion, 5 min

Moderator: Mohammad Mehdi Salari

Members: Mostafa Alavi-Moghadam Mitra Zandi Maryam Mohammadi Nasrabadi Mitra Ranjbar Bita Behnava

HB2 Viral Hepatitis for Surgeons

13:30-15:00

Titles and Speakers:

• Surgeons are at Higher Risk for HBV and HCV Hosein Khedmat (Iran), 20 min

•Recommendations for Post Exposure Prophylaxis to Hepatitis B Virus Masoud Ziaee (Iran), 20 min

• Approach for Prevention after Needle Stick with HCV-infected Patients Shahnaz Sali (Iran), 20 min

• Prevention of HIV Transmission after Needle Stick Nematollah Joneidi (Iran), 20 min

•Discussion, 10 min

Moderator: Hosein Khedmat

Members: Shahnaz Sali Nematollah Joneidi Zahra Ahmadinejd Alireza Jalali

HB3 The Status of Viral Hepatitis in Iran

15:00-17:00

Titles and Speakers:

•The Status of Viral Hepatitis in the Province of South Khorasan Masoud Ziaee (Iran), 15 min

•The Status of Viral Hepatitis in Sistan and Balouchestan Province Soheila Khosravi (Iran), 15 min

•The Status of Viral Hepatitis in Isfahan Mohamad Minakari (Iran), 15 min

• Status of Hepatitis B Virus in Tehran during Last Decade Masoud Mardani (Iran), 15 min

• The Status of Viral Hepatitis in Mazandaran Mohammad Reza Hasanjani-roshan (Iran), 15 min

•The Status of Viral Hepatitis in Fars Ahad Eshraghian (Iran), 15 min

• Distribution and Risk Factors of Hepatitis B Virus Infection in the General Population of Central Iran (Qom) *Mohammad Reza Ghadir (Iran), 15 min*

•The Status of Viral Hepatitis in Hormozgan Seyed Hamid Moosavy (Iran), 15 min

Discussion,

Moderator: Mohamad Hosein Somi

Members:

Masoud Mardani Mohammad Reza Hasanjani-roshan Mohammad Reza Ghadir Seyed Hamid Moosavy

HB4 Challenges in Liver Disease and Viral Hepatitis

17:30-19:00

Titles and Speakers:

• The Current Importance of Hepatitis A in Iran Roya Ghasemian (Iran), 20 min

• Epidemiology of Hepatitis E in Iran Khashayar Hesamizadeh (Iran), 20 min

•DC-based Immunotherapy: A New Horizon in Treatment of Chronic Hepatitis B Mostafa Alavi-Moghadam (Iran), 20 min

•O31 Comparison of Invasive and Non-Invasive Tests for Assessment of Liver Fibrosis in the Patients with Chronic Hepatitis B and C *Fariba Keramat (Iran)*, 10 min

•O174 High Burden of Hepatitis B Virus Infection in the Esfandiar Region of Southern Khorasan Province, Iran: A Comprehensive Comparative Study

Davod Javanmard (Iran), 10 min

•Discussion, 10 min

Moderator: Mostafa Alavi-Moghadam

Members: Roya Ghasemian Khashayar Hesamizadeh

Second Day, 7th September, 2017

HB5 Blood Safety and Viral Hepatitis

08:30-10:30

Titles and Speakers:

• Infections as a Threat for Blood Safety Maryam Zadsar (Iran), 20 min

• Donor Selection and Blood Safety Mahtab Maghsudlu (Iran), 20 min

• Transfusion Transmitted Infections Surveillance System for Blood Safety in Iran, 2016 *Abas Sedaghat (Iran)*, 20 min

•O54 Frequency of Transfusion Transmitted In-

fections among Ardabil Blood Donors Based on Demographic Characteristics from 2012 to 2016 Behrooz Ghezelbash (Iran), 10 min

•O74 Frequency of HBc-Ab, HBs-Ab and HBV-DNA among HBs-Ag Negative Healthy Blood Donors in Yazd *Mahtab Vaziri (Iran), 10 min*

•O102 Occult Hepatitis B Virus Infection and Anti-HBc among Blood Donors *Amir Pouremamali (Iran), 10 min*

•O200 Risk Factors for Hepatitis C in Volunteered Iranian Blood Donors: A Case-Control Study Fahimeh Ranjbar Kermani (Iran), 10 min

•Discussion, 20 min

Moderator:

Sedigheh Amini-Kafiabad

Members:

Maryam Zadsar Mahtab Maghsudlu Abas Sedaghat Masoomeh Sofian Bashir Hajibeigi Zohreh Sharifi

HB6 Autoimmune Liver Disorders

11:00-13:00

Titles and Speakers:

• Laboratory Diagnosis of Autoimmune Disorders Mahdi Shekarabi (Iran), 25 min

• Treatment of Autoimmune Hepatitis Sepideh Haghazali (Iran), 25 min

•Controversies in the Management of Primary Sclerosing Cholangitis Nasser Ebrahimi Daryani (Iran), 25 min

•O45 Epidemiologic and Demographic Survey of Autoimmune Hepatitis in Khuzestan Province *Pezhman Alavinejad (Iran), 15 min*

•O161 Enhanced Th17 Responses in Patients with Autoimmune Hepatitis Zohreh Jadali (Iran), 15 min

•Discussion, 15 min



Moderator:

Sepideh Haghazali

Members:

Mahdi Shekarabi Nasser Ebrahimi Darvani Homayoun Vahedi Faramarz Derakhshan Kioumars Fattahi

HB7 Cirrhosis and Hepatocellular Carcinoma

14:00-16:00

Titles and Speakers:

•Epidemiology, Diagnosis and Staging of HCC Mohsen Nassiri-Toosi (Iran), 20 min

•Update of Interventional Procedures for HCC Hossein Ghanaati (Iran), 15 min

 Applications of UES in Liver Diseases Siavosh Mansouri (Iran), 15 min

• Targeted Therapy for HCC Farhad Shahi (Iran), 20 min

•O35 Expression Pattern of P53 and Ki-67 in HBV Related Hepatocellular Carcinoma: A Quantitative Real-Time PCR and Immunohistochemical Study

Bita Moudi (Iran), 10 min

•O169 Study on Plasma Levels of miRNA-625 in Patients with Liver Cirrhosis in Comparison with Healthy Controls Mohabbat Ghaempoor (Iran), 10 min

•O189 Application of Non-Mixture Long-Term Models in Survival Analysis of Cirrhotic Patients Saeede Khosravi Bizhaem (Iran), 10 min

•Discussion, 20 min

Moderator:

Mohsen Nassiri-Toosi

Members:

Hossein Ghanaati Siavosh Mansouri Farhad Shahi

Sodeif Darvish Moghadam

HB8 Workshop on FibroScan Elastography, Non-invasive Assessment of Liver Diseases

16:30-18:30

Titles and Speakers:

Introduction, 15 min

• Experience of FibroScan Shahin Merat (Iran), 30min

• FibroScan Role in Fatty Liver Disease Seyed Moayed Alavian (Iran), 30 min

• FibroScan Principles and Interpretation Hossein Poustchi (Iran), 30 min

 Practical Exam of FibroScan Members, 15min

Members:

Shahin Merat Seyed Moayed Alavian Hossein Poustchi

Third Day, 8th September, 2017

HB9 Monitoring and Evaluation of HCV Elimination Program

08:30-10:00

Titles and Speakers:

•Monitoring and Evaluation of HCV Elimination Program in Australia Behzad Hajarizadeh (Australia), 20 min

•Pilot Study of Screening, Diagnosis and Treatment of Hepatitis C in Iranian Prisons Hossein Poustchi (Iran), 20 min

•Elimination of Hepatitis C in Hemophilia, Thalassemia and Patients with Chronic Kidney Disease

Seyed Moayed Alavian (Iran), 20 min

•Elimination Program of Hepatitis C in Iran Mohammad Mehdi Gouya (Iran), 20 min

Scientific Program-Hall B

Discussion, 10 min

Moderator: Behzad Hajarizadeh

Members:

Hossein Poustchi Seyed Moayed Alavian Mohammad Mehdi Gouya Mehrnaz Rasouli nejad

HB10 Hepatitis C: Clinical, Epidemiology and Molecular Studies

10:30-12:00

Titles and Speakers:

•O179 The Role of Polymorphisms Near IFNL3 Gene as Predictors of Residual HCV RNA in Buffy Coat after Successful Antiviral Therapy Seyyed Mohammad Miri (Iran), 15 min

•O182 Effectiveness of Sobiovir® (Sofosbuvir) and Daklibiox® (Daclatasvir) for Treatment of Hepatitis C in Patient with Thalassemia Jamshid Vafaeimanesh (Iran), 15 min

•O216 Evaluation of the Prevalence HBV and HCV and Related High Risk Behaviors among Prisoners in Iran: Result of National Bio-Behavioral Survey, 2015 *Ghobad Moradi (Iran)*, 15 min

Gilobaa Moraal (Trait), 15 min

•Hepatitis C in Leprosy: Baba Baghi Study Heidar Sharafi (Iran), 15 min

•Treatment of HCV/HIV co-infection with DAAs: Iranian Experience Mehri Nikbin (Iran), 15 min

•Discussion, 15 min

Moderator: Mahboubeh Hajiabdolbaghi

Members:

Heidar Sharafi Mehri Nikbin Ehsan Arefian Fereidoun Rahmani

HB11 Hepatitis B: Clinical, Epidemiology and Molecular Studies

13:00-14:30

Titles and Speakers:

•O9 Construction of a Hepatitis B Virus Neutralizing Chimeric Monoclonal Antibody Recognizing Escape Mutants of the Viral Surface Antigen (HBsAg)

Forough Golsaz-Shirazi (Iran), 10 min

•O43 Association of MicroRNA-146A and MicroR-NA-196A2 Genetic Variants with Concequence of Hepatitis B Virus Infection *Behnaz Riazalhosseini (Iran), 10 min*

•O47 Hepatitis B Virus X Gene Deletions and Insertions in Gorgan City Patients: Chronic Hepatitis-B versus Cirrhosis *Farzanhe Salarnia (Iran), 10 min*

•O77 Investigation of the HBsAg Mutation Patterns Correlation with Disease Progression in Asymptomatic Carriers and Hepatocellular Carcinoma/Cirrhotic HBV Infected Patients *Neda Sanaei (Iran), 10 min*

•O131 An Investigation of Occult Hepatitis B Infection Among Anti-HBc Only Positive Patients in the Southern Khorasan Province: An Iranian Community Based Study *Davod Javanmard (Iran)*, 10 min

•O155 Hepatitis B Infection in Iranian Institutionalized Mentally Retarded Patients Maryam Vaezjalali (Iran), 10 min

•O201 Characterization of OBI Prevalence among Vaccinated Children from Alborz General Population, Iran; Vertical OBI, Myth or Truth *Azam Ghaziasadi (Iran), 10 min*

•Discussion, 20 min

Moderator:

Ashraf Mohamadkhani

Members: Shervin Shokouhi Iradj Maleki

HB12 Viral Hepatitis and Socio-preventive Medicine

14:30-16:00

Titles and Speakers:

•A Review on Social Interventions for Prevention and Control of Viral Hepatitis *Tolou Hasandokht (Iran), 15 min*

Scientific Program-Hall B

•A Review on Last Iranian Schedule and Guideline of HBV Immunization (2015) Mohammad Reza Hedayati-Moghaddam (Iran), 15 min

•Intrafamilial Seropositivity of Hepatitis in Patients with Hepatitis B and C Virus *Leila Seddigh (Iran), 15 min*

• Evaluation of Scientific Evidences of Systematic Reviews and Meta-Analyses on Hepatitis in Iran Masoud Behzadifar (Iran), 15 min

•Discussion, 30 min

Moderator:

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Mohammad Reza Hedayati-Moghaddam

Members:

Tolou Hasandokht Leila Seddigh Masoud Behzadifar •

W1 Plagiarism: How to Prevent?

6th September, 13:30-15:00 in Hall D **By Seyed Mohammad Miri (Iran)**

Wrongful appropriation of text within your academic paper is able to destroy the whole of your academic life just as easy as falling down to a river.

Researcher must be aware of narrow points of writing plagiarized manuscripts and avoid from further threats. This workshop is designed as a fast and quick review for both students and researchers. Basic knowledge and attitude toward one of the most important and recent changes among researchers: our ultimate goal is considering ethic in publishing. During a half-day workshop we talk about: Definition of plagiarism, prevention form plagiarism, and preparations prior to submission.

W2 How to Sell Yourself in Academia

6th September, 15:00-17:00 in Hall D **By Behzad Hajarizadeh (Australia)**

Content: In this seminar, we will discuss the strategies and skills to improve communication for academic purposes. We focus primarily on writing resume, looking for an academic position or scientific collaboration, and presenting in the scientific conferences.

Who benefits from this seminar? The seminar is intended for students, post-doctoral fellows, and other early career researchers in biomedical sciences who are willing to develop their careers through academic networking.

Speaker: Dr Behzad Hajarizadeh, MD, MPH, PhD is an epidemiologist, and a lecturer in the University of New South Wales (UNSW Sydney) in Australia. He had more than 100 presentations in medical conferences and published more than 70 papers in peer-reviewed medical journals, including high-rank journals such as Nature Reviews Gastroenterology & Hepatology (Impact factor: 13.7), Hepatology (Impact factor: 13.2), Journal of Hepatology (Impact factor: 12.5), Journal of Infectious Diseases (Impact factor: 6.2), and The Lancet Gastroenterology & Hepatology (a recently launched journal of The Lancet).

W3 How to Publish a Paper?

7th September, 08:30-10:30 in Hall D **By Mario Mondelli (Italy)**

Writing a scientific paper is one of the most challenging endeavor faced by scientists. Before writing whatever data one has generated from clinical or translational research, one has to think why should the findings be communicated to the scientific community. It is expected that the research has identified a clear scientific objective from which solid findings have emerged out of impeccable methodology. However, a scientific experiment is not complete until the results have been published: this is why we should report our data in a paper. Notably, a well-written paper will convey a clear message and increase your credibility and prestige within your community. Writing "mechanics" suggests to use short simple sentences and active, not passive style. Avoid non-standard abbreviations. Ask native speakers or persons proficient in English to read your paper. Make it beautiful!

An additional task is to find a suitable journal to publish which will also have to be commensurate to the importance of the scientific message. High-impact factor journals should be preferred but it is important "what" rather than "where" you publish. Read instructions to authors. Regarding authorship, avoid inserting an army of authors as a pure gift. ALL authors must have significantly contributed to at least one of: study concept, protocol design, data collection, data analysis, drafting manuscript, and: revision and final approval of manuscript, according to the guidelines of the International Committee of Medical Journals Editors (ICMJE).

Ethics in science is a crucial point. Scientists are accountable for what they write. Data falsification, fabrication and plagiarism should be pursued, as well as unethical research. Journals are responsible for safeguarding the research record and hence have a critical role in dealing with suspected misconduct. This is recognized by the Committee on Publication Ethics (COPE) which has issued clear guidelines. Publication is linked to a honor code: production of reliable data, accurate presentation of results, human/animal investigation approval, informed patient consent, disclosure of financial support and conflict of interest. Once your paper is returned for revision do your best to respond to the reviewers' critiques. Try to do all

THC7 Workshops

new experiments required and clarify what you have done in an itemized fashion. If for whatever reasons you are unable to perform an experiments requested by a reviewer try to explain why. Never be confrontational. If your paper is rejected, do not try to rebut unless you think the reviewers have been grossly unfair or wrong. Again, it is important to maintain good manners all along. The best tip is to improve the manuscript according to the reviewers' suggestions and submit it elsewhere. Be optimistic!

W4 Peer-review

7th September, 11:00-13:00 in Hall D **By Peter Karayiannis (Cyprus)**

During this workshop the importance of peer-review before publication of research articles in scientific and clinical journals, the process that is followed, the expectations of editors and authors, and the ethics of the process will be discussed and analyzed with audience participation.

W5 A Simple and Rapid Guideline for Diagnosis, Prevention and Control of Chronic Hepatitis B

7th September, 14:00-16:00⁻ in Hall D

By Mohammad Reza Hedayati-Moghaddam, Hosein Froutan (Iran) and Hosein Keyvani (Iran)

Target groups:

Specialists of infectious diseases
 General practitioners
 Medical students

Topics:

1. Who should be screened for chronic HBV infection?

- 2. What is a difference between chronic HBV infection and chronic Hepatitis B?
- 3. How can you interpret the results of HBV screening tests?
- 4. What should you do for a person with HBsAg positivity and normal ALT?
- 5. What should you do for a person with HBsAg positivity and elevated ALT?

W6 Sample Size Calculation for Clinicians

8th September, 08:30-10:00 in Hall D By Siamak Sabour (Iran)

At the end of the workshop, participants will be familiar with the principals of the sample size calculation in clinical researches. This workshop will be applied to the sample size calculation in clinical researches in accordance with the needs of academic staff and clinicians in research projects and student dissertations. The workshop has been organized as 60% theoretical aspects of sample size calculation and 40% practical issues using software.

W7 Brief Workshop on Systematic Review and Meta-analysis

8th September, 10:30-12:00 in Hall D

By Ali Kabir (Iran)

Review studies are necessary because of daily increasing of the literature. Systematic review, as a special type of review studies, assess all published and non-published studies and evaluate quality of related studies. Then, quantitative analysis of selected studies will be done to determine final idea of all scientists about a specific subject. It may also determine is there any controversy in the literature about the subject? Why such difference exist? Is that related to the quality of studies, place, time, etc? Such studies may be able to provide a final solution, guideline or help for scientists.

In this workshop, concept and necessity of systematic review studies, search strategy principles, study selection, quality assessment, meta-analysis concept and primary rules, data preparation and synthesis, drawing and inference of graphs and main commands for doing meta-analysis using Stata will be discussed. We hope be able to prepare an opportunity for interested students and researchers to run high-quality researches.

W8 Assessment of Autophagy and Autophagic Cell Death

8th September, 13:00-14:30 in Hall D **By Behzad Yeganeh (Canada)**

Autophagy is a highly conserved lysosomal dependent degradation and turn-over of long-lived proteins and organelles in the cell, which can be subjected to suppression or further induction in response to different stimuli. Autophagic cell death has been implicated in several pathologies including cancer, viral infections and neurodegenerative disorders resulting in new approaches to the treatment of such diseases. This workshop provides an overview of methodologies for assessment of autophagy both in vitro and in vivo as well as monitoring autophagy via numerous assays and approaches to measure autophagy in living cells and in mammalian tissue. It will include questions & answer sessions on autophagic gene knockdown approach used to the study autophagy as well as the measurement of the autophagosome microtubule, LC3B and lysosome recruitment during the autophagic process in numerous fields of cell biology.



Additional Day, 10th September, 2017

Birjand Hepatitis Conference

B1 Birjand Hepatitis Conference

08:15-10:15

Titles and Speakers:

•Management of Hepatitis B in 2017 Cihan Yurdaydin (Turkey), 30min

•Molecular Pathogenesis in Hepatitis C Virus-associated Liver Tumorigenesis Pascal Pineau (France), 30 min

•Hepatocellular Carcinoma and Role of Liver Transplantation *Bijan Eghtesad (USA), 30 min*

•Use of Data for Formulation of Public Health Policy - Case Study: HCV Homie Razavi (USA), 30 min

B2 Birjand Hepatitis Conference

11:00-12:50

Titles and Speakers:

•The Mechanisms of Action of Antiviral Drugs for Treatment of Hepatitis *Behzad Yeganeh (Canada), 30 min*

• Strategies to Decrease the Burden of Hepatitis B and C Seyed Moayed Alavian (Iran), 30min

•Management of HBsAg Inactive Carriers Hossein Poustchi (Iran), 20 min

•Vertical OBI, Myth or Truth? Seyed Mohammad Jazayeri (Iran), 15 min

•Vertical OBI in South Khorasan Davod Javanmard (Iran), 15min

B3 Birjand Hepatitis Conference

14:15-16:15

Titles and Speakers:

•Treatment of HCV Infection with DAAs in Iran Shahin Merat (Iran), 20 min

• Laboratory Diagnosis of Hepatitis Seyed Abdorahim Rezaei (Iran), 15 min • Fatty Liver and Cardiovascular Diseases Tooba Kazemi (Iran), 15 min

• Prevalence of Diabetes in People with Hepatitis B and Healthy People Azadeh Ebrahimzadeh (Iran), 15 min

•Hepatitis Vaccination Farshid Abedi (Iran), 15 min

• Panel of Hepatitis Prevention Moderator and Members, 40 min

BW1 How to Perform a Peer Review for a Journal Article?

By Behzad Yeganeh, 10th September, 16:45-18:15

BW2 Understanding a Meta-Analysis; Eating a Piece of Cake!

By Mohammad Saeid Rezaee-Zavareh, 10th September, 18:30-20:00

43

IMC

Additional Day, 10th September, 2017

Shiraz International Conference on Hepatitis

S1 Shiraz International Conference on Hepatitis

08:30-10:30

Titles and Speakers:

• Burden of Liver Diseases in Iran Kamran Bagheri Lankarani (Iran), 15 min

• Management of HBV in Adult Patients Mohammad Reza Fattahi (Iran), 15 min

•Upcoming Treatments of Hepatitis B Robert Gish (USA), 25 min

•Approach to Persistent Abnormal Liver Function Tests in Pediatric Age Group Mahmood Haghighat (Iran), 15 min

•How Autophagy and Unfolded Protein Response Affect Liver Response to HBV and HCV Infection? Saeid Ghavami (Canada), 25 min

• HEV: One Coin, Two Faces Mario Mondelli (Italy), 25 min

S2 Shiraz International Conference on Hepatitis

11:00-13:00

Titles and Speakers:

•The Contribution of Hepatitis C Virology to the Treatment of HCV Infection Jean Dubuisson (France), 25 min

• Management of Hepatitis C Peter Ferenci (Austria), 25 min

•Future Options in the Treatment of Chronic Hepatitis C in Non-Responding Patients Peter Karayiannis (Cyprus), 25 min

• When to Refer for Liver Transplantation Maryam Moeini (Iran), 15 min

•Challenges in Liver Cancer Therapy Massimo Colombo (Iran), 25 min

•Wrap Up

Kamran Bagheri Lankarani (Iran), 5 min

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Paper Poster Presentation Tour in Basic & Laboratory Science; 6th September, 09:00-17:00, Poster Hall

P6 COMPARISON OF DIAGNOSTIC VALUES OF THE FOURTH GENERATION ANTI HCV TESTS (INNOTEST HCV AB IV, DIASOURCE ANTI HCV ELISA V 4.0) WITH THIRD GENERATION ANTI HCV TESTS, by Recep Kesli

P33 INVESTIGATION OF DIAGNOSTIC VALUES OF DIFFERENT ANTI HCV REACTIVES BASED ON IM-MUNOASSAY METHOD USED IN THE LABORATORY DIAGNOSIS OF HEPATITIS C INFECTION IN TUR-KEY, *by Recep Kesli*

P37 IMPACT OF HOST GENE POLYMORPHISMS ON SUSCEPTIBILITY TO CHRONIC HEPATITIS B VI-RUS INFECTION, *by Bita Moudi*

P38 CCR5, MCP-1 AND VDR GENE POLYMORPHISMS ARE ASSOCIATED WITH THE SUSCEPTIBILITY TO HBV INFECTION, *by Bita Moudi*

P39 THE RELATIONSHIP BETWEEN LAMC1 GENE POLYMORPHISM AND SUSCEPTIBILITY TO THE CHRONIC HEPATITIS B VIRUS INFECTION IN AN IRANIAN POPULATION, *by Bita Moudi*

P40 POLYMORPHISMS OF SURVIVIN GENE AND ITS PROTEIN EXPRESSION ARE ASSOCIATED WITH CHRONIC HBV INFECTION IN IRANIAN POPULATION, *by Bita Moudi*

P41 ASSOCIATION OF TNF-A GENE POLYMORPHISMS WITH THE OUTCOMES OF CHRONIC HEPATI-TIS B INFECTION IN IRANIAN POPULATION: LOOKING AT THE PROTEIN LEVEL, *by Bita Moudi*

P42 INTERFERON GAMMA GENE POLYMORPHISMS AND CHRONIC HEPATITIS B INFECTIONS IN AN IRANIAN POPULATION, *by Bita Moudi*

P57 A META-ANALYSIS FOR TUMOR NECROSIS FACTOR-A POLYMORPHISMS AND RISK OF HEPA-TOCELLULAR CARCINOMA, *by Shahnaz Sali*

P60 EFFECTS OF CURCUMIN ON NF-KB SIGNALING PATHWAY IN HEPATITIS B VIRUS INFECTION, by AmirReza Hesari

P61 MICRORNAS AND HEPATITIS C VIRUS: BIOMARKERS, FUNCTIONS AND THERAPY, by AmirReza Hesari

P62 NEW OPTIONS FOR CHRONIC HEPATITIS B VIRUS INFECTION TREATMENT: \" MANIPULATION OF REGULATORY CELLS' RESPONSES \", *by Soheil Tavakolpour*

P66 EVALUATION OF HBV RESISTANCE TO TENOFOVIR IN PATIENTS WITH CHRONIC HEPATITIS B USING ZNA PROBE ASSAY IN KERMAN, SOUTHEAST OF IRAN, *by Hamid Reza Mollaei*

P91 HAPLOTYPE ANALYSIS OF THE INTERLEUKIN-1 GENE CLUSTER POLYMORPHISM IN THE CHRONIC HEPATITIS B VIRUS INFECTION, *by Bita Javan*

P105 ABSENT OF HBV PROTECTIVE CCR5-DELTA32 MUTATION IN THE SOUTHERN KHORASAN POPULATION (EAST OF IRAN), *by Hamidreza Safari*

P117 ASSOCIATION OF IL-28B RS12979860 C/T AND RS8099917 T/G HAPLOTYPE WITH HEPATITIS C INFECTION OUTCOME IN IRAN: SPONTANEOUS CLEARANCE VERSUS CHRONIC INFECTION, by Jamal Sarvari

P122 APTAMERS AGAINST HEPATITIS C VIRUS: A REVIEW ARTICLE, by Amir Shamshirian

P123 COMBINED EVALUATION OF AFP, CA15-3, CA125 AND CA19-9 TUMOR MARKER IN PATIENTS WITH HEPATITIS B AND C, *by Sara Yeganeh*

P125 ANTI-CANCER EFFECTS OF ADMINISTRATION OF TILORONE DIHYDROCHLORIDE ON THE HEPA1-6, MOUSE HEPATOMA, CELL LINE, *by Mahsa Alem*

P130 RELATION BETWEEN IFN-Y POLYMORPHISM AND THE OUTCOME OF HEPATITIS B INFECTION IN AN IRANIAN POPULATION, *by Mohammad Sadegh Naghizadeh*

P139 VIRAL LOAD IS ASSOCIATED WITH SERUM ADENOSINE DEAMINASE AND ORNITHINE DECAR-BOXYLASE LEVEL IN PATIENTS WITH GENOTYPE 3A HEPATITIS C INFECTION, *by Galia Amirbozorgi*

P140 ASSOCIATION OF INTERLEUKIN 18 GENE SINGLE NUCLEOTIDE POLYMORPHISM (RS360719) WITH CHRONIC HEPATITIS B VIRUS INFECTION, *by Haleh Sarrafnia*

P160 DESIGN AND DEVELOPMENT OF A ONE STEP TAQMAN REAL TIME RT-PCR ASSAY TO QUAN-TIFY HEPATITIS C VIRUS RNA, *by Fahimeh Ranjbar Kermani*

P168 RESISTANT ASSOCIATED VARIANTS (RAVS) INVESTIGATION IN THE NAÏVE HCV PATIENTS, by Samira Salman-Tabar

P171 EFFECT OF SILICON DIOXIDE NANOPARTICLES ON LIVER CYSTATIN ISOLATED FROM BUFFA-LO KIDNEY: AN IMPLICATION FOR LIVER DISEASES, *by Mohd Anas Shamsi*

P172 MUTATION FREQUENCY OF THE SW172* MUTANTS AMONG IRANIAN CHRONIC HBV PATIENTS WHO PARTIALLY RESPONDED TO LAMIVUDINE PLUS ADEFOVIR DIPIVOXIL THERAPY, *by Mostafa Ma-habadi*

P180 POTENTIAL OF PROBIOTICS AGAINST AFLATOXIN ABSORPTION IN CACO-2 CELLS, by Seyed Amir Behtash Ladan

P190 A NOVEL INDUCTIVE IMMUNOBIOSENSOR BASED ON MODIFIED MAGNETIC NANOPARTICLES FOR DETECTION OF HEPATITIS B SURFACE ANTIGEN, *by Elias Alipour*

P207 DEVELOPMENT OF AN ELECTROCHEMICAL IMMUNOSENSOR USING MAGNETIC BEADS FOR DETECTION OF HEPATITIS B SURFACE ANTIGEN, *by Sara Nourani*

P210 INVESTIGATION OF COVALLENT ATTACHMENTS BETWEEN STREPTAVIDIN AND ANTI- HEPA-TITIS B ANTIBODY USING DOCKING, *by Mostafa Sourian*

P215 ASSOCIATION STUDY ON HUMAN LEUKOCYTE ANTIGEN (HLA-DPB1) POLYMORPHISM RS1042151 IN IRANIAN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION, *by Shahrzad Shoraka*

P217 LACK OF ASSOCIATION BETWEEN INTERLEUKIN-21 GENE POLYMORPHISM (RS3117229) AND CHRONIC HEPATITIS C VIRUS INFECTION, *by Shahrzad Shoraka*

P218 ANALYSIS OF BASELINE RESISTANCE-ASSOCIATED VARIANTS (RAVS) IN HCV-INFECTED GENOTYPE 1A TREATMENT-EXPERIENCED PATIENTS, *by Ali Namvar*

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Electronic Poster Presentation Tour in Basic & Laboratory Science, Moderated by Dr. Hadi Karimzadeh; 6th September, 13:30-15:00, Poster Hall

E36 COMBINED USE OF HEAT-SHOCK PROTEIN 70, GLYPICAN-3 AND GLUTAMINE SYNTHETASE IN DIAGNOSIS OF HBV-RELATED HCC, by Bita Moudi, 7 min

E56 MUTATIONS AT NUCLEOTIDE 1762, 1764 AND 1766 OF HEPATITIS B VIRUS X GENE IN PATIENTS WITH CHRONIC HEPATITIS B AND HEPATITIS B RELATED CIRRHOSIS, *by Farzanhe Salarnia, 7 min*

E58 THE COMPARISON OF ISG15 GENE EXPRESSION IN PBMCS OF CHRONIC ACTIVE AND INAC-TIVE CARRIER HEPATITIS B INFECTED PATIENTS WITH HEALTHY INDIVIDUALS, *by Seyed Mohammad Ali Hashemi, 7 min*

E59 THE COMPARISON OF USP18 GENE EXPRESSION IN PBMCS OF CHRONIC ACTIVE AND INAC-TIVE CARRIER HEPATITIS B INFECTED PATIENTS WITH HEALTHY INDIVIDUALS, *by Seyed Mohammad Ali Hashemi, 7 min*

E67 THE ASSOCIATION OF NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE POLYMORPHISM WITH MARKERS OF HEPATIC INJURY AND DE NOVO LIPOGENESIS IN NONALCOHOLIC FATTY LIVER DIS-EASE, *by Bahareh Amirkalali, 7 min*

E93 NO ASSOCIATION OF PD-1.3 G/A AND PD-1.5 C/T HAPLOTYPE WITH OUTCOME OF HEPATITIS C VIRUS INFECTION IN SOUTHWEST OF IRAN, *by Jamal Sarvari, 7 min*

E132 TLR7 GENE EXPRESSION IN CHRONIC RESPONDER AND NON-RESPONDER HEPATITIS C PA-TIENTS, *by Razieh Dowran, 7 min*

E166 IN SILICO INVESTIGATION OF THE ATP7B PROTEIN: INSIGHTS FROM THE ROLE OF RCCS MU-TATION THAT EFFECT ON PROTEIN STRUCTURE AND FUNCTION, *by Abdorrasoul Malekpour, 7 min*

E213 DESIGN OF POLY EPITOPE PROTEIN-BASED VACCINE FOR HCV CORE PROTEIN, HBSAG AND POLIO VP AND ANALYSIS OF ITS IMMUNOREACTIVITY IN DENDRITIC CELLS, by *Armina Alagheband Bahrami*, 7 min

Paper Poster Presentation Tour in Epidemiology of Liver Diseases; 7th September, 09:00-17:00, Poster Hall

P29 SURVIVAL ANALYSIS OF LIVER TRANSPLANT PATIENTS WITH PORTAL VENOUS THROMBOSIS: A REPORT FROM SHIRAZ, IRAN, *by Behnam Honarvar*

P34 DETECTION OF SEROPOSITIVITY RATES OF BLOOD-BORNE VIRUSES AMONG DENTISTS IN PROVINCE OF AFYONKARAHISAR, *by Recep Kesli*

P44 FREQUENCY OF HEPATITIS D VIRUS INFECTION IN CHRONIC HEPATITIS B PATIENTS IN ARAK, by Masoomeh Sofian

P49 HEPATITIS B VACCINATION COVERAGE AND HEPATITIS B SURFACE ANTIBODY IN IRANIAN PREGNANT WOMEN: A SYSTEMATIC REVIEW AND META-ANALYSIS, *by Milad Azami*

P53 ASSESSMENT OF RISK FACTORS IN PATIENTS WITH CHRONIC HEPATITIS B REFERRED TO DR.LABBAFI NEJAD'S HOSPITAL HEPATITIS CLINIC 2012-2014, *by Sara Abolghasemi*

P65 EVALUATION OF THE FREQUENCY OF PRECORE/CORE MUTATION IN PATIENTS WITH CHRONIC HEPATITIS B, KERMAN, SOUTHEAST OF IRAN, *by Hamid Reza Mollaei*

P68 HEPATITIS E VIRUS AND SERUM LEVEL AMINOTRANSFERASES IN BLOOD DONORS, *by Abdolreza Sotoodeh*

P69 TT VIRUS INFECTION IN SOUTH IRANIAN VOLUNTEER BLOOD DONORS, by Abdolreza Sotoodeh

P72 PREVALENCE OF HEPATITIS C VIRUS IN IRANIAN DRUG ABUSERS, by Nastaran Norouzi Parashkouh

P73 CORRELATION BETWEEN HUMAN DEVELOPMENT INDEX AND HBV/HCV RATE IN THE EU IN 2012, by Maryam Mirzaei

P78 THE DOMINANT PREVALENCE OF HBV GENOTYPE D AMONG INFECTED PATIENTS FROM SOUTHERN OF IRAN, by Seyed Younes Hosseini

P82 IMMUNITY TO HBV IN TABRIZ, HIV POSITIVE PATIENTS, by Golamreza Gahremani

P83 IMMUNE RESPONSE TO HEPATITIS B VACCINE AMONG NORTH IRANIAN HEALTHCARE WORK-ERS AND ITS RELATED FACTORS, *by Fariborz Mansour-Ghanaei*

P84 NEEDLE STICK INJURIES AMONG HEALTH CARE WORKERS; WHY NOT TO REPORT? *by Farahnaz Joukar*

P87 EXPLANATION OF LOCAL COMMUNITIES' VIEWS ON HEPATITIS IN ILAM CITY: A QUALITATIVE STUDY, by Milad Borji

P89 PREVALENCE OF HEPATITIS C VIRUS INFECTION AMONG BLOOD DONORS IN BUSHEHR PROV-INCE, *by Reza Taherkhani*

P100 THE PREVALENCE OF HEPATITIS B SURFACE ANTIGEN AND HEPATITIS C VIRUS IN REFER-RING TO IMAM REZA HOSPITAL, SIRJAN FROM APRIL TO NOVEMBER 2016, *by Mojtaba Rahim nezhad*

P106 PREVALENCE OF HEPATITIS C VIRUS INFECTION AND ASSOCIATED RISK FACTORS AMONG PEOPLE WHO INJECT DRUGS IN KERMANSHAH, IRAN, *by Asaad Sharhani*

P107 THE PREVALENCE OF HEPATITIS B IN MARRIAGE APPLICANTS IN ZABOL IN 2011-2012, by Khalil Shahriari **P109** HEPATITIS B, HEPATITIS C, AND HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN MULTI-TRANSFUSED THALASSEMIC PATIENTS, KERMANSHAH, IRAN, 2015, *by Maryam Foroughikia*

P112 IDENTIFYING AND ASSESSING THE IMPROVEMENT SCALE OF INFECTION- CONTROL CRITERION FOR HEPATITIS B VIRUS IN REGARD TO THE KNOWLEDGE, ATTITUDES AND PREVENTIVE HEALTH BE-HAVIORS, *by Sedigheh Sameti*

P113 REPORT OF OCCUPATIONAL EXPOSURE AND COVERAGE OF HEPATITIS B VACCINE IN HEALTH CARE WORKERS, by Mahnaz Mohammadpouri

P114 HEPATITIS B IN EXPOSED HEALTHCARE WORKERS: PREVALENCE, HBS ANTIBODY AND REASON OF INJURY, *by Zhaleh Zeinali*

P121 PREVALENCE AND RISK FACTORS OF HEPATITIS B IN A LARGE MILITARY POPULATION, by Saeed Soleiman Meigooni

P126 LIVER CANCER MORTALITY AT NATIONAL AND PROVINCIAL LEVELS IN IRAN BETWEEN 1990 AND 2015: A META REGRESSION ANALYSIS, *by Negar Rezaei*

P128 PREVALENCE OF HEPATITIS D VIRUS INFECTION IN INDIVIDUALS WITH HEPATITIS B SURFACE ANTIGENEMIA IN MASHHAD, NORTHEAST OF IRAN, *by Sanaz Ahmadi Ghezeldasht*

P136 PREVALENCE OF HEPATITIS E VIRUS INFECTION AMONG PREGNANT WOMEN IN BUSHEHR PROV-INCE, SOUTH OF IRAN, *by Reza Taherkhani*

P138 PREVALENCE OF HEPATITIS B VIRUS INFECTION IN A REPRESENTATIVE SAMPLE OF DIABETIC PATIENTS RESIDENT IN BUSHEHR PROVINCE, SOUTH OF IRAN, *by Fatemeh Farshadpour*

P143 INTRAFAMILIAL SEROPOSITIVITY OF HEPATITIS IN PATIENTS WITH HEPATITIS B AND C VIRUS IN HEPATITIS CLINIC IN HAMADAN, IRAN, *by Leila Seddigh*

P152 HBSAG, ANTI-HBS, ANTI-HAV IGG AND ANTI-HCV SEROPREVALENCE OF THE PATIENTS WHO HAS APPLIED TO AFYONKOCATEPE UNIVERSITY ANS APPLICATION AND RESEARCH HOSPITAL FOR THE LAST FIVE YEAR, *by Recep Kesli*

P153 PREVALENCE AND RISK FACTORS OF HEPATITIS D INFECTION AMONG INTRAVENOUS DRUG US-ERS, 2016, *by Behnoosh Eshraghi Mosa Abadi*

P156 A SYSTEMATIC REVIEW AND META-ANALYSIS FOR ESTIMATION OF OCCULT HEPATITIS B VIRUS INFECTION PREVALENCE AMONG DIFFERENT POPULATION OF IRAN, *by Mohammad Reza Hedayati-Moghaddam*

P163 SEROPREVALENCES OF THE ANTI HAV IGM/IGG, HBSAG, ANTI-HBS, AND ANTI HCV IN PATIENTS APPLIED TO AFYON KOCATEPE UNIVERSITY ANS APPLICATION AND RESEARCH HOSPITAL IN PROVINCE OF AFYONKARAHISAR, TURKEY (2012-2017), *by Recep Kesli*

P167 SYSTEMATIC REVIEW OF HEV SEROPREVALENCE AMONG EMRO AND MIDDLE EAST COUNTRIES, by Mohammad Hadi Karbalaie Niya

P184 BURDEN OF HEPATITIS IN IRAN FROM 1990 TO 2015, by Hossein Mirzaei

P185 INVESTIGATING THE STATUS OF IMMUNITY AGAINST HEPATITIS B IN THE STAFF OF TEHRAN'S HEALTH CENTER IN 1394-1395, *by Maryam Hosseiny rad*

P191 THE ROLE OF TRAINING IN THE PREVENTION OF HEPATITIS IN THE COMMUNITY: AN OVERVIEW ARTICLE, *by Fateme Dashkhaneh*



P193 THE PREVALENCE OF HEPATITIS B SURFACE ANTIGEN AND HEPATITIS C VIRUS IN PEOPLE REFERRING TO DR.SHAFAZAND LAB, SIRJAN FROM MARCH TO JUNE 2017, *by Fateme Fathi*

P194 THE PREVALENCE OF HEPATITIS A SURFACE ANTIBODY AND THE RELATIONSHIP BETWEEN HAV AB AND THE ALT AND AST ENZYMES IN REFERING TO DR.SHAFAZAND LAB, SIRJAN, FROM MARCH TO JUNE 2017, *by Fateme Fathi*

P197 EFFICACY OF HEPATITIS B VIRUS VACCINATION ON IRANIAN PATIENTS WITH HEMOPHILIA AND THALASSEMIA, *by Toomaj Sabooteh*

P199 EVALUATION OF KNOWLEDGE, ATTITUDE AND BEHAVIOR OF ACTIVE DENTISTS IN THE HEALTH SYSTEM OF MASHHAD UNIVERSITY OF MEDICAL SCIENCES FOR PEOPLE WITH HEPATITIS B AND C (2017), by Ali Mohammad Hosseinpour

P204 CONTENT AND STRUCTURE ANALYSIS OF IRAN NOHEP SOCIAL NETWORK: NEW PERSPECTIVE FOR NEEDS ASSESSMENT, by Elham Maserat

P206 KNOWLEDGE AND ATTITUDE LEVELS TOWARD HEPATITIS B AMONG NURSING STUDENTS IN TREATMENT AND EDUCATIONAL CENERS OF URMIA UNIVERSITY OF MEDICAL SCIENCES, URMIA, IRAN, *by Nader Aghakhani*

P209 PREVALENCE OF HEPATITIS D VIRUS IN HEPATITIS B VIRUS INFECTED PATIENTS REFERRED TO SHAHID MOHAMMADI HOSPITAL IN BANDAR ABBAS, SOUTH OF IRAN, *by Mirzaali Nazarnezhad*

P214 EPIDEMIOLOGY OF HEPATITIS B & C DURING 2014- 2016 IN RAZAVI KHORASAN PROVINCE, by Seyyed hossein Hosseini

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50

T

Electronic Poster Presentation Tour in Epidemiology of Liver Diseases; 7th September, Moderated by Dr. Behzad Hajarizadeh, 11:00-13:00, Poster Hall

E25 CHANGES IN DITRIBUTION OF HCV GENOTYPES IN AHVAZ CITY, SOUTH-WEST OF IRAN, by Mojtaba Hamidi-Fard, 7 min

E28 NUTRITION PREDICTORS OF NAFLD: A COMPARATIVE STUDY IN SHIRAZ, SOUTHERN IRAN, by Behnam Honarvar, 7 min

E90 DECREASING TREND OF TRANSFUSION TRANSMISSIBLE HEPATITIS B VIRUS INFECTION IN SOUTH OF IRAN, *by Fatemeh Farshadpour*, 7 *min*

E108 HEPATITIS D VIRUS INFECTION IN KERMANSHAH, WEST OF IRAN: SEROPREVALENCE AND VI-REMIC INFECTION IN HBSAG POSITIVE POPULATION, *by Yosra Naderi, 7 min*

E111 DISTRIBUTION OF HEPATITIS C VIRUS GENOTYPES IN KERMANSHAH, WEST OF IRAN, *by Maryam Bahadori*, *7 min*

E124 EPIDEMIOLOGY OF HEPATITIS B IN GENERAL POPULATION OF IRAN FROM 2000 TO 2016 IN NATIONAL AND PROVINCIAL LEVELS: A META REGRESSION ANALYSIS, *by Negar Rezaei*, *7 min*

E145 HIV/HCV CO-INFECTION IN I.R.IRAN, CHALLENGES, POLICIES AND SOLUTIONS, 2017, by Katayoun Tayeri, 7 min

E183 THE DISTRIBUTION OF HEPATITIS B VIRUS GENOTYPES IN HAMADAN CITY, by Farid Azizi Jalilian, 7 min

E186 PREVALANCE OF HEPATITIS A, B AND C VIRUS INFECTION AMONG STREET URCHINS, by Sukran Köse, 7 min

E205 FREQUENCY OF HEPATITIS A VIRUS RNA IN RAW MILK SAMPLES FROM ZANJAN PROVINCE IN IRAN, *by Angineh Parsadanians, 7 min*

E208 PRE-TRANSPLANT MORTALITY PREDICTION OF PATIENTS WITH END-STAGE LIVER DISEASE: A COMPARATIVE STUDY BETWEEN MACHINE LEARNING METHODS AND THE TRADITIONAL MELD SCOR, by Sina Famouri, 7 min

E212 THE PRELIMINARY DATA OF THE IRANIAN LIVER CIRRHOSIS REGISTRY, by Ahad Eshraghian, 7 min

Paper Poster Presentation Tour in Clinical Hepatology; 8th September, 09:00-17:00, Poster Hall

P3 RELATIONSHIP BETWEEN SERUMAL LEVELS OF ALT, AST, FBS, ANTI FASCIOLA HEPATICA IGG AND NON-ALCOHOLIC FATTY LIVER DISEASE, *by Mohammad Taghi Ahady*

P14 THE EFFECT OF AEROBIC EXERCISE ON TNF-ALPHA AND ADIPONECTIN IN MILITARY MEN WITH NONALCOHOLIC FATTY LIVER, *by Alireza Shamsoddini*

P23 HCV IN CHILDREN, by Enayatollah Nematkhorasani

P24 OPIUM CONSUMPTION AND RISK OF LIVER FIBROSIS IN CHRONIC HEPATITIS B AND C, by Seyed Ehsan Asadi

P26 PAIN OR SUFFER IN HEPATITIS: A BIOPSYCHOSOCIAL MODEL OF PAIN SEVERITY, by Manijeh Firoozi

P46 VITAMIN D LEVELS IN DIFFERENT STAGES OF CHRONIC HEPATITIS B, by Shahnaz Sali

P51 HOW TO HEAL PATIENTS WITH B HEPATITIS THROUGH HOMEOPATHY, by Seyedaghanoor Sadeghi

P55 THE RELATIONSHIP BETWEEN REPRODUCTION TECHNIQUES AND LIVER DYSFUNCTION, CASE SERIES AND LITERATURE REVIEW, *by Neda Nozari*

P71 HEPATITIS B PREGNANT WOMEN AND HEALTH NEEDS, by Elham Ebrahimi

P88 COMPARING THE EFFECTS OF PENDER'S HEALTH BELIEF MODEL AND NURSING CARE AT HOME ON THE HEALTH OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: A RANDOMIZED CLINI-CAL TRIAL, *by Milad Borji*

P98 SPECIFIC IMMUNOTHERAPY IN HEPATOCELLULAR CANCER: A SYSTEMATIC REVIEW, by Nastaran Khalili

P101 IMPACT OF HIV INFECTION IN PATIENTS INFECTED WITH CHRONIC HCV, by Rasoul Baharlou

P110 HBV/HCV COINFECTION: A CHALLENGE IN TREATMENT OF CHRONIC HEPATITIS C WITH DI-RECTLY ACTING ANTIVIRALS, *by Maryam Bahadori*

P115 EFFECT OF PROBIOTICS AND PREBIOTIC ON ANTROPOMETRIC INDEX AND SERUM LIPID PRO-FILE IN ACUTE NON ALCOHOLIC FATTY LIVER FATTY LIVER DISEASES: A DOUBLE BLIND RANDOMIZED CLINICAL TRIAL, by Leila javadi

P116 THE SUSTAINED VIROLOGIC RESPONSE AND COMPLICATIONS OF PEG INTERFERON ALFA AND RIBAVIRIN IN IRANIAN PATIENTS WITH CHRONIC HEPATITIS C, *by Azadeh Laali*

P118 THE EXPERIENCES OF THE HEPATITIS B CARRIERS IN ADAPTATION WITH THE DISEASE: A QUALITATIVE STUDY, *by Ali Zabihi*

P119 A COMPARISON BETWEEN THE STANDARD PEGYLATED INTERFERON AND RIBAVIRIN REGI-MEN WITH AND WITHOUT VITAMIN B12 SUPPLEMENTATION ON SUSTAINED VIROLOGIC RESPONSE RATE IN CHRONIC HCV HEPATITIS IN IRAN, A RANDOMIZED CLINICAL TRIAL, *by Marjan Mokhtare*

P120 FREQUENCY AND RISK FACTORS FOR DRUG-INDUCED HEPATITIS IN TUBERCULOSIS AT TWO HOSPITALS IN TEHRAN DURING 2009-2015, *by Saeed Soleiman Meigooni* P133 EVALUATION OF HEMOGLOBIN OVERSATURATION IN CIRRHOTIC PATIENTS, by Ali Adib

P135 COGNITIVE FUNCTION IN IRANIAN PATIENTS WITH HEPATITIS C, by Zahra Amirsardari

P137 COMPARISON STUDY OF CAROTID INTIMA MEDIA THICKNESS IN NONALCOHOLIC FATTY LIVER AND CONTROL GROUP, by Tahereh Fakharian

P150 CHRONIC HEPATITIS B INFECTION AND PREGNANCY, by Farzaneh Gholamalian

P151 THE ASSOCIATION BETWEEN HEPATITIS INFECTION AND ORAL LICHEN PLANUS: REVIEW STUDY, *by Maryam Koopaie*

P158 ORAL MANIFESTATION OF HCV INFECTION (A REVIEW STUDY), by Maryam Koopaie

P164 TREATMENT RESPONSE RATES IN PAKISTANI HEPATITIS C VIRUS PATIENTS; CURRENT PROS-PECTS AND FUTURE CHALLENGES, by Muhammad Ali

P187 DETERMINING THE ASSOCIATION OF PROGNOSTIC FACTORS ON SURVIVAL OF LIVER CIRRHOSIS PATIENTS: A FRAILTY MODEL APPROACH, *by Elnaz Saeedi*

P188 ETIOLOGY OF HEPATIC CYSTIC HYDATIDOSIS IN BIRJAND, EASTERN IRAN, by Mehdi Karamian

P195 OUTCOME OF INACTIVE CARRIERS OF HBV IN 10 YEARS FOLLOW-UP IN IRAN, by Zahrasadat Seghatoleslami

P203 REGULATION OF HEPATIC FUNCTION BY CENTRAL FATTY ACIDS, by Sepideh Ghodousifar

Electronic Poster Presentation Tour in Clinical Hepatology, Moderated by Dr. Raika Jamali; 8th September, 11:00-13:00, Poster Hall

E5 APPLICATION OF SCALE MODEL FOR END – STAGE LIVER DISEASE TO PREDICT THE LIFE EX-PECTANCY OF PATIENTS WITH HEPATIC CIRRHOSIS AND PORTAL HYPERTENSION, AND HEPA-TORENAL SYNDROME TYPE II, *by Lukmonov Saidrakhim Nodirovich*, *7 min*

E12 FAMILIAL CLUSTERING OF NONALCOHOLIC FATTY LIVER DISEASE AMONG THE FAMILY MEMBERS OF NONALCOHOLIC STEATOHEPATITIS CIRRHOTIC PATIENTS, by Saiful Islam, 7 min

E64 INTERPRETATION OF SERUM VISFATIN LEVEL IN RELATION TO HEPATIC INJURY IS PROBA-BLY SEX DEPENDENT IN NONALCOHOLIC FATTY LIVER DISEASE, *by Bahareh Amirkalali, 7 min*

E86 CLINICAL STUDY ON HEPATOCELLULAR CARCINOMA IN BABYLON IRAQ, by Monem Makki Alshok, 7 min

E144 DIETARY PATTERNS IN RELATION TO NONALCOHOLIC FATTY LIVER DISEASE, by Ghazaleh Eslamian, 7 min

E154 THE STUDY OF STIGMA RATE IN PATIENTS WITH HEPATITIS B AND THE EFFECT OF COGNI-TIV EBEHAVIORAL THERAPY ON ITS REDUCTION IN BIRJAND CITY, *by Nasrin Riyahi, 7 min*

E196 INTRAMUSCULAR HEPATITIS B IMMUNOGLOBULIN AND ITS WITHDRAWAL AFTER A YEAR OF LIVER TRANSPLANTATION IN COMBINATION WITH LAMIVUDIN AND/OR TENOFOVIR IN PRE-VENTING HEPATITIS B REINFECTION AFTER LIVER TRANSPLANTATION, *by Ali Jafarian, 7 min*

E198 HIGH PREVALENCE OF THYROID PATHOLOGY IN INTERFERON-NAÏVE HEPATITIS C VIRUS PATIENTS IN PAKISTAN, *by Shan Elahi, 7 min*

HEPATITIS B VIRUS REACTIVATION DURING IMMUNOSUPPRESSIVE DRUG THERAPY: PREVENTION, DI-AGNOSIS AND TREATMENT

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Abstract

HBV persists in the body of all patients with infection, even those with evidence of serological recovery. Patients with serologic evidence of HBV infection (HBsAg-positive or anti-HBc-positive) are at risk for HBV reactivation if they receive immunosuppressive therapy. Hepatitis B virus reactivation (HBVr) after immunosuppressive therapy is associated with significant morbidity and mortality. All patients undergoing chemotherapy, immunosuppressive therapy, hematopoietic stem cell transplantation, or solid organ transplantation should be screening for active or prior hepatitis B viral infection by testing for hepatitis B surface antigen and the antibody to hepatitis B core antigen in serum. Presence of antibody to hepatitis B surface antigen (anti-HBs) may provide additional protection against reactivation.

Who is at risk for HBV reactivation:

1-Patients receiving chemotherapy: HBV reactivation has been described in patients receiving cancer chemotherapy for a variety of

Hematologic and solid tumors and in patients receiving chemoembolization for hepatocellular carcinoma and chemoradiation.

2-Patients being treated for autoimmune disorders

3-Patients undergoing transplantation: HBV reactivation can occur in patients who are HB-sAg-negative and undergoing solid organ or hematopoietic stem cell transplantation.

How to assess risk:

HBV serologic status

Individuals who are HBsAg-positive are at greater risk for HBV reactivation compared with those who are HBsAg-negative. HBsAg positive individuals who are hepatitis B e antigen (HBeAg)-positive and/or have high baseline levels of HBV DNA may be at highest risk. The most important risk factor for reactivation was a HBV DNA level of >105 copies/mL.Patients who have resolved infection (eg, HBsAg-negative, anti-HBc-positive) are also at risk for reactivation with immunosuppressive Therapy but this most occur in those receiving anti-CD20 agents (eg,rituximab) or bone marrow/hematopoietic stem cell transplant(reverse seroconversion). Reactivation was seven-fold higher among patients who were HBsAg-positive (38%) compared to those who were HBsAg-negative but anti-HBc-positive (5%). Type of immunosuppressive therapy

1-Anti-CD 20 agents: most experts believe that anti-CD20 agents are associated with the highest risk of HBV reactivation among immunosuppressive therapies. The frequency of reactivation may be less for HBsAg-negative patients receiving treatment for rheumatologic conditions. the "lower" risk may be related to differences in other concomitant immunosuppressive agents used in rheumatology versus oncology patients. 2-Glucocorticoids: HBV reactivation has occurred with both high-dose (>20 mg prednisolone daily), rapidly tapered regimens and moderate-dose (10-20 mg prednisolone daily), prolonged regimens(\geq 4 weeks). Despite the increase in viral replication, serum aminotransferases tend to decline.

3-TNF inhibitors: HBV reactivation is uncommon in those who are HBsAg-negative.

Therapy	HBsAg- Positive	HBsAg- Negative,
Anti-HBc-Positive		
Anti-CD20		
Hematopoietic stem cell transplantation	Very high	Moderate
High-dose corticosteroids*		
Other cytokine inhibitors (e.g., anti-CD52)	High	Low
Combination cytotoxic chemotherapy† (without corticosteroids)		
Anti-tumor necrosis factor		
Anti-rejection therapy for solid organ trans- plant recipients	moder- ate	Rare
Methotrexate		
Azathioprine	Low	Rare
Androgen deprivation therapy		
Estrogen and progesterone blockers	No known effect	No known effect

very high risk could be considered to be in excess of 20%, high in the 11%- 20% range, moderate somewhere between 1% and 10%, and low less than 1%.

*high-dose(>20 mg prednisolone daily)

Clinical manifestations of reactivation: Most patients with HBV reactivation are asymptomatic, Severe flares can be associated with jaundice, hepatic decompensation, and death; poor outcomes are more likely to occur in patients who have underlying cirrhosis.

Diagnosis of reactivation: HBV reactivation is diagnosed when a patient with serologic evidence of HBV has:1- A detectable HBV DNA level when ************************************

Abstracts-Invited Speakers

they previously had undetectable HBV DNA.2- A rise in HBV DNA of more than 2 log10 international units/mL in patients who had HBV DNA present at baseline.3- Reverse seroconversion (when a patient previously HBsAg-negative/anti-HBc-positive becomes HBsAg-positive).

Treatment of HBV reactivation: Antiviral treatment with Tenofovir or Entecavir(Interferon should never be used) is recommended for all patients who develop HBV reactivation and who are treatment-naïve. Lamivudine should only be used when these first-line agents are not available. Among those who are asymptomatic, the goal is to prevent a flare of their disease. Tenofovir is prefered, rather than entecavir, for patients who received prior lamivudine therapy. If antiviral therapy is not started, these patients must be monitored closely.

Prevention of Hepatitis B Virus Reactivation: Prophylactic (starting antiviral therapy prior to or at the same time as starting chemotherapy) is more effective than preemptive (starting when viral levels begin to rise) antiviral therapy in preventing HBV reactivation. Prophylaxis is associated with an 87% relative risk reduction of reactivation and an 84% relative risk reduction of HBV associated hepatitis flares.

The decision to administer preventive therapy depends upon the level of risk:

•Moderate to very high risk: Most experts agree that antiviral therapy should be administered concurrently or prior to initiating immunosuppressive therapy to patients who are at moderate to very high risk of HBV reactivation. for patients with a high baseline serum HBV DNA level (eg, >4 log10 international units/ml), we prefer to delay immunosuppressive therapy until the HBV DNA level is suppressed

to <3 log10 international units/mL.

•Low risk or very low risk: Monitoring HBV DNA levels during immunosuppressive therapy for early detection and treatment of HBVr.

Duration of treatment: Most studies have continued therapy for 3 to 6 months after the last cycle of chemotherapy, though many experts favor continuing for up to 12 months when anti-CD20 is used. In addition, certain HBsAg-positive patients (eg, those with a baseline HBV DNA >2000 international units/mL or evidence of cirrhosis) may need prolonged treatment.

HBV FLARE: A HBV flare is typically defined as a rise in aminotransferases with an alanine aminotransferase (ALT) that is at least three to five times the baseline value and beyond the reference range. Patients with a flare secondary to HBV reactivation should have an increase in the ALT level that is consistent with a flare and evidence of HBV reactivation.

Differential diagnosis:

- •Acute HBV
- •Immune clearance phase of chronic HBV
- •Emergence of drug-resistance
- •Hepatotoxins
- Infection with other viruses
- •Other causes of liver disease

Management: Among patients experiencing a flare, antiviral treatment should be started as soon as HBV reactivation has been identified as the cause. The goal of antiviral therapy is to prevent progression to hepatic decompensation. After initiation of therapy, patients should be monitored closely. Aminotransferase levels and prothrombin time should be monitored at least monthly until the ALT becomes normal; after that,laboratory monitoring can be performed every three months.

EARLY DETECTION AND TREATMENT: We should monitoring patients at low risk or very low risk for HBV reactivation rather than administering preventive antiviral therapy. We obtain HBV DNA and liver chemistries while immunosuppressive therapy is being administered, and for six months after treatment is discontinued. The optimal frequency of monitoring has not been established; however, we determine the interval based upon the baseline

HBV DNA level:

• For patients with a detectable HBV DNA at baseline, we perform laboratory monitoring monthly.

•For patients with an undetectable HBV DNA at baseline, we perform laboratory monitoring every three months.

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T CELL THERAPY FOR MANAGE-MENT OF CHRONIC HEPATITIS B IN-FECTION

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Abstract

There is a big appetite in the field of viral hepatitis to develop an effective immune-based therapeutic approach. T helper cells play a central role in development and differentiation of virus-specific T cells with cytotoxic capacity. Strong Th1-type T cell response is associated with successful clearance of HBV infection. Th1 master transcription factors are T-bet and Eomes which trigger IFN-g production and cytotoxic activity. We previously showed the correlation between dysfunctional HBV-specific CD8 T cells and low expression of T-bet. Little is known about how the balance of T-bet and Eomes influences the CD8 and CD4 T cell response during the course of HBV infection. To determine the signatures of protective immune responses we need to characterize the transcriptional phenotype of T cells during acute and chronic HBV infection and investigate the functional signatures of the different transcriptional T-cell subsets. Therefore, patients with acute HBV (n=24), chronic HBV (n=45) and acute EBV infection (n=9) were enrolled. We analyzed the virus-specific CD8 and CD4 T cell response by using HLA-A02 and HLA-DRB01-restricted tetramers targeting immunodominant epitopes from the HBV core region (HBc 18-27 and HBc 61-80). We combined Enrichment-based Tetramer staining with intracellular assessment of transcription factors such as T-bet and Eomes. Intracellular cytokine staining (ICS) was performed after 3 days of in vitro culturing of peripheral blood mononuclear cells (PBMCs) with anti-CD3/CD28, antigen with or without rhIL-2 and rhIL-12 and anti PD-L1/2. Virus-specific T cells were also expanded by cultivating PBMCs at the presence of antigen for 10 days in various conditions including rhIL-2, rhIL-12 and anti-PD-L1/2 before staining for T-bet, Eo-

mes and Intracellular cytokines. From these studies we learned that T-bet and Eomes are highly expressed on virus-specific CD8 T cells during acute HBV but not during chronic HBV infection. Self-limiting infections are characterized by a high proportion of T-bet+Eomes+ and T-bet+Eomes-CD8 T cells which probably represent protective transcriptional phenotypes. Strong TCR stimulation by anti-CD3/28 induces T-bet and Eomes expression on CD8 as well as on CD4 T cells. T-bet+Eomes+ T cells selectively produce IFN- γ upon CD3/28 stimulation. We divided CD8 and CD4 T cells to high and low T-bet/Eomes expressing subsets. The [T-bet/Eomes] high cells are characterized by high Perforin and IFN- γ production, which was not observed in the T-bet and Eomes low expressing subset. IL-12 selectively induces this [T-bet+Eomes+] high subset of IFN producing T cells. HBV-specific CD8 T cell proliferation is especially generated from [T-bet+Eomes-] high and [T-bet+Eomes+] high cells. These cells can be generally induced by PD-L1/2 blockade up to 55% of tetramer positive CD8 T cells.

Conclusions: T cell differentiation through regulation of transcription factors such as T-bet and Eomes will represent a unique chance for prospective immuno-based antiviral treatment strategies against chronic HBV infection.

NUC THERAPY OF HEPATITIS B: THE LONG TERM CONSEQUENCES

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Abstract

Roughly 240 million people are chronically infected by the hepatitis B virus (HBV) facing the risk of progression to cirrhosis, clinical decompensation, hepatocellular carcinoma and liver related deaths. To stop progression of liver disease, international societies recommend either a short course of pegylated :

Abstracts-Invited Speakers

58]]]]]

interferon(in carefully selected patients) or the long-term administration of third generation nucleot(s)ide analogs(NUCs) like entecavir (ETV), and tenofovir disoproxil fumarate (TDF). Recently, a new tenofovir endowed with less renal toxicity, tenofovir alafenamide (TAF), has been licensed. Permanent suppression of HBV aimed to prevent progression of infection to end-stage liver disease and anticipated liver-related death may be attained with long-term treatment with the ETV and TDF as these regimens cause universal virological and biochemical remission, histological improvement and prevention or reversal of liver decompensation. However, despite HBV suppression, hepatocellular carcinoma remains a threat particularly for cirrhotic patients and those with additional risk factors, including male sex, advanced age, elevated alfa-fetoprotein, metabolic syndrome and alcohol abuse. The survival of a large cohort of Caucasian patients treated for 5 years with ETV or TDF, was excellent (>95%) with a significant proportion of deaths coming from liver unrelated causes. Liver cancer development stands as a major factor affecting the overall mortality and the only factor affecting liver related mortality in such patients. While TDF monotherapy suppresses viral replication in most patients with previous resistance to nucleoside analogues, ETV is effective in adefovir resistant patients who are lamivudine sensitive, only. NUCs are generally well tolerated, but clinical manifestations like myopathy, nephropathy, neuropathy, hepatic steatosis, pancreatitis, macrocytosis, hyperlactaemia and lactic acidosis have been described in few cases. Ten cases of TDF-associated Fanconi syndrome, an acute and severe form of proximal tubular toxicity, have been described while no cases have been linked to the administration of ETV. While TDF to ETV switch is the currently recommended strategy to rescue for this severe though rare complication, TAF could be an alternative strategy that requires validation. The need for long-term, perhaps indefinite, treatment is the main limitation of the NUCs therapy with possible associated costs, unknown long-term safety and the low rates of hepatitis B surface antigen (HBsAg) seroclearance. The latter remains the best stopping rule for NUCs-treated cirrhotic patients. The are several unmet medical needs which include stopping rules

for patients on long-term NUC who remain HBsAg seropositive and sensitive propensity scores to identify responders at risk of liver cancer, all considered useful in order to optimize surveillance in hyperendemic regions.

TREATMENT OF HEPATITIS B WITH PEGYLATED-INTERFERON-BASED REGIMENS

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Abstract

Current treatment of chronic hepatitis B (CHB) consist of treatment with nucleos(t) ide analogs (NAs) and interferon based treatments. While the former treatment is attractive due to negligible side effects and potent antiviral efficacy in all treated patients, prolonged and may be indefinite treatment duration is required since the aim of NA treatment is to keep the infection under control and not target cure. Interferon treatment is still being considered for the treatment of chronic hepatitis B due to its finite treatment duration and the potential of leading to sustained off treatment viral response. It is a treatment option where at least a functional cure can be targeted in a subgroup of patients receiving treatment. Due to its antiviral and immunomodulatory properties. Preclinical studies reveal that interferon alpha may be effective at every step of the HBV life cycle including HBV cccDNA degradation where molecular mechanisms of epigenetic repression by interferon alpha have been elucidated by several groups. Pegylated interferon (peg-IFN) enabling once weekly dosing due to better pharmacokinetics is used today. In general, the drawbacks of peg-IFN therapy are side effects on the one hand and genotype dependent efficacy on the other. However, the realistic surrogate marker of treatment efficacy in HBeAg-positive CHB, HBeAg seroconversion is more durable with

IFNs than with NAs. In HBeAg-negative CHB, peg-IFN treatment can be seen as efficacious when six months post-treatment HBV DNA is below 80IU/mL which can be achieved in around 20% of patients, depending on genotype. Such patients are likely to clear HBsAg on long-term follow-up and to lead to functional cure whereas this is not observed with NAs. Combination of peg-IFN with NAs using very different approaches have been studied in numerous studies. Superiority over peg-IFN monotherapy was only marginal and not conclusive and the current guidelines do not recommend combination therapy outside clinical trials. The optimal way of using peg-IFN therapy in CHB today should rely on on-treatment assessment of efficacy with serum HBV DNA and quantitative HBsAg determinations in both HBeAg-positive and HBeAg-negative CHB.

NEW TREATMENTS FOR HBV: WHAT IS THE PATHWAY FOR DRUG DEVEL-OPMENT?

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Abstract

Chronic hepatitis B (CHB) is the world's most common serious liver infection1 and is a widespread global health issue that is under-diagnosed and under-treated. CHB will progress in about a third of untreated patients, causing liver damage, cirrhosis, liver transplant and hepatocellular carcinoma (HCC) as well risk of death. Although hepatitis B virus (HBV) infection is not currently curable, it can be effectively controlled (defined by DNA undetectable) using pegylated interferon-alpha $(pegIFN-\alpha)$ and/or one of the two nucleos(t) ide analog (NUC) antivirals (entecavir or tenofovir) in sequence or combination or as a single therapy. Determination of which therapy to use and which approved combination includes careful consideration of duration of treatment, stopping rules, drug efficacy, use

of quant(s)Ag, potential side effects and potential for antiviral resistance with NUCs. PegIFN- α has the advantage of a fixed duration of therapy with the option of response-guided therapy based on HBsAg levels and can be an ideal option for some patients with high ALT and medium to low DNA noting that less than 20% of patients have a durable response defined by HBV DNA being undetectable. While resistance can be a limiting factor for the long-term use of early 2nd and 3rd level NUCs such as lamivudine, telbivudine and adefovir, more recent first line agents (entecavir and tenofovir) have very high barriers to resistance and are the dominant recommended therapies worldwide and the emergence of resistant variants in patients treated with these agents has been extremely rare. TDF has a risk of bone and renal injury and has led to a safer prodrug TAF that is liver targeting at a lower dose. Treatment is now indefinite for most patients (with treatment termination defined by loss of sAg in patient with HBV DNA <LOQ). Importantly, entecavir and tenofovir, are able to maintain extended virologic control over several years, in compliant patients, resulting in histologic improvement over time and leading to a significantly reduced risk of cirrhosis, death, liver transplant and HCC are supported by moderate quality grade criteria. There is also evidence that hepatic cccDNA levels can be modestly decreased with NUC therapy there is no cccDNA clearance. The success of long-term NUC treatment prompts new questions for future treatment strategies. Is it possible to permanently eliminate HBV infection with therapies that specifically target the cccDNA pathway or should we be aiming to achieve a "functional cure" using HBsAg elimination as an endpoint as the ultimate maker that we are changing outcomes? What is the new role for HBV RNA and HBcrAg testing? Will there be a role for FNA and liver sampling for cccDNA and intracellular intermediates of HBV replication including HBV pgRNA and mRNA testing? Many clinicians and scientist believe the answer is "yes" to each and all of these questions, but the use of new technologies and anti-viral tools including iRNA, anti-sense, blocking viral entry, inhibiting viral release, using cellular mechanisms of viral replication such as cyclophilins, capsid inhibitors, anti-sense, release inhibitors, gene edit-

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Abstracts-Invited Speakers

ing and new immune modulators including PDL1 antagonists, TLR7 and 9 agonists, epigenetic modifiers, vaccines with adjuvants and extended preS1 epitopes. The new tools that can attack the virus in the nucleus by CRSPR-Cas9, change histones and modify acylation patterns may also lead to viral clearance. Ultimately, we need to next clear HBsAg, then clear cccDNA and finally clear all cells with HBV DNA integration (which can produce viral intermediates) and prevent HBV integration from occurring in those patients with early phases of disease. The new therapies need to target multiple sites in the HBV genome and /or the immune system. The major concept moving forward with HBV therapeutics is the use of new combination therapies, or new therapies in sequence. The new Guidelines from APASL, AASLD and EASL will guide current therapy application, but are place holders while we need to further suppress virus, stop the regeneration of cccDNA, clear cccDNA directly and awaken the sleeping giant: the immune system that will ultimately have the final "word" in viral control and clearance. One-shot, single drug therapy is the "pie-in the-sky", realistically this next phase in the search for the grail of HBV therapeutics will require an integrated approach with pharma, clinicians and scientists. We now have the attention of the investment community that see HBV as the new "C". Now let's have the WHO, CDC and all a governments join with Pharma, advocates and researchers in the fight to eliminate HBV from the world.

THE GLOBAL BURDEN OF HEPATI-TIS B

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Abstract

Introduction: HBV vaccination has had a dramatic impact on reducing HBsAg prevalence in the younger age cohorts while HBV treatment has been effective in slowing the progression of disease burden. However, adoption of birth dose and three dose vaccination varies across different regions and countries within regions.

Materials and Methods: To develop an estimate of the global burden of hepatitis B, the Polaris Observatory developed a dynamic model that took into account the impact of vaccination and treatment on prevalence and HBV related morbidity and mortality. Over a two year period, a literature search was conducted to identify all indexed and non-indexed publications reporting HBsAg prevalence. WHO HBV vaccination rates, by country, were also gathered. Each study was reviewed by two epidemiologists and scored. The findings were then reviewed by a panel of experts in each country and updated based on their feedback. The inputs were used in the Markov model to forecast HBsAg prevalence in 2016 for each country.

Results: HBsAg prevalence and vaccination data were available in 120 countries. The weighted average prevalence estimates in each region were used to estimate the HBsAg prevalence in countries with missing data. The overall HBsAg prevalence was estimated at 291 million (255-350 million) corresponding to 3.9% (3.5-4.5%) prevalence. However, most of these infections were in the older age groups. Prevalence of HBsAg among five year olds was estimated at 1.6% (1.5-2.1%).

Conclusion: Hepatitis B vaccination has resulted in a significant drop in prevalence in younger age cohorts. However, birth dose vaccination is absent in most of the African region, and three dose vaccination rates are below 90% in many countries around the world. HBV elimination requires a wide scale effort to increase vaccination and prevention programs.

NON-INVASIVE DIAGNOSIS: FROM VIRAL HEPATITIS TO NAFLD

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Abstract

Liver biopsy, which was traditionally considered to be the "gold" standard for the staging of fibrosis in chronic liver disease, has been challenged over the past decade by non-invasive methods. These methods rely on two distinct but complementary approaches: a "biological" approach, based on the quantification of biomarkers of fibrosis in serum and a "physical" approach, based on the measurement of liver stiffness using elastography-based technologies for which transient elastograpy (TE) (FibroScan) (Echosens, Paris, France) has been the pioneer. Advantages of serum biomarkers include their high applicability (>95%) and good reproducibility. However, as none are liver specific their results can be influenced by co-morbid conditions and ALT levels. TE has the advantage of being a user's friendly procedure that can be performed at the bedside or in an outpatient clinic with high performance for detecting cirrhosis. However, its applicability is lower (80%) than that of serum biomarkers (particularly in case of ascites, obesity and limited operator experience) with the risk of false positive results in case of ALT flares. Nevertheless, TE is currently the most widely available and validated technique worldwide. Although non-invasive tests were initially developed in patients with chronic viral hepatitis (B and C), they are now increasingly used in patients with NAFLD, reducing the need for liver biopsy. In that respect, the recent availability on FibroScan of CAP (Controlled Attenuation Parameter), a technology allowing to grade hepatic steatosis, is an asset for assessing NAFLD. Finally, the use of non-invasive tests in clinical practice is now recommended by several international guidelines, including the EASL-ALEH Clinical Practice Guidelines.

HBV AND BURDEN OF HCC

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Abstract

Hepatitis B virus infection is a very common cause of chronic liver disease worldwide. In spite of nationwide vaccination of newborns against HBV virus since 1992, hepatitis B virus infection remains a very common cause of chronic liver disease in Iran which should be dealt with for at least the next 30-50 years. In total, Iran was classified within the low-intermediate HBV prevalence areas (2%-a4%), while according to recent data (after 2010), Iran was classified within the low HBV prevalence areas (< 2%), indicating that preventive measures conducted in Iran have been effective. According to systematic reviews and meta-analysis, it is estimated that 3% of Iranians are chronically infected with hepatitis B virus. However, the collected data was very heterogenic, even within a single province, which made it hard to estimate a single-point prevalence. HBV is a main cause of hepatocellular carcinoma. More than 70% of all new cases of liver cancer were diagnosed in Asia, a region that 75% of all those chronically infected with HBV in the world. The prevalence of this cancer is high in Eastern and South-Eastern Asia, But Middle Eastern countries are characterized as moderate prevalence rate of HCC region and central Asia and some part of Middle Eastern countries are known as low prevalence rate. There is an increase in the rate of hepatocellular carcinoma incidence in Iran. However, the rate of this increasing is not homogenous for all parts of country. Provinces with more medical facilities of Iran including Tehran (capital of the country), Razavi Khorasan in northeast of Iran, East Azerbaijan in north-west of the country, Isfahan in central part and near to Tehran, Khozestan and Fars in south and Mazandaran in north of the Iran, had an expected coverage more than their expectation. These provinces had significantly higher rates of hepatocellular carcinoma than their neighboring provinces which some of them indicated higher rate of HBV prevalence. According to a Bayesian analysis, it seems that, in years 2004 to 2008, there were 22%-47% under-estimation and misclassification of HCC incidence for those low facilitated

Abstracts-Invited Speakers

provinces including Sistan and balochestan, Hormozgan, Kogiloye and boyerahmad, etc, which also showed high prevalence of HBV. Besides, the rate of HCC mortality and YLL due to this cancer, moderately increased in recent year for Iranian patients and according to our prediction it seems that these rates are going to level off. Also HCC mortality and YLL was higher for older age and was considerably greater in men than in women. In conclusion, the incidence of HCC is still increasing and the mortality is level off, also accounting and correcting the regional misclassification is necessary for identifying high risk areas and planning for reducing the HCC burden. The main challenge which still infected patients with HBV in high prevalence provinces, which could corresponding to increasing the burden in future decades.

IS OBI THE FIFTH PHASE IN HBV NATURAL HISTOTY?

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Abstract

Recovery from acute hepatitis B virus (HBV) infection and spontaneous or antiviral treatment-induced loss of hepatitis B surface antigen (HBsAg in chronic infection, leads to the production of virus neutralizing anti-HBs antibodies. The longevity of this antibody as well as that of non-virus neutralizing antibodies such as anti-HBc (against core antigen) and anti-HBe (against e antigen) is variable over time. Individuals who are HBV DNA positive in liver tissue (mainly covalent closed circular DNA, cccDNA) and negative for HBsAg in serum with or without detectable anti-HBs but positive for anti-HBc, are thought to have "occult HBV infection" (OBI). 20% of OBI patients are seronegative for all HBV markers. A minority of cases are due to genomic mutations (surface escape mutants) that evade serological detection. The prevalence of OBI varies

depending on risk group and may constitute the fifth phase in the natural history of HBV infection, the others being the immune tolerant, immune clearance, inactive carrier and reactivation phases. Progression to phase 5 is not unidirectional or sequential and its establishment is largely controlled by the immune system and epigenetic control of transcriptional activation, or not of cccDNA, resident in hepatocyte nuclei. Thus low level replication of the virus may occur which is however kept in check by the host's immune defence mechanisms. In such cases however, overt infection may occur accompanied with seropositivity for HBsAg and active viral replication in individuals receiving immune suppressive drugs, cytotoxic treatments for malignancies or Direct Acting Antivirals against hepatitis C virus in co-infected individuals, all of which may tilt the balance in favour of the virus.

EXPERIMENTAL OBI IN THE WOOD-CHUCK HBV INFECTION MODEL

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Abstract

Molecular, pathogenic and oncogenic properties of woodchuck hepatitis virus (WHV) are highly compatible to those of HBV. Both viruses are hepatotropic but they also invade and propagate in the immune system. Woodchuck-WHV infection model significantly contributed to the understanding of the natural course, virological and immunological properties and pathological consequences of occult HBV infection (OBI). WHV invariably persists for life irrespective of whether infection is symptomatic and serologically detectable (i.e., serum HBsAg and HBV DNA reactive) or asymptomatic and serologically silent (i.e., occult; serum HBsAg negative and low HBV DNA positive). Two forms of occult hepadnaviral persistence were uncovered in the woodchuck-WHV model. Secondary occult

infection (SOI) that continues after resolution of acute hepatitis and apparent clearance of circulating WHsAg and is accompanied by antibodies to WHV core antigen (anti-WHc; an equivalent of anti-HBc in HBV infection) and low levels WHV DNA in serum, liver and immune system. The liver in SOI can display minimal to moderate inflammation with periods of normal morphology, nonetheless hepatocellular carcinoma (HCC) develops in up to 20% of animals. The related study confirmed that the detection of anti WHc alone, in the absence of serum WHsAg, is a reliable indicator of low-level WHV replication and assembly of infectious virus. Primary occult infection (POI) is another form of silent hepadnavirus persistence that was originally uncovered in offspring born to woodchuck dams convalescent from experimental acute hepatitis and then confirmed in animals infected with WHV doses lower than 103 virions. POI progresses in the absence of detectable serum WHsAg, anti-WHc and antibodies to WHsAg (anti-WHs), and biochemical and histological evidence of liver inflammation but trace WHV replication is detectable in the immune system and with time (2-3 years later) in the liver. WHV-specific T cell, but not B cell, response emerges, however, unlike in SOI, protective immunity against virus is not established in POI. Further, POI coincides with virus DNA integration into the host's genome and the persisting virus retains its liver pro-oncogenic potency. In this regard, 20% of animals with POI develop HCC. This strongly emphasizes a role for primary occult HBV infection in the pathogenicity of cryptogenic HCC in patients without past clinical evidence of hepatitis B. Other study showed that multiple intravenous injections with WHV doses causing POI (i.e., <103 virions) do not culminate in serologically detectable infection and hepatitis. This study also revealed that, although WHV-specific T cell response was mounted, no immune protection was induced, confirming that the virus-specific antibody response is essential in protection against reinfection with hepadnavirus. In summary, highly pathobiologically relevant and reproducible models of OBI in woodchucks were established. The expertise gained should facilitate investigations on the emerging aspects of OBI, including recognition of the mechanisms underlying reactivation of OBI and arise of severe hepatitis B and liver failure due to usage of some clinically highly valuable immunomodulatory, cytotoxic and anti-cancerous therapies and to test the efficacy of novel approaches aimed at eradication of HBV and OBI.

CHARACTERIZATION OF OBI PREV-ALENCE AMONG VACCINATED CHILDREN FROM ALBORZ GENER-AL POPULATION, IRAN; VERTICAL OBI, MYTH OR TRUTH?

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Abstract

Background: Occult hepatitis B infection (OBI) has been described in various clinical settings; however, studies on the prevalence of OBI among immunized general population are scarce.

Methods: 1200 sera samples obtained from children between 7 and 15 years old selected randomly from different schools located in Alborz Province, Iran, who already had completed doses of HBV vaccine according to standard schedule. None had received HBIg. All were checked by HBV serology and real time PCR. The parents of OBI-positive subjects were investigated by the same methodology.

Results: Mean age was 8.5 years old. All subjects were negative for HBsAg and anti-HBc. 548(46%) and 652 (%54) were responders (anti HBs >10IU/ml) and nonresponders (anti-HBs <10 IU/ml), respectively. One hundred individual from the group who contained low levels of anti-HBs were selected randomly to check the presence of HBV DNA. 27% (27/100) OBI were OBI- positive. Upon recalling of parents of OBI-infected children, 30 (64%) of either

mother or father were positive for OBI. None of parents were positive for HBsAg. 30.4% of OBI-positive parents had anti-HBc. We extended the same approach for another 320 samples (that never had been checked for HBV DNA). 59 cases (18%) were OBI- positive. We checked the parents and only one father of an index child that was positive in PCR.

Conclusion: HBV occult infection seems to be relatively frequent in immunized children from Alborz province. However, the initial HBV DNA positivity during childhood (vertical infection), does not necessarily indicate a prolonged persistence of HBV DNA (occult infection). Adequate levels of anti-HBs after vaccine following birth could eventually clear the virus as time goes by. Periodic monitoring of these children at certain time intervals is highly recommended.

ANTI-HBC (+) TESTS: GETTING TO THE CORE OF THE ISSUE

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Abstract

About 2 billion people have been infected with hepatitis B virus (HBV) as defined by anti-HBc (+). An estimated 257 million people are actively infected with chronic HBV (CHB). CHB-related complications result in approximately 686,000 deaths annually. CHB accounts for more than 50% of all hepatocellular carcinoma worldwide. When a non-immune person acquires this viral infection, after a 4-10 week incubation period, hepatitis B surface antigen (HBsAg) is detectable in the blood. Antibody to core antigen (anti-HBc) appears shortly thereafter. Anti-HBc is IgM (+), the first test to become positive in the disease process; IgG then appears in the serum a few weeks to a month later. Anti-HBc IgM titers in the serum disappear after 6-12 months with clearance of the infection or with chronic disease evolution. However, 2-3% of HBsAg (+) patients can have +anti-HBc with chronic

disease, with high replication and very active liver disease. Almeida first reported that anti-HBc is present in the serum of hepatitis B-infected patients in the convalescent state, with hepatitis B antibodies that were reacting with the nucleocapsid core but not with the outer surface component (HBsAg). Hoofnagle et al first demonstrated anti-HBc transfusion-associated hepatitis. At that time, they considered this biomarker to be a more sensitive indicator of persistent viral replication than the standard HBsAg test for screening blood samples. Cohen et al and others reported that anti-HBc IgM is reflective of acute HBV infection and anti-HBc IgG is reflective of long-term viral persistence. On the other hand, anti-HBc IgG also develops during acute infection and persists for life, irrespective of activity or chronicity of infection. Anti-HBc can be accompanied by either anti-HBsAg or anti-HBs; rarely, all three appear in the same patient, depending upon the status of the HBV. Hepatitis B core antigen (HBcAg) is the most immunogenic component of hepatitis B virus and, thus, high titers of anti-HBc are produced during acute and chronic disease. Titers of anti-HBc can be indicative of the disease state/phase of the patient. Since anti-HBc is considered the most sensitive and reliable marker of HBV exposure and HBV is an incurable disease, this test indicates the presence of persistent viral intermediates in the liver cell, with no need for vaccination but risk for reactivation. In addition, organ donation from anti-HBc (+) donors carries a substantial risk of HBV transmission, most importantly in liver organ donation. In western countries, with low HBV infection burden, 1-4% of the population is positive for anti-HBc alone (10-20% of all subjects with HBV biomarkers); 10% of those are positive for HBV DNA High sensitivity is needed for any epidemiological biomarker. The above mentioned characteristics of anti-HBc makes it the ideal biomarker for population-based HBV screening; by extension this biomarker can be used as a test for HBV exposure. The false positive rate, even in low risk populations, is probably 3/1000 patients tested. Anti-HBc along with HBsAg and anti-HBs can represent three distinct clinical scenarios.7 Anti-HBc along with HBsAg reflects current HBV infection. Anti-HBc along with anti-HBs represent previous infection

with "recovery"; there is no such term or condition as natural immunity. People who are anti-HBs-negative but positive for anti-HBc are a third group termed "anti-HBc alone/ only", presuming that they are not in the "window phase" of acute HBV infection; in the latter, anti-HBc IgM and HBV DNA would both be positive. When anti-HBc alone is positive, it could be reflective of occult HBV, a form of chronic hepatitis B carrier with undetectable levels of HBsAg/anti-HBs and a low level of HBV DNA; infection with an HBV (HBsAg) mutant must also be considered, or coinfection with other hepatoviruses.

OCCULT HEPATITIS B VIRUS INFEC-TION (OBI) IN IRANIAN BLOOD DO-NORS

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Abstract

About 2 billion people have evidence of past or present infection of HBV and 248 million of these are chronic carriers of HBV in worldwide. Most of the people currently living with HBV infection are persons that were born before hepatitis B vaccination. The Prevalence of HBV in Iran is around 2% in general populations. There was a significant and impressive drop in HBsAg prevalence from 0.73% in 2004 to 0.08% in 2016. Despite the above-mentioned measures, the occult hepatitis B infection is the main concern in blood safety due to transmission of the HBV via HBsAg seronegative blood components. Overall, a prevalence of occult HBV infection depends on; geographical region, a sensitivity of HBsAg kits, HBV DNA amplification methods and co infections with HCV/HIV. The gold standard assay for detection of OBI is sensitive HBV DNA amplification testing. The anti-HBc screening strategy may

prevent some HBV transmission by transfusion. Prevalence of anti-HBc rates among Iranian blood donors between 2.1 and 11.5 % has been reported. For blood detection of occult hepatitis B requires high sensitivity HBsAg screening (<0.1 ng/mL) or individual donornucleic acid testing (ID-NAT) with clinical sensitivity <4 IU/ml. HBsAg tests with high sensitivity (<0.1 ng/mL) are predicted to have a comparable yield to MP-NAT. The frequency of OBI is low in Iran. Prevalence of HBV DNA and OBI in HBsAg negative blood donors has been reported in most studies ranging from 0.0 % to 0.9 % among Iranian blood donors. The occult hepatitis B infection is the main concern in blood safety. Anti-HBc screening strategy in areas with high prevalence of anti-HBc affects the blood Supply. HBsAg with high sensitivity (<0.1 ng/mL) and individual NAT with clinical sensitivity <4 IU/ml requires for blood detection of occult hepatitis B.

AN UPDATE ON THE VIROLOGY AND MOLECULAR BIOLOGY OF HEPATI-TIS D VIRUS

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Abstract

Hepatitis D virus (HDV) is responsible for 15-20 million cases of chronic infection worldwide. It is a defective virus closely related to plant viroids and virusoids. The virus, which to-date remains unclassified, relies on hepatitis B virus (HBV) for the provision of its outer envelope which consists of hepatitis B surface antigen (HBsAg). This entails that both viruses utilize the sodium taurocholate co-transporting polypeptide as a receptor for cell entry. Its replication is unique among viruses in that it does so through use of the host RNA polymerase II and has other unique features such as ribozyme activity, RNA editing and rolling-circle RNA replication. The RNA genome of the virus is 1700 nucleotides long, circular :

Abstracts-Invited Speakers

in nature and of negative polarity. It forms a rod-like structure through extensive intramolecular nucleotide base -pairing. It contains a single open reading frame that encodes for the hepatitis D antigen (HDAg), which in turn forms the ribonucleoprotein core of the virus. In fact, two forms of HDAg are produced, the short and the long forms, through an RNA editing event, with unique roles in the replication cycle of the virus. Infection is through co-infection with both HBV and HDV or superinfection of chronic HBV carriers by HDV. Epidemiological studies indicate that HDV infection causes more severe chronic liver disease accompanied by more frequent progression to cirrhosis and hepatocellular carcinoma in comparison to mono-infection with HBV.

HDV CLASSIFICATION AND IMMU-NOBIOLOGY

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Abstract

Hepatitis D virus (HDV) infection affects millions of people worldwide. Only a very few number of patients are able to clear the virus. HDV isolates so far have been divided into eight major genotypes with different geographic distributions. We aimed to investigate whether the worldwide distributed HDV genotype-1 contains subtypes within the European isolates. The large Hepatitis Delta Antigen (L-HDAg) nucleotide sequences of 116 HDV genotype-1 isolates from this study were analyzed along with additional 570 sequences of HDV genotype 1-8 isolates retrieved from GenBank, NCBI. Phylogenetic analysis of selected L-HDAg sequences of European isolates was performed to identify plausible subtypes within HDV genotype 1. Pairwise genetic distances for L-HDAg sequences were calculated to estimate the inter-genotype and inter-subtype differences. The HDV genotype-1 isolates phylogenetically formed five distinct clusters (Genotype 1a-1e), each of them corresponding to a certain geographic region. Using the same approach, we identified for HDV genotype-2 and -4 distinct subtypes (i.e. -2a and -2b; -4a and -4b respectively). We could demonstrate so far that the defined genotypes 1-8 contain an inter-genotypic difference of $\geq 10\%$. Additionally, the newly defined subtypes show an inter-subtype difference of >3% to \leq 9%. The viral evolution can be also affected by the host immune response by developing new variants which are able to evade virus-specific T cells. Here, we investigated the role of CD8 T cell immune pressure in evolution of HDV and how they fail in eliminating this virus. In patients with chronic HDV infection, we detected escape mutations within the identified CD8 T cell epitopes which could lead to viral evolution and evasion from CD8+ T cell responses and possibly persistence of the virus. These results have important implications for the clinical prognosis of HDV infection and for the development of vaccines against HDV.

INTERFERON THERAPY OF CHRON-IC HEPATITIS D

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Abstract

Conventional antivirals aimed at directly inhibiting the replication of HDV are not efficacious in chronic hepatitis D (CHD), as the virus has no independent enzymatic outfit and relies on the replicative machinery of the hepatocyte. The only licensed therapy is alfa-interferon (IFN). The current recommended schedule is peg-interferon alfa (Peg-IFN) given weekly for 48 weeks; however, the optimal duration of treatment has not been established. Treatment is indicated in patients with active HDV disease; in patients with advanced cirrhotic disease, the expected benefits of therapy should be balanced against the adverse effects of Peg-IFN and the lower rate

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of response. The mechanism of action of IFN has not been determined. In vitro it has no effect on HDV-RNA, the virus may directly inhibit IFN α signaling; IFN appears to delay the entry of HDV into hepatocytes. Interferons have limited efficacy in CHD, they induce a sustained viral response (HDV-RNA clearance) in no more than 20-25% of the patients in the large HepNet International Delta Hepatitis Intervention Trial (HIDIT) 90 patients were randomly assigned to receive Peg-IFN plus adefovir, Peg-IFN plus placebo or adefovir alone. Overall 6 months post-therapy HDV RNA was negative in only 28% of patients given Peg-IFN, either alone or with adefovir, compared with only 8% of the patients given adefovir alone. In the HDIT 2 study of Peg-IFN monotherapy vs Peg-IFN plus tenofovir for 96 weeks, the combination treatment had similar efficacy and safety profiles compared to Peg-IFN alone. Relapses of HDV viremia and disease are frequent after apparently successful therapy, because very low titers of HDV, undetectable by current testing, can persist in the liver despite the apparent clearance of HDV-RNA. Elimination of the HBsAg is the most reliable end-point of therapy but this goal is seldom attained.To push for eradication of HDV, longterm therapy with Peg-IFN may be considered in patients who exhibit a significant decline of HBsAg during initial therapy.

UPCOMING TREATMENTS OF HEPA-TITIS D

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Abstract

Chronic hepatitis D (CHD) represents the only hepatotrop viral infection where new drugs have not entered clinical practice despite being the most severe form of chronic viral hepatitis. Current treatment with interferons is unsatisfactory. In the last 5 years new drugs

have been explored for the management of CHD. These drugs tailor various steps in the life cycle of HDV. However, as a general comment, it is clear that any management strategy leading to a functional or complete cure in HBV would be beneficial in CHD as well. After all, the ideal surrogate marker for effective treatment is HBsAg clearance and the reason we use quantitative HDV RNA testing as a surrogate in daily practice and not HBsAg clearance is that the latter is so rarely achieved. However, patients who have a lasting virologic response to treatment have a high chance of clearing HBsAg on long-term follow-up. In a study from our own institution we were able to show that 37% of patients with virologic response to conventional or pegylated interferon did loose HBsAg during a median follow-up of 5 years. New compounds are currently explored with relevance to the management of CHD. The main drivers among new compounds are hepatocyte entry inhibitors, farnesyl transferase inhibitors and nucleic acid polymers. All of these compounds have shown some efficacy in phase 2 clinical trials in CHD. For all 3 groups of compounds studies are ongoing and we are at the stage where large phase 3 studies leading to registration are awaited.

HCV CASCADE OF CARE AND THE REQUIREMENT TO ACHIEVE THE ELIMINATION TARGETS IN DIFFER-ENT REGIONS

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Abstract

Introduction: The introduction of the direct acting antivirals has provide sustained viral response rates of >90%. However, any strategies to increase treatment require an understanding of the total number of HCV infections and the number of diagnosed patients available for treatment. :

Materials and Methods: To develop the HCV cascade of care, the HCV prevalence estimates were extracted from the Polaris Observatory. When available, national registry data was analyzed by taking into account mortality and cure rates to estimate the number of individuals diagnosed with HCV who are alive and have not achieve SVR. When available, the number of patient treated was taken from the unit sales data of the common medicine to treat HCV. A panel of experts in each country was interviewed to validate the estimates, or to provide estimates for the number individuals diagnosed and treated.

Results: Globally, treatment increased from 1.1 million in 2015 to 1.7 million in 2016. However, in most Western countries, the number of treated patients decreased in 2016 due to the depletion of the diagnosed population.

Conclusion: Screening will be required to maintain treatment rates to achieve WHO targets. In addition, programs are needed to re-engage those already diagnosed with HCV.

HEPATITIS C ELIMINATION PRO-GRAM IN GEORGIA

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Abstract

Georgia is a middle-income Eastern European country with a population of 3.7 million people. According to the nationwide serosurvey conducted by the National Center for Disease Control and Public Health (NCDC) with support of the US Centers for Disease Control and Prevention (CDC) in 2015, seroprevalence of hepatitis C (HCV) in Georgia is 7.7% with 5.4% prevalence of active disease. Recognizing HCV burden as one of the main public health problems in the country, Georgian Government announced HCV as a priority and committed to eliminate the disease by 2020. In April 2015, in collaboration with US CDC and Gilead Sciences, Georgia launched the unprecedented Hepatitis C Elimination Program using curative regimens based on new direct-acting antivirals (DAAs). All patients receive regimens based on sofosbuvir or sofosbuvir/ledipasvir, provided free-of-charge by Gilead Sciences; Georgian Government purchases additional medications (i.e., Pegylated interferon and ribavirin) and provides them at no cost to patients who need alternatives to DAAs. Screening is available free of charge in every region of the country and is coordinated by the NCDC. Ministry of Labour, Health and Social Affairs of Georgia (MoLHSA) with NCDC and local experts, with support of CDC, WHO and other international partners, developed a Hepatitis C Elimination Strategy and action plan for 2016-2020. To achieve elimination goal, the country of Georgia has set forth the following 2020 targets: identifying 90% of HCV-infected persons, treating 95% of people with chronic HCV infection, and curing 95% of persons treated of their HCV infection.

Public health impact: From April 28, 2015 through June 30, 2017, more than 800 000 screening tests were conducted, 40 676 RNA positive individuals were registered in the program, 31 840 patients already completed the treatment with different regimens based on Sofosbuvir and Harvoni, and among those with SVR result available, overall cure rate reached 95%, whereas cure rate for Sofosbuvir/Ledipasvir-based regimens was 98%. HCV elimination became a flagship program for Georgian healthcare and public health. Activities within this program are aimed not only at reducing morbidity and mortality due to HCV, but also contribute to improving infection control and blood safety measures, establishing laboratory quality control system and reducing disease-related stigma and discrimination.

Why is this program innovative? The concept of disease elimination in Georgia is an ambitious but viable goal, given small size of population, experience with implementation of HIV prevention and control programs, strong political will and public support. The program is a unique example of a public-private partnership with a comprehensive approach to delivering a public health program. The public-private partnerships are twofold: first, between the Government of Georgia, US CDC and Gilead Sciences and second between the Government of Georgia and the Georgian

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service providers, the vast majority of which are from the private sector. Georgia has committed to the planning and capacity-building needed to implement this comprehensive public health program that has impact across various public health sectors, with the ultimate goal of eliminating the HCV burden.

HCV ELIMINATION IN IRAN: NEXT STEP AFTER GENERIC DAA

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Abstract

Development of highly effective, well tolerated and easy-to-administer direct acting antiviral (DAA) regimens for hepatitis C virus (HCV) infection has resulted in a realistic optimism to reach ambitious WHO HCV elimination targets in many settings. The availability of generic DAA in Iran is a major step towards broadening the treatment access which is crucial for treatment scale-up. However, there are also other requirements to ensure the feasibility of any treatment scale-up program and achieving WHO targets. Affordability is central to the HCV treatment uptake. Although the current price of Iranian generic DAA is much lower than that for the branded drugs, the total cost of a treatment course, including drugs and pre-treatment and post-treatment laboratory tests is still not affordable for majority of people who inject drugs as the main target population. Enhanced HCV diagnosis and linkage to care is required given that only 35% of people with chronic HCV infection have been diagnosed in Iran. Point-of-care diagnosis and integration of substance use care and HCV care can facilitate HCV diagnosis and linkage to care. High-coverage harm reduction can provide both an access point for people who inject drugs to engage in HCV care and the means to limit HCV re-infection after successful treatment. An efficient surveillance system is required to monitor HCV

prevalence and incidence, diagnosis rate, and treatment uptake.

SIMPLIFIED HCV DIAGNOSIS

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Abstract

According to WHO hepatitis C virus (HCV) is a serious public health threat. As a part of worldwide effort for elimination of HCV infection, the aim is dramatic and large-scale reductions in new transmissions of HCV, as well as in the number of people becoming ill and dying from HCV, to a level where HCV no longer represents a major health concern. In Numeric terms, the WHO proposed reductions of 60% in HCV-related mortality and 90% in HCV transmission globally in member countries by 2030. As a part of test and treat strategy, HCV screening is an important part of overall effort to contain the infection. Here we want to look into most significant barriers to HCV testing. We also want to discuss ideas about how to improve the quality of testing and maintain the standards. It is also vital to explore methods for reaching out to risk groups and link patients to care system where they will be taken care of in a safe environment and cured of HCV infection. Improving HCV testing depends on following factors: scope and setting for use for POC tests, QC assurance cycle, role and responsibilities of stakeholders, developing and review of policies, implementation plans, financial plans, selecting the right site, selection of right product, evaluating, improving and sustaining the quality assurance. To facilitate "ACCESS", health systems need to provide: the right product, at the right price, in the right quantities, in the right places, at the right time. We look deeper into how to improve access to diagnostics via availability of simple, affordable, high quality screening and diagnostic tests, clear and appropriate linkage to diagnosis and care, integration of diagnosis and management of HCV into existent programs rather than cre.

ating vertical programs, screening, diagnosis and treatment availability in health facility, knowing ones status and demand access to affordable treatment. We aim to provide an exclusive review of testing and screening in context of public health concept, as a part of overall test and treat strategy.

UPDATES ON HCV VACCINES

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Abstract

Hepatitis C virus (HCV), the major cause of chronic hepatitis was discovered in the late 1980s. Despite of efforts during last 28 years to develop an HCV vaccine, none is available to date. The high sequence divergence among the seven major genotypes and HCV evasion from humeral and cellular immune responses were major obstacles for development of a pan-genotypic vaccine. Since it is the "persistence" of HCV infection that result to established liver diseases and cirrhosis, any HCV vaccine capable of inhibiting the "progress to the chronic state" might be considered as an efficient preventive HCV vaccine. In 1990s, formulation of recombinant HCV envelope proteins in MF59 adjuvant and immunization studies in chimpanzee suggested that protective immunity might be generated against persistent HCV infection (even if not sterilizing) for both homologous and heterologous virus challenges with efficacies around 70%. However, difficulties of HCV vaccine studies in human trials and elucidation of the role of CD4 helper and CD8 CTLs in resolution of the infection in 2003, directed the further studies towards invention of T-cell vaccines via utilization of HCV-Nonstructural proteins and application of novel vaccine modalities (recombinant proteins, viral vectors, yeast-based) for therapeutic aims in monotherapy or joint-therapy with Interferon+ribavirin. But revolutionary emergence of direct antiviral agents (DAAs) with SVRs of >90% in 2012 limited the impact of such therapeutic vaccines (such as: MVA-based TG4040 or whole yeastbased GI-5005) and raised the question, "if it is still worthy to continue research studies on HCV vaccines"?. However, recent modeling studies predicted the potential of eradication by DAAs alone only for patient populations with a HCV prevalence <25%, while in higher prevalence rates (like drug users with prevalence's around 40%), a preventive vaccine is needed to stop HCV transmission. Moreover, without national screening programs, there will be no control of hepatitis C with DAAs, while access to these new therapies is itself one of the most important issues. In addition, resistance-associated variants (RAVs) which present around 15% of patients (preexisting NS5A RAVs) are at risk of treatment failure with DAAs. Moreover, recent data on positive effect of DAA therapy on T cell recovery and restoration of immune responses have proposed the need for an HCV vaccine for both prevention and therapy, while co-administration of NS3-protease inhibitor-DAAs with immunotherapeutics for enhancement of innate immunity against HCV infection is recently suggested. Indeed, Currently a prophylactic T-cell viral vector-based prophylactic HCV vaccine (Adeno-Prime, MVA-boost) containing HCV non-structural proteins is in phase 2 clinical trial (NCT01436357) on injecting drug users (IDUs; as subjects with highest risk of HCV infection) and results are expected to be released in July 2018. In addition, recent successes in crystallography and characterization of E2 core domain and identification of inter-genotypic conserved epitopes with cross neutralization potential in this domain (amino acids 421-446 and the CD81 binding loop) as well as pan-genotype prevention of infection by specific E2-mAbs like Ap33 (which identifies the conserved linear epitopes in E2 region: 412-423) may yield a basis for a rational vaccine design.

HCV VIRAL PARTICLE AND LIFE CY-CLE

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Abstract

Despite recent progress in treatments, Hepatitis C virus (HCV) still represents an important global health problem. The search for new antiviral drugs has been a major drive for basic research on this virus. However, our picture of the HCV life cycle is far from being complete. An intriguing feature of this virus is the peculiar overlap between the infectious cycle and lipid metabolism. This association, which has clinical consequences, begins to be understood at the molecular level, and the whole HCV life cycle relies on lipid metabolism. One of the most striking features is the association between HCV particle and very low density lipoproteins (VLDL) which is the result of HCV hijacking the VLDL assembly pathway. As a consequence, apolipoproteins are found at the surface of HCV virion. This specific interaction has an impact on HCV cellular entry since several lipoprotein receptors have been identified as entry factors. Viral replication also induces the formation of novel membranes derived from the endoplasmic reticulum which contribute to the replication factory. Finally, cellular lipid droplets have been shown to play a central role in HCV replication and assembly since both the replication complex and the assembly site converge towards this organelle. A comprehension of HCV interaction with lipid metabolism will help to better understand the physiopathological consequences of this viral infection. It could also provide opportunities for the development of a new generation of antiviral molecules.

INNATE IMMUNITY TO HCV: THE ROLE OF NK CELLS

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Abstract

Natural killer (NK) cells are a major component of the innate immune system that are instrumental in establishing a coordinated and efficient adaptive immune response in viral infections. Most studies suggest that they are functional and activated in the peripheral blood of patients with chronic HCV infection, but are polarized toward cytotoxicity as a consequence of chronic exposure to endogenous IFN-α, resulting in deficient IFN-γ secretion. The significance of this finding with respect to the natural history and pathogenesis of chronic hepatitis C is unclear, but it has been hypothesized that failure to produce adequate amounts of IFN- γ , a potent non-cytolytic mechanism of virus control, would contribute to inability to eradicate HCV, whereas enhanced cytotoxic function would be responsible for persistent inflammation. Current evidence suggests that direct-acting antivirals (DAAs) promptly reconstitute innate immune homeostasis, with a rapid reconstitution of NK cell IFN-γ secretion and reduced NK spontaneous cytotoxicity. However, the HCV effect on innate immunity may be more pervasive tha hitherto recognized, as antibody-dependent cell-mediated cytotoxicity may require a significant amount of time for regeneration, as a result of HCV-induced prolonged FcyRIII down-modulation. Recent data suggest that monocytes play a significant role in NK immune regulation. Deficient monocyte-derived IL18 and increased IL18 binding protein may inhibit NK cell function. Of note, during HCV infection, certain NK cell subsets display reduced expression of Siglec-7 which results in altered function (reduced degranulation and TNF- α and IFN- γ secretion). This may significantly impinge on the quality of the innate immune response in this setting, allowing a relatively simple pathogen to survive unchecked within the liver.

IMMUNE CELL RESERVOIRS OF PER-SISTING HCV AND RELATED POTEN-

TIAL PATHOGENIC CONSEQUENCES

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Abstract

Accumulated experimental and clinical evidence indicate that the immune system, in addition to liver, is target of HCV and a site where HCV may hide from immune surveillance and elimination. The ability of HCV to infect immune cells is consistent with a higher prevalence of certain lymphoproliferative disorders in patients chronically infected with HCV. Regression of these diseases following treatment with anti-HCV therapies suggests a direct pathogenic role of HCV in these disorders. Studies on HCV compartmentalization in the immune system showed virus presence in all main types of circulating immune cells, including B and T lymphocytes and monocytes. The data showed that HCV lymphotropism is not just the mere detection of HCV RNA positive (non-replicative) strand. The detection of virus RNA negative (replicative) strand and intracellularly located viral proteins in immune cells, both in HCV-positive patients and cells in vitro infected with authentic HCV, have been reported. Other evidence came from identification of unique HCV variants in immune cells distinct from those in rearverified that the cells are the site of active replication. Also, HCV released from in vivo or in vitro infected immune cells transmitted infection in culture resulting in production of HCV virions that were precipitated with anti-E2 envelope antibody and visualized by immunoelectron microscopy. The recent identification of CD5 as a molecule essential to infection of human T lymphocytes and that a co-stimulatory receptor B7.2 (CD86) is involved in infection of B cells by a HCV variant further advanced understanding of the nature of HCV lymphotropism. HCV infection of immune cells may affect their functions and proliferation kinetics. In this regard, upregulation of B cell receptor signaling and suppression of CD4+ T cell proliferation due to infection with HCV were reported. HCV ability

to infect both CD4+ and CD8+ T cells may also directly impair the efficacy of HCV-specific immune cell response, lessen virus clearance and favor its persistence. The likelihood of a direct induction of immune cell dysfunctions by HCV validates importance of further studies on HCV lymphotropsim and its pathogenic implications.

EPIGENOMIC CHANGES AND NON-CODING GENOME SEGMENTS INVOLVED IN HCV-ASSOCIATED HCC

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Abstract

Hepatitis C virus (HCV) is still a major cause of Hepatocellular Carcinoma (HCC) as it is considered to have recently overtaken hepatitis B virus (HBV) in terms of annual death toll for malignancy. In addition, it represents currently the main cause of mortality from HCC in most regions of the world. At variance with HBV, HCV is not associated with a high rate of chromosomal instability in tumors and it was not described to act synergistically with a carcinogenic compound such as aflatoxin B1 to promote liver tumorigenesis. It appears, thus, that the oncogenic potential of HCV is subtle and predominantly associated with alterations of liver cells transcriptome and epigenome. It has been shown recently that various categories of non-coding genetic materials are playing an instrumental role in the development of HCV-associated HCC. At the genomic level, several non-coding segments either expressing long non-coding RNA (IncRNA) such as NEAT1 or MALAT1 or promoter regions (eg. TERT) are recurrently affected by somatic small deletions or point mutations. In addition, various expressions of non-protein encoding transcripts such as microRNAs (eg miR-21), lncRNA (eg HULC), or circular RNAs (eg ANRIL) are consistently deregulated

in HCV-associated HCC. The presentation will review the situation of this rapidly expanding field of HCC research.

TREATMENT OF PATIENTS WITH HCV GENOTYPE 1 OR 4 INFECTION

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Abstract

Direct acting antivirals (DAAs) now represent the standard of care for all patients with chronic HCV infection. Current international guidelines recommend that all treatment-naïve and treatment-experienced patients with compensated or decompensated chronic liver disease due to HCV must be considered for therapy. Although clinical trials and real-life experience show a virtually universal success in HCV eradication, special caution must be exercised to optimize treatment. Thus, geno/ subtyping, seeking RASs in case of treatment failure, evaluating co-morbidities and extrahepatic manifestations, drug-drug interactions, particularly in polytreated elderlies, prior treatment experience and severity of liver disease. Treatment of patients with GT1 or 4 infections is relatively straightforward with wide options of safe and effective drug combinations. Current treatment recommendations from major liver societies indicate that combinations of NS5B and NS5A inhibitors, eg sofosbuvir + ledipasvir or daclatasvir (both unfortunately not available in some countries anymore) or velpatasvir may represent a safe approach also in patients with decompensated cirrhosis. Triple combinations including protease inhibitors (PIs) such as paritaprevir/r + ombitasvir ± dasabuvir are also effective but should not be used in decompensated patients. Caution should also be exercised when using drugs that may interfere with the pharmacokinetics of PIs. Combinations of PIs

and NS5A inhibitors such as grazoprevir + elbasvir may also be safely used in patients with severe renal insufficiency or on hemodialysis. Ribavirin is still part of the HCV pharmacopeia and is generally used in cirrhotic or treatment experienced patients, to increase efficacy or to reduce treatment duration. This can be reduced to 8 weeks in non-cirrhotic naïve patients for sofosbuvir + ledipasvir or paritaprevir/r + ombitasvir + dasabuvir (for subtype 1b only). One additional triple drug combo has been approved by FDA: sofosbuvir + velpatasvir + voxilaprevir (Vosevi[™]) with results similar to the sofosbuvir/velpatasvir combo. New drug combinations are presently being tested in order to reduce standard treatment duration to 8 weeks. One, glecaprevir + pibrentasvir (Mavyret), has just been approved by FDA, showing success rates >92% for all genotypes. An additional one, grazoprevir + ruzasvir + uprifosbuvir, is currently being considered. Data from controlled clinical trials indicate very promising SVR12 rates of 93% in GT1a, 98% GT1b and 100% GT4.

TREATMENT OF PATIENTS WITH HCV GENOTYPE 2 OR 3 INFECTION

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Abstract

Hepatitis C virus (HCV) genotype 3a is the second most common genotype in chronic hepatitis C worldwide. In the pre-DAA era both genotypes 2 and 3 were considered as easy to treat genotypes. Patients treated with peginterferon/ribavirin (RBV) who became HCV-RNA negative by week 4 achieved an almost 100% cure rate after treatment for a total of just 12 weeks (1,2). In 2011 a combination of Sofosbuvir (SOF) with RBV cured all 10 patients in that phase 2 study; and is considered as the birth of interferon (IFN)-free treatment with DAA. Unfortunately, subsequent studies with SOF/RBV did not repeat his success, combinations clearly showing the need for combinations with other DAA. Some of these combinations market authorization within the last year. Unfortu:

nately not all of these new drugs are available worldwide. In resource restricted countries treatment-naïve, noncirrhotic patients can be treated with REG/RBV (3) for 12-24 weeks depending on the rapidity of viral decline. In patients with a < 2 log decline after 4 weeks SOF may be added (not part of the guidelines). Not all the potential problems are solved, the most important one is the treatment for patients who failed an interferon-free regimens, especially if NS5A resistance associated substitutions (RAS; ie. Y93H). Because of the inclusion of a protease inhibitor Vocevi® and Maviret® cannot be used in patients with decompensated cirrhosis

Licensed and recommended DAA combina-	
tions for GT 2 and 3 infected patients (4,5):	

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Drug	Poly- merase inhibitor	NS3 protease inhibi- tor	NS5a Inhibitor	RBV	weeks	
					F0-3, naive	TE, Cir- rhosis
HARVONI®	Sofosbuvir		ledipasvir	х	12-24	?
EPCLUSA®*	Sofosbuvir		velpatasvir	±	12	12
VOCEVI® 6	Sofosbuvir	voxila- previr	velpatasvir		12	12
MAVIRET® 7,8		gleca- previr	pibrentasvir		8	16
SOF/DAC*	Sofosbuvir		daclatasvir	±	12	24

TE= treatment experienced; * according EASL/AASLD guide-lines.

RETREATMENT OF PATIENTS WITH TREATMENT FAILURE WITH DAAS

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Abstract

The new treatments for hepatitis C are extremely effective. Almost all studies report success rates above 95%. Studies from Iran also confirm this number and in some cases, even better. Nevertheless, some patients fail these treatments for various reasons. How should we treat these? Various reasons might be involved. First, of course, non-compliance. Regular use of medicine is important in achieving SVR and might be a challenge in subjects with less motivation such as prisoners, or active drug abusers. In prisons, for instance, Directly Observed Therapy (DOT), as used in tuberculosis treatment, might be required in some cases. In very high-risk groups, such as active IV drug abusers, early reinfection can also be confused with lack of response to treatment. Sometimes a change in genotype can help make the diagnosis but re-infection with the same genotype might not be easy to differentiate from lack of response. One other reason for failed treatment might be lack of therapeutic blood level due to interaction with other concomitant medicine. This is rarely an issue of concern in the everyday patient but in some cases, eg patients co-infected with HIV and on efavirenz, a modification of DAA therapy might be in order. It is the duty of the managing physician to identify concomitantly used medicine and whether they effect DAA treatment or not. He can then choose to either temporarily hold the medicine in question or modify the DAA dose. The most challenging reason for treatment failure is drug-resistant viruses. It is well known that some mutations in the viral genome offer resistance to various classes of DAAs. Fortunately, many of these so-called Resistance Associated Strains or Variants (RAS, RAV) offer a survival disadvantage and are gradually lost once the DAA is discontinued. Thus, waiting a couple of months and repeating the same treatment will result in over 95% response. Unfortunately, not all RASs are easily lost by time. One notable exception is the Y93H mutation which might confer resistance to NS5A inhibitors such as those available in Iran for years. For patients with NS3 inhibitor RASs and no NS5A inhibitor RASs detected, retreatment with sofosbuvir and an NS5A inhibitor with ribavirin for 24 weeks is recommended. For patients who have NS5A inhibitor RASs and no NS3 inhibitor RASs detected, treatment with simeprevir, sofosbuvir, and ribavirin for 24 weeks is recommended. In either case retreatment with the previous failed regimen for 24 weeks and adding ribavirin offers at least 60% response which in many cases is quite acceptable. Frequently, e.g. in a young female without liver fibrosis, it is acceptable to defer treatment pending availability of more effective medicine.

TREATMENT OF HCV INFECTION WITH GENERIC DAAS IN IRAN; AN UPDATE ON IRANIAN CONSENSUS FOR TREATMENT OF HEPATITIS C

Seyed Moayed Alavian

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Abstract

Hepatitis C virus (HCV) infection is a major public health issue worldwide. This infection is one of the major causes of chronic hepatitis with the risk of progression to cirrhosis and development of Hepatocellular Carcinoma (HCC). Treatment of HCV infection has been revolutionized by introduction of direct acting antiviral agents (DAAs). In many countries, people don't have access to a course of brand-name direct-acting antiviral drugs due to their high cost as much as between \$30,000 -\$94,000 a patient. Generic medications have a significant cost advantage because they do not require the background research and development studies to support registration. There is a higher motivation to use the generic drugs in therapy of HCV infected patients in developing and developed countries. India, Egypt and Iran are pioneer in developing generic brands for therapy of HCV infection. In developed countries, Australia is a good model. Importation of the novel hepatitis C direct-acting antiviral therapy into Australia before it was registered in the country is an illustrative case study. Access to hepatitis C (HCV) treatment provides an excellent illustration of the issues related to generic medication. Australia is a good model for affordability of low cost drugs. Prior to the commencement of the Australian government-funded HCV treatment program in March 2016, an estimated 1400 Australian patients had been treated with the assistance of FixHepC, a web-based platform for the importation of HCV therapies. In Iranian guideline consensus therapy in HCV infection, Sofosbuvir/Ledipasvir (SOF/LED) and Sofosbuvir/Daclatasvir (SOF/DCV) according to their affordability are suggested. The experiences regarding generic brand presented to scientific community. Preliminary data about the efficacy of 12 Weeks of Sofosbuvir-Daclatasvir, and Ribavirin in treating hepatitis C patients with cirrhosis, Genotypes 1 and 3 showed precious outcome with high achievement of SVR12 (98%, per-protocol, 92% intention-to-treat. In-press data reported a similar result in Sofosbuvir-Daclatasvir with higher number of enrolled cases. In conclusion, the fixed-dose combination drugs of Sofosbuvir and Daclatasvir given together with weight-base Ribavirin for 12 weeks is extremely effective and safe in treating

HCV patients with Genotypes 1, 3 and cirrhosis. Efficacy and safety of Generic Sofosbuvir/Ledipasvir fixed-dose combination in Iranian patients with chronic hepatitis C virus infection was acceptable as well. In the preliminary study, 30 patients with the mean age of 52.9 years were enrolled and treated with SOF/LDV. Most of the patients were male (73.3%), had cirrhosis (53.3%), infected with HCV-1a (46.7%) and had previous history of HCV antiviral therapy (62.1%). All the patients completed the course of treatment. Rapid virologic and sustained virologic responses were observed in 29 (96.7%, 95%CI = 83.3% - 99.4%) and also 29 (96.7%, 95%CI = 83.3% - 99.4%) cases, respectively. The only case of treatment failure was a relapse. No serious adverse-event was observed during the treatment course. In conclusions, the generic SOF/LDV was efficacious and safe to treat Iranian patients with chronic HCV infection. Finally, we should discuss more the possibility of omission of HCV genotyping test in naive and non-cirrhotic HCV infection patients for using pan genotyping protocol. The role of longer duration with adding Ribavirin in cirrhotic patients with HCV-G3 will be discussed more in presentation. We can conclude that Iranian generic medicines provide greater access to the treatments due to their greater affordability. They also enhance health-system efficiency.

LIVER TRANSPLANTATION FOR AUTOIMMUNE HEPATITIS IN IRAN (MANAGEMENT AND OUTCOMES)

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Abstract

Autoimmune hepatitis (AIH) is a common indication of liver transplantation (LT) in Iran. From 3191 patients who received LT in Shiraz till end of 2015, 14% had AIH making this disease entity as the third most common cause of LT after cryptogenic cirrhosis and HBV in our center. AIH was not only common in our patients with end stage chronic liver disease but also was the cause of 25% of patients who received LT for acute liver failure. Of these 447 patients who received LT for AIH, 68.2% were female and 21.9% aged less than 20 years. The minimum age of these patients was 3 years old and maximum 71 years and mean 30.19+/- 12.31 years. :

65.86% of them are still alive with 10 years survival of 82%. Nine patients received re transplantation making AIH as the most common cause of re Tx in our center. LT had a better survival when female patients received liver from female donors compared to other groups {Mean ±SE survivals were with 12.11±0.29 in female donor to female recipient, 11.89±0.23 in male donors to male recipients, 11.41±0.21 in male donor to female recipients and 10.30±0.35 in female donors to male recipients, respectively (P=0.037)}. Comparing between those transplanted before 2005 and those who received LT more recently, the percentage of AIH decreased from 19.4 to 13.6 substituted with more LT for hepatocellular carcinoma and metabolic liver disease. Out come of LT is excellent after AIH but few patients may need re transplantation.

MANAGEMENT OF HEPATITIS B IN LIVER -TRANSPLANTED PATIENTS

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Abstract

All patients with terminal HBV disease waiting for liver transplantation must be given oral HBV antivirals, in order to abate HBV viremia (HBV-DNA) at surgery and prevent flares of hepatitis B which may be fatal. The combination of hepatitis B immune globulins (HBIG) with lamivudine was the regimen most widely used for the last 15 years, with recurrence of HBV limited to 6% of the patients with low HBV-DNA at transplantation. However, HBIG is expensive and current prophylactic efforts aim to dispense with their use in order to diminish costs and inconvenience to patients. Strategies were first developed to stop HBIG after a few months of combination therapy but recent studies have demonstrated that Entecavir and Tenofovir alone without the use of HBIG are effective in preventing HBV reinfection and hepatitis of the graft, achieving excellent long term outcome; the efficacy of newer antivirals without HBIG is related to their lower rates of resistance compared with lamivudine. Monoprophylaxis with antivirals is effective for patients without pre-existing resistant mutations while in those with resistant strains, the combination of a nucleoside and a nucleotide antiviral is recommended. Attempts

to raise immunity against the HBV by therapeutic vaccination have led to conflicting results, because of the impaired immune response of transplanted patients given immunosuppression. Combination of HBIG with an antiviral is generally advocated for the prevention of HDV reinfection; however, recent studies have reported that full protection can be achieved also in this virologic setting by monotherapy with HBV antivirals, without the use of HBIG.

INTRODUCING A CASE WITH ELE-VATED LIVER ENZYME

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Abstract

In this session, we introduce a case with elevated aminotransferase levels and discuss about the appropriate diagnostic approach. The lecture would be completely interactive and the presenter ask the audiences opinion. The information regarding the case is provided in each section and the next part is planned according to the recent guidelines. While introducing the case, the hallmarks in the patient history that are associated with the metabolic syndrome and NAFLD are reviewed. Special clues to differentiate other causes of abnormal Liver function tests are also provided. This session briefly goes through the medications that cause fatty liver. Different para-clinic diagnostic tools including laboratory, imaging, Fibroscan, and liver biopsy for discrimination of NAFLD are issued in the panel. Controversies exists in choosing the best technique for estimation of liver cell damage in NAFLD. Some important scoring systems regarding steatosis, lobular inflammation, and fibrosis are addressed in the meeting and pros and cons of each method is discussed. This conference also comprises updates on NAFLD pathogenesis, application of Fibroscan, and management strategies.

PATHOGENESIS OF NAFLD – AN UP-DATE

Peter Ferenci

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Abstract

Hepatic fat accumulation is a common condition which may lead to serious liver disease and hepatocellular carcinoma. The pathogenesis of hepatic steatosis is complex and involved endogenous and exogenous factors. The driving force to advanced liver disease is lipotoxicity which leads to inflammation, fibrosis and finally to cancerogenesis. However it is not a disease entity and reflects various causes affecting hepatic fat metabolism. Thus, the pathogenesis of fatty liver is multifactorial. This spectrum includes:

The consequences of metabolic syndrome (including obesity, diabetes mellitus and hyperlipidemia/hypercholesteremia. Hepatic lipid accumulation is the hepatic presentation of the metabolic syndrome and is usually called nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) in its advanced form. At least in Western countries it is frequently associated with increased alcohol consumption and it can be difficult to differentiate from alcoholic steatohepatitis (ASH).

Conditions not directly associated with metabolic syndrome:

A, Toxin-induced steatosis: A variety of drugs (ie. tamoxifen) and industrial toxins (ie. solvents) leads to impaired hepatic fat metabolism.

B, Certain viruses (i.e. HCV genotype 3a, Reye syndrome): inhibit hepatic fat transfer and cause massive steatosis.

C, Genetic diseases: Wilson disease: Steatosis is the most common histologic feature of early hepatic Wilson disease and is partly related to copper toxicity Lysosomal acid lipase A (LIPA) deficiency (Cholesterylester storage disease, Wolman's disease): leads to reduced or absent production of the LIPA, yielding increased cholesterol ester storage in the lysosomes By early diagnosis and treatment progression of these two diseases can be prevented.

D, Gene variants of enzymes involved in hepatic fat metabolism: PNPLA3 (Adiponutrin): It functions as both a triglyceride hydrolase (suggesting catabolic lipase activity) and acetyl-CoA-independent transacylase (suggesting anabolic lipogenic activity). Mutation of PNPLA3 leads to steatosis and augments the effects of the metabolic syndrome. TMS6S2 (transmembrane superfamily 6 member 2): Decreased levels correlate with altered expression of multiple genes involved in triglyceride synthesis (including PNPLA3). They lead to increased size and number of hepatocytic lipid droplets, but with no effect on cell damage and proliferation. MBOAT (Membrane Bound O Acyltrasferase): was recently identified as a potential genetic risk gene for NAFLD.

PRACTICAL APPROACH TO NAFLD TREATMENT

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Abstract

There are three important steps in assessing a patient with suspected NAFLD: 1.confirming the diagnosis 2.determining the patient's risk of liver-related outcomes (cirrhosis, HCC) 3. Monitoring and treatment plan based on the patient's metabolic risk profile and risk for liver-related outcomes. Risk of liver outcomes can be assessed using transient elastography, Fibrosis-4 (FIB4) index, (APRI index) and NAFLD fibrosis Score (NFS). Low-risk subjects at low risk for liver-related outcomes (obesity without additional features of metabolic syndrome, age<40 years, FIB4<1.3, APRI<0.5, NFS< -1.455, and LSM<5 kappa) should be managed by interventions with a similarly low-risk profile. The cornerstone of treatment consists of a hypocaloric diet and exercise to create a caloric deficit of 500-1,000 cals per day. Intermediate-risk subjects for those with intermediate-risk (hepatic fibrosis but with- out cirrhosis), treatment is mainly directed towards reducing disease activity with pharmacological agents. High-risk subjects Careful management of high-risk NASH patients (bridging fibrosis or NASH-related cirrhosis) is of utmost importance. There are no completed clinical trials to demonstrate efficacy of any pharmacological agents in this population.

IMPACT OF AUTOPHAGY AND APOP-TOSIS ON VIRAL HEPATITIS

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Abstract

All viruses are obligate intracellular pathogens. They have evolved diverse strategies to exploit and manipulate different host cell signaling mechanisms to evade from host defenses and survive in a hostile cellular environment. Among these host cell signaling mechanisms are autophagy and apoptosis, two catabolic pathways essential for the cell survival and death balance in the cell. Autophagy is a tightly regulated catabolic process, which is essential in many cellular events including development, differentiation, survival and homeostasis. Autophagy is usually considered a very important step for numerous virus life cycles and it is apparently used by cells to eliminate invading pathogens via targeting viral particles for lysosomal degradation as well as initiating innate and adaptive immune responses to viral infections. Consistent with this antiviral role of host autophagy, many viruses including hepatitis C virus (HCV), hepatitis B virus (HBV), have learned to block host autophagy by encoding virulence factors that interact with the host autophagy or to subvert the host autophagic process to foster their own intracellular replication. Apoptosis is also a tightly regulated process of programmed cell death that plays an important role in development and homeostasis. Additionally, it may function as a host defense mechanism against viruses. Both, HCV and HBV induce autophagy and apoptosis; however, the relationship between HCV or HBV-induced autophagy and apoptosis as well as the influence of autophagy and apoptosis on virus virulence are not fully understood as yet. Here, we present an overview of the interactions between HCV and HBV viruses and host cells in regards to cellular autophagy and apoptosis. This presentation highlights the cellular states and signaling mechanisms that participate in, and are crucial for this interplay, the significance of which during HCV and HBV infection. A full understanding of these signaling mechanisms could be highly relevant for the development of alternative therapeutic strategies in control of viral hepatitis infection.

IMMUNOPATHOLOGY AND MO-LECULAR PATHOGENESIS OF VIRAL HEPATITIS

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Abstract

Viral hepatitis is caused by several distinct viral pathogens preferentially invading hepatocytes, which can initiate either transient, spontaneously resolving infections or chronic infections that at a high frequency progresses to cirrhosis, hepatic failure and/or cancer. Hepatitis A virus (HAV), hepatitis B virus (HBV) and hepatitis C virus (HCV) cause most of viral hepatitis worldwide. The mechanisms underlying liver injury, course of hepatitis and its outcomes significantly vary depending upon the molecular characteristics of virus, its cytopathic properties and immunological responses induced. All viruses triggering hepatitis initiate innate and virus-specific adaptive immune responses, however their magnitude, contribution to the development and perpetuation of liver damage and to protection against re-infection are highly divergent. In this regard, while HAV and HBV cause minimal induction of the innate interferon (IFN) and IFN-stimulated gene (ISG) response, HCV strongly augments expression of IFN and ISG in the infected liver and circulating immune cells, which pre-determines susceptibility of patients with chronic hepatitis C to the IFN-based therapy. Comparing the pathogenic relevance of virus-specific T lymphocyte responses, contributions of cytotoxic CD8+ and helper CD4+T cells to induction of hepatocyte injury and resolution of acute hepatitis B and C are well recognized, whereas there is no such compeling evidence regarding acute hepatitis type A. A strong protective immunity provided by HAV-specific and anti-HBV surface antigen (HBsAg)-specific antibodies, but only transient, strain-specific protection observed under experimental conditions against HCV is another example of a distinctive immunobiology of viruses commonly causing viral hepatitis. Other similarities and differences in the molecular mechanisms

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contributing to the immunopathogenesis of liver damage caused by infections with different hepatitis viruses will be discussed.

GENOTYPE F OF HEPATITIS B VIRUS: BENIGN COMMENSAL OR STEALTH DESTROYER?

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Abstract

In Peru, Hepatocellular carcinoma (HCC) is characterized by an unusual bimodal distribution for age and the absence of fibrotic/cirrhotic process in the liver (90% of cases). Factors responsible for such situation are currently unknown but Hepatitis B virus (HBV) is serologically associated with HCC in less than half of cases. We decided to explore HBV presence in 65 younger and older Peruvian patients with HCC, half of them positive for HBV surface antigen. HBV DNA was found in the tumor or the corresponding liver tissue in more than 80% of cases by qPCR (n=53/65). All HBV strains isolated were belonging to subtype F1b. We observed very low viral loads in tumor or non-tumor liver tissues, with only a fraction of the cells potentially bearing a copy of HBV genome (median value: 0.1-6.5 copy of HBV for 100 cells). HBV DNA was more abundant in young patients than in elder ones and in non-tumor livers (NTL) than in tumor parts. Viral DNA isolated from young patients was significantly less mutated than isolates from older patients but presented higher rates of monotonous dipyrimidines (TpT or CpC) changes. Microfluidic analysis of genes (n=121) on 40 pairs of tumors and NTL revealed drastic differences in DNA repair pathway gene expression between young and older patients. Considering the young age of many patients, our observations are at odds with the current vision that associates high HBV loads and faster tumor development. We concluded, that in Peru, HBV-associated liver tumorigenesis differs significantly from that generally observed in the rest of the world.

EFFECT OF END-STAGE LIVER DIS-

EASE ON DRUGS' PHARMACOKI-NETICS AND PHARMACODYNAMICS

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Abstract

Lack of sufficient data on pharmacokinetic and pharmacodynamic changes of drugs in patients with end-stage liver diseases and cirrhosis induces concerns in gastroenterologists and hepatologists for drug prescribing. Specific drug prescribing information is often lacking. Main concerns include fear of drug-induced liver injury by hepatotoxic drugs that may rapidly deteriorate the damaged liver and also fear of deterioration of some cirrhosis patients' complications such as gastrointestinal and variceal bleedings and provoking renal failure or hepatic encephalopathy by drugs in these patients. Main pharmacokinetic changes of drugs in cirrhosis patients include reduced first pass metabolism of some drugs due to decreased hepatic blood flow, increased free fraction of highly albumin bound drugs, increased volume of distribution of hydrophilic drug in patients with severe ascites, decreased drug absorption due to portal gastropathy, decreased systemic clearance of some drugs and consequent increased in their blood concentrations due to decreased metabolic activity of CYP 450 microsomal enzymes and decreased biliary and renal excretion. Pharmacodynamic changes of some drugs happen due to up-regulation or down-regulation of some drug receptors and changes in receptor sensitivity. As a general rule, lower doses of drugs with intermediate to high hepatic excretion ratio are generally recommended in cirrhosis patients. Hepatotoxicity of few drugs such as anti-tuberculosis or antiretroviral agents used for HIV or viral hepatitis may increase in cirrhosis patients. Neurotoxicity and sedative effects of anticonvulsants and sedative/hypnotic drugs also may potentiate in these patients. Paracetamol can be used safely when prescribed in small doses of maximum 2-3 g per day for short durations and is recommended as firstline analgesic agent. In contrast, NSAIDs should be preferably avoided in advanced cirrhosis. Proton pump inhibitors have been linked to an increased risk of spontaneous bacterial peritonitis in cirrhosis.

IMAGING FINDINGS AND INTER-PRETATION IN PATIENTS WITH END-STAGE LIVER DISEASE

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Abstract

Cirrhosis is the final result of chronic damage to the liver and is characterized by parenchymal injury leading to extensive fibrosis and nodular regeneration. Wide spectrum of intra and extra hepatic findings on imaging in patients with cirrhosis are seen. Cirrhosis leads to diffuse parenchymal and morphology changes and interpretation of some focal lesion could be difficult due to parenchymal distortion. Cirrhosis is the main risk factor for development of hepatocellular carcinoma the sixth most common malignancy worldwide and the third most common cause of cancer related death. Early detection of HCC is essential to improve patient survival. Periodic ultrasonography (every 3 to 6 months) allows early HCC detection and dynamic CT or MRI permits an accurate assessment of the tumor in developed countries with a high incidence of HCC.LI-RADS (Liver Imaging Reporting and Data System) is a set of standardized terminology and a classification system for imaging findings in liver lesions. The LI-RADS score for a liver lesion is an indication of its relative risk for HCC.

LIVER FIBROSIS IN HBV OR HCV IN-FECTED PATIENTS: ROLE OF AUTO-PHAGY AND UNFOLDED PROTEIN RESPONSE

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Abstract

Bridging fibrosis is one of the major etiologies of liver damage and is initiated by chronic viral hepatitis B and C. Its pathological characterization includes interface hepatitis and portal-central vein bridging necrosis which results in the formation of portal-central fibrotic septa. Interestingly in many cases hepatic fibrosis is almost asymptomatic therefore its progression to cirrhosis provides significant risk of morbidity and mortality. It has been well defined that hepatic fibrosis can be reversed and is accompanied by accumulation of extracellular matrix (ECM) (collagen, fibronectin) following liver injury. However if there is continuous injury and chronic inflammation in the liver it will cause irreversible accumulation of ECM and leads to a progressive replacement of liver parenchyma by scar tissue. The progress to this end stage is naturally depended on both genetic and environmental factors and may take 5 to 20 years. Autophagy (macroautophagy) is the mechanism by which cells sequester, degrade via lysosomal enzymes and recycle long-lived proteins and even entire organelles. Autophagy is induced by different physiological stimuli or pathological situations. It is now widely accepted that autophagy plays crucial roles in cellular and tissues homeostasis as well as metabolism, development, immunity and the clearance of pathogens. The endoplasmic reticulum (ER) is involved in the regulation of cellular stress and protein folding processes and serves as an early gateway in response to unregulated cellular stress. The ER is involved in the creation of a series of tightly adaptive mechanisms that assist cells in resuming normal conditions and preventing cell death. These adaptive responses are referred to as the unfolded protein response (UPR). It is important to emphasize that the UPR has a threshold for its response to stresses. If there is too much stress on the ER and the ER cannot compensate this condition and return the cell to its normal status this will eventually trigger cell death. Several recent investigations have showed that both autophagy and UPR are involved in positive/ negative regulation of tissue fibrosis in different models. Our team beside many other investigators have reported that HBV and HCV infection induce autophagy and UPR in infected liver therefore it is important to find out the relation of HBV and HCV infection induced autophagy and UPR in modulation of liver fibrosis. Here I will focus on the role of autophagy and UPR in regulation of liver fibrosis in HBV and HCV patients. I will also discuss how autophagy and UPR might be involved in HBV or HCV induced liver fibrosis, progress of fibrosis and possible therapeutic approach for preventing liver fibrosis in these patients for future develop-

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ment of new generation of drugs.

HEPATITIS C IN HEMODIALYSIS CENTERS

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Abstract

Blood borne virus (BBV) infection is recognized as an important hazard for patients and staff in hemodialysis units since 1960s. During recent decades, increasing number of patients on hemodialysis (HD) give us this alarming message that hemodialysis units should be alert for the threat of BBV transmission through patient to patient and from patients to staff and vice versa. The prevalence of HCV infection in HD patients varies geographically both inside and between countries. The prevalence of HCV infection varies widely between 5.5% and 24% among different HD patients among Iranian population. There are known risk factors for acquiring HCV infection among patients undergoing HD including: long hemodialysis duration, three or more HD sessions per week, male gender, old age, history of previous blood transfusion. Presence of positive Anti-HCV among patients undergoing HD increase their mortality and it also diminish graft survival rate among HD patients' candidate for renal transplantation. Strict implementation of universal precaution strategies of infection prevention in HD units, proper disinfection of equipment's in HD unit, routine initial and surveillance serologic screen of HCV and avoiding blood transfusion as least as possible in patients undergoing HD are main strategies to decrease impact of HCV in HD units. Consideration as soon as possible of therapy of HD patients with chronic hepatitis C, is also important. There is not enough evidence yet to support segregation of patients or dedication of machines among patients of positive Anti-HCV undergoing HD could lead to more benefit to control of HCV in HD units.

PREVENTION OF HEPATITIS B IN NURSES

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Abstract

Hepatitis B is the most important infectious occupational hazard which the healthcare workers (HCWs) encounter. Healthcare personnel specially nursing staff represents a high risk population for Hepatitis B virus (HBV) infection, but they do not recognize all exposures to potentially infectious blood or body fluids and, even if exposures are recognized, often do not seek post-exposure prophylactic management. The objective of the study was to review of preventive practices regarding Hepatitis B among nurses.

Content: Health care personnel are at increased risk of contracting blood borne pathogens due to their occupational exposure to blood and body fluids. More than twenty diseases can get transmitted through needle stick injuries including Hepatitis B, Hepatitis C and HIV. Among the health care personnel, HBV is transmitted by the skin prick with an infected, contaminated needles and syringes or through accidental inoculation of minute quantities of blood during the surgical and dental procedures. Global burden of HBV due to contaminated sharp injuries in HCWs is estimated to be 66,000 cases and 261 deaths annually. In developing countries 40-60% HBV infections in HCWs are attributed to sharp injuries. When compared to other health personnel, the nursing staff is the group that is most frequently victimized by accidents with cutting and piercing objects, since these professionals are also the ones who most often handle such material while performing their tasks. Nurses often have to deal with spilt blood, needle stick and sharps injuries, which can transmit blood-borne infections between patients and healthcare staff, and infection with the HBV is a common result. The risk of contracting HBV infection in an unvaccinated person from an HBV-infected needle stick or sharp injury ranges from 6–30%. Various measures of preventive practices which should to be taken by the nurses include use of gloves, gowns, use of sterilized instrument, blood testing, taking vaccines and use of condoms. Hepatitis B is a vaccine preventable disease for which a safe, immunogenic and effective vaccine is recommended since 1982 though its implementation is still insufficient and a sizable proportion of HCWs never get vaccinated



despite potential occupational risk. Iran has been conducting the vaccination program for high-risk groups, such as medical staff and clinical students, at intervals of 0, 1, and 6 months since 1993. WHO (2015) is developing consolidated guidelines on hepatitis B. It provided recommendations on the use of safety-engineered syringes for intramuscular, intradermal and subcutaneous therapeutic injections in health-care settings (www.who.int/ injection_safety/en). This guidance helps prevent the reuse of syringes on patients and decrease the rate of needle-stick injuries in health-care workers related to injection procedures.

Conclusion: Since nurses are at increased risk of acquiring needle stick injury, and exposed to blood and blood products in their clinical practice, they should be vaccinated upon entry into the professional life, Education programs should be focused on increasing nurse's perceived severity to occupational exposure to hepatitis B.

MANAGEMENT OF HEPATITIS B: FOR NURSES

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Abstract

HBV infection is a global public health problem. It is estimated that there are more than 250 million HBV carriers in the world of whom approximately 600,000 die annually from HBV-related liver disease. Despite the availability of HBV vaccines, the rate of HBV-related hospitalizations, cancers and deaths have more than doubled during the past decade.

Acute Infection: The diagnosis of acute HBV infection is based upon the detection of hepatitis B surface antigen (HBsAg) and IgM antibody to hepatitis B core antigen (anti-HBc). Treatment of acute HBV depends upon the clinical setting. However, appropriate measures should be taken to prevent infection in all exposed contacts and hepatitis B immune globulin and hepatitis B vaccine. For most patients, treatment is mainly supportive. The likelihood of liver failure from acute HBV is less than 1 percent and in immunocompetent adults, the likelihood of progression to chronic HBV infection is less than 5 percent. As a general rule, we treat patients with a severe or a protracted course (eg, those who develop a coagulopathy [international normalized ratio (INR) >1.5], those with persistent symptoms or marked jaundice [bilirubin >10 mg/dL] for more than four weeks after presentation). We also treat patients with acute liver failure due to HBV to reduce the likelihood of reinfection post-liver transplant.

Chronic Hepatitis B: The diagnosis of chronic HBV infection is based upon the persistence of hepatitis B surface antigen (HBsAg) for greater than six months The initial evaluation of patients with chronic HBV infection should include: A history and physical examination, emphasizing: risk factors for coinfection with hepatitis C virus (HCV), hepatitis delta virus (HDV) and/or HIV; use of alcohol; family history of HBV infection and liver disease and signs and symptoms of cirrhosis. Laboratory tests, including: a complete blood count with platelets, liver chemistry tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], total bilirubin, alkaline phosphatase, albumin), international normalized ratio (INR) and tests for HBV replication (hepatitis B e antigen [HBeAg], antibody to HBeAg [anti-HBe], HBV DNA). Testing for immunity to hepatitis A virus (HAV) with HAV IgG antibody should be performed in patients who are not known to be immune. Screening for fibrosis using noninvasive tests (eg, vibration-controlled transient elastography, serum fibrosis panel) or liver biopsy. The decision to initiate treatment is primarily based upon the presence or absence of cirrhosis, the alanine aminotransferase (ALT) level and the HBV DNA level. Patients who are not deemed to be treatment candidates at presentation and those who decide to defer treatment, should undergo monitoring of liver biochemical tests, HBV DNA and HBeAg status since liver disease and/or HBV replication may become active later. The goals of antiviral therapy are suppression of HBV DNA, loss of HBeAg (in patients who were initially HBeAg-positive) and loss of HBsAg. Antiviral agents for chronic HBV include pegylated interferon (PegIFN) or nucleos(t)ide analogs (eg, entecavir and tenofovir). Patients should be monitored while on therapy to assess for virologic response and medication toxicity. Most patients receiving nucleos(t)ide analogue therapy will require at least four to five years of treatment and some may require indefinite treatment.

MANAGEMENT OF HEPATITIS C: FOR NURSES

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Abstract

Hepatitis C is a major cause of liver failure and hepatocellular carcinoma worldwide. The main aim of HCV therapy is to achieve sustained virologic response (SVR), defined as undetectable HCV RNA 12 weeks after the end of therapy. Iran will possibly eliminate HCV by 2030. Patients finding in necessary step for HCV elimination. All cases who at risk for HCV infection should be assessed, including: persons with a history of transfusion before 1996 in Iran, thalassemic and hemophilic patients, patients with organ transplant, HIV infected patients, persons with a history of IV addiction, sex workers, prisons, neonates of HCV infected mothers. We should consider at least three parameters prior to HCV therapy. First, fibrosis stage of liver disease should be assessed by non invasive assays. Initially HCV genotyping (and subtyping) should be assessed. Another parameter is treatment history of HCV therapy by pegylated interferon and ribavirin or other regimens. Direct acting antiviral (DAA) regimens including: A. simeprevir+sofosbuvir, B. daclatasvir or ledipasvir or velpatasvir+sofosbuvir ±ribavirin, C. grazoprevir+elbasvir±ribavirin, D. pa ritaprevir+ombitasvir+dasabuvir+ritonavir±ribav irin, E. velpatasvir+voxilaprevir+sofosbuvir. These regimens can improve SVR \geq 95% with minimal adverse effects. The duration of DAAs therapy is 12 or 24 weeks.

SURGEONS ARE AT HIGHER RISK FOR HBV AND HCV

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Abstract

Surgeons are at risk of acquiring infection with Hepatitis B virus (HBV), Hepatitis C virus (HCV) during surgical procedures. The prevalence of HBV and HCV among surgeons is at least as high as in the general population. The rate of transmissi-

bility from needle stick is 6-37% for HBV and 1-2% for HCV. The risk of transmission of HBV and HCV from surgeons to patients during surgical procedures are small, but there are documented instances of its occurrence, despite the availability of HBV vaccine and less transmissibility of HCV, thus the infected surgeon should consider the possibility of transmitting the infection to the patient during surgery. The likelihood of transmission is greatest during exposure prone procedures. What are the ethical issues when a surgeon is infected with HBV or HCV? Does the surgeon an ethical or professional responsibility to disclosure his condition to the hospital or to the patient? What should an infected surgeon do to protect his patients? HBV infection alone should not disqualify persons from the practice or study of surgery. Use HBV-DNA serum levels rather than Hepatitis B e-antigen status to monitor infectivity. Threshold value of serum HBV-DNA considered safe for practice is <1000 IU/ ml. For most chronically HBV-infected providers and students who conform to current standards for infection control, HBV infection status alone does not require any curtailing of their practices or supervised fearing experiences. Surgeons are generally required by hospitals to undergo testing for the HBV, in the future this requirement may be extended to HCV. Recently drugs have become available for the treatment of HCV that are highly effective with a shorter duration of treatment. Surgeons should consider being tested voluntarily for HCV but should understand the consequences of a positive test. According to published guidelines, the surgeon infected with HBV or HCV has an ethical duty to curtail his practice until treatment has reduced the risk of transmission to patients to an acceptable levels.

RECOMMENDATIONS FOR POST EX-POSURE PROPHYLAXIS TO HEPATI-TIS B VIRUS

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Abstract

More than 30 different pathogens have caused documented occupational infection following ex-

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posure to blood or body fluids in healthcare workers (HCWs) or hospital laboratory personnel. The most important of these are hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The risk of acquiring HBV from a needle stick injury ranges from 1% to 6% (source patient HBsAg-positive, HBeAg-negative) to 22%-31% (source patient HBsAg-positive, HBeAg-positive). The average incidence of anti-HCV seroconversion after accidental percutaneous exposure from an HCV-positive source is 1.8%.

The recommendations for management of blood borne exposure to HBV are summarized below.

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APPROACH FOR PREVENTION AF-TER NEEDLE STICK WITH HCV+ PA-TIENTS

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Abstract

Individual institutions should establish policies and procedures for HCV testing of persons after percutaneous or permucosal exposures to blood and should ensure that all personnel are familiar with these policies and procedures. Immune globulin and antiviral agents are not recommended for post-exposure prophylaxis of hepatitis C. When a needle stick, sharps or mucosal exposure to blood occurs, the source of the exposure should be tested for antibody to HCV (anti-HCV), and all repeatedly reactive results by enzyme immunoassay should be confirmed by recombinant immunoblot testing for anti-HCV. If the source is anti-HCV positive, the exposed person should be tested for anti-HCV and alanine aminotransferase level at baseline and follow-up (e.g., at 4 to 6 months). For earlier diagnosis of HCV infection, testing for HCV RNA may be performed at 4 to 6 weeks. There are no recommendations for restriction of activities during the post-exposure follow-up period. Limited data indicate that antiviral therapy might be beneficial when started early during the course of acute hepatitis C, but no guidelines exist for administration of therapy during the acute phase of infection. Most patients with acute hepatitis C are asymptomatic, but a high rate of chronicity is expected (50-90%). Symptomatic disease with jaundice, female gender, a young age, and genetic polymorphisms in the region upstream of the IL28B gene have been associated with spontaneous viral clearance. Patients with acute hepatitis C should be considered for antiviral therapy in order to prevent progression to chronic hepatitis C. Some investigators estimate that the onset of ALT elevation, with or without clinical symptoms, may be the ideal time point for treatment. High SVR rates (>90%) have been reported in a small number of patients with sofosbuvir-based IFN-free regimens. The ideal duration of treatment of acute hepatitis C with IFN-free regimens remains unknown. Three trials were performed with the fixed dose combination of sofosbuvir and ledipasvir in patients infected with genotype 1. The SVR rates were: 93% (13/14) after 4 weeks of treatment in injection drug users [5], 77% (20/26) after 6 weeks of treatment in HIV-positive individuals [6] and 100% (20%) after 6 weeks of treatment in HIV-negative, non-injection drug users [7]. Because of the small number of Patients included in these trials, of the differences in their results and by analogy with chronic hepatitis C for which at least 8 weeks of therapy are required to maximize SVR rates, patients with acute hepatitis C should be treated with the combination of sofosbuvir and an NS5A inhibitor for 8 weeks, pending additional data establishing the ideal treatment regimen and duration. There is currently no indication for antiviral therapy as post exposure prophylaxis in the absence of documented HCV transmission. There is no indication for antiviral therapy as post-exposure prophylaxis in the absence of documented HCV transmission. Other treatment regimens are at the clinical developmental stage and will reach the market within the next two years.

THE STATUS OF VIRAL HEPATITIS IN THE PROVINCE OF SOUTH KHO-RASAN

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Abstract

Background and aim: Despite the existence of an effective vaccine, hepatitis B is still considered one of the main problems of global health, which is the main cause of hepatocellular carcinoma. Given the extent of the Khorasan province and sharing border with Afghanistan and reports of high prevalence of HBV in some rural areas (the Esfandiar village around the city of Tabas), we decided to conduct a deep comparative investigation.

Material and methods: This study started at 2013 by performing a community based screening project in the city of Birjand, to evaluate the prevalence of HBV, HCV and HIV. According to cluster sampling method, 5235 cases (15-70 years old) were included. Blood samples were collected and questionnaires have been completed. The status of anti-HBc, HBsAg and sero- markers of HIV, HCV, HDV and HAV was determined with ELISA test. In the course of this project, the initial screening plan for Esfandiar region began in 2016; a comparative comprehensive study included the Esfandiar region in compare to two neighboring villages (Marghoub and Zenoghan). The whole Esfandiar and partly of comparing group were included (1243 cases). The positivity for HBs Ag, anti- HBc along with seromarkers of HIV, HCV and HDV were assayed using ELISA tests.

Results: The mean age of Birjand's participants was 39.07-±14.04 y, and 52.2% subjects were female; in the Esfandiar study, it was 35.6-±19.9 y, with 54.3% females. The prevalence of HBsAg and anti- HBc in Birjand was 1.6% and 15% respectively, corresponding result for Esfandiar was 17.8 and 48.7% respectively. In the comparing villages, the seropositve rates of HBsAg and anti- HBc in Marghoub were 1.7% and 20.3%, respectively, 0.5% and 7.8% among the population of Zenoghan. The rate of HBsAg positivity in the city of Birjand was significantly higher in subjects with a history of cupping, a positive history of familial HBV or HCV infection and older subjects. In the project of Esfandiar, the HBV was more prevalent among those with dental treatment history, traditional phlebotomy and endoscopy, inter familial routs and war veteran.

Conclusion: The prevalence of HBsAg in Birjand

was close to that observed in the overall Iranian population but the rate of anti-HBc was higher, possibly due to the exposure of the elderly to more risk factors and also positive effect of vaccine. It seemed that HBV is high endemic in the Esfandiar village. The high rate of anti- HBc indicates declining disease due to more control and vaccine program. In spite of familial affinities between villages, this low level of disease in Marghoub and Zenoghan is interesting and requires more studies.

THE STATUS OF VIRAL HEPATITIS IN SISTAN AND BALUCHESTAN PROV-INCE

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Abstract

Background: Viral hepatitis is one of the most important health problems in the worldwide, that a high rate of morbidity and mortality. The condition of the disease varies in different parts of Iran. The aim of this study was to determine the status of viral hepatitis in Sistan and Baluchestan province, as well as risk factors and frequency of disease in high-risk populations.

Method: A systematic review was conducted to evaluate the studies performed in the past 20 years(1997-2017) that reported prevalence acute and chronic viral hepatitis infection and its risk factor in the general population and among high risk group including: Family members of patients, thalassemic and hemophilic patients, prisoners, IV drug abuser, barbers ,municipal solid waste workers and etc.

Results: Data was extracted from 22 papers. In the discussion of acute hepatitis, only one study was carried out 15 years ago that the frequency of viral hepatitis was respectively HAV (71.5%), HBV (17.9%), HCV (2.3%) and HDV (1.9%). The frequency of chronic hepatitis B and C in recent years in the general

population was 3.38 and 0.5%, respectively. The prevalence HBsAg in Family members of patients, thalassemic and hemophilic patients, prisoners, IV drug abuser, barbers and municipal solid waste workers was 19.3%, 0.3%, 4.9%, 8.4%, 25.9%,8.7% and 6.8%. The prevalence HCV in thalassemic and hemophilic patients and prisoners, IV drug abuser was 5.9%, 29.6%, 9.1% and 29.6%. The most serious risk factor for hepatitis B was the history of hepatitis B in the family and for hepatitis C injecting drug abuse.

Conclusion: This study shows information on the status of viral hepatitis in Sistan and Baluchestan province. Due to the high prevalence of hepatitis virus, preventive measures such as public education, screening of high-risk groups, vaccination program, prevention of addiction and Screening of hangouts in the province is seriously considered.

THE STATUS OF VIRAL HEPATITIS IN ISFAHAN

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Abstract

Isfahan is a province in center of Iran, with more than 5 million of population. Viral hepatitis, especially hepatitis B, C are among major health related issues in Isfahan. Actually, the history of identification & treatment of viral hepatitis patients began about 20 years ago, when diagnostic & therapeutic tools became generally available. In the first years, only a few specialists were involved in management of hepatitis B & C patients. However with global improvements in diagnosis & treatment of these cases, more & more gastroenterologists, internists & infectious disease specialists are now involved. There are 2 clinics dedicated to visit these patients. Large epidemiologic studies about the prevalence & incidence of viral hepatitis are lacking, but more than 100 small studies have been conducted in special populations such as IV-DU's, health care workers, sex workers, prisoners, etc. Hepatitis A is usually happening in children & young adults, so most people in Isfahan are immune by the age 30. The incidence & prevalence of hepatitis B has been decreasing in the past 20

years, probably as a result of national vaccination programs. The main route of transmission oh HBV in Isfahan is maternal. There has been limited studies about HDV prevalence in Isfahan. The HDV prevalence in HBS-Ag + patients is estimated to be 2-4%, most of them due to super-infection. The main route of transmission of HCV is through IV drug use. High risk behaviors, unsafe sex, tattooing, transfusion are other known routes. A large study in 2011, which recruited about 1800 volunteer IVDU's in Isfahan showed that about 35% of them were HCV-Ab positive. It is estimated that there are about 4000 IVDU's in Isfahan province, so, there should be about 14000 undiagnosed HCV +, IVDU's in the province, who can be a source for spreading the infection to the community. Isfahan is going to have an active role in the national program for HCV eradication. Since the medications are becoming free for every patient, the most important challenge in the future, will be case finding, which needs to be improved rapidly, so we can identify new cases with about 10 times higher rate than now. The incidence of cirrhosis due to chronic hepatitis B has been gradually decreasing in the recent 10 years, probably because of availability of diagnostic & therapeutic measures. But we see more cirrhotic patients with chronic hepatitis C. Fortunately, liver transplantation is now available in Isfahan & about 50 liver transplant operations have been performed in Isfahan in the past 2.5 years. Hepatitis E is rare in Isfahan & only few cases have been reported to have acute hepatitis E. The current situation of the management of viral hepatitis patients in Isfahan seems to be good. There are more than 10 laboratories who can perform molecular diagnostic tests. There are more than 30 specialists who are active in the treatment of viral hepatitis. There are at least 5 experts in the field, with more than 15 years of experience in treatment of viral hepatitis. Most patients have access to these facilities, either freely or with the least expense. So Isfahan can be a pioneer province in management of viral hepatitis, particularly HCV eradication in Iran.

STATUS OF HEPATITIS B VIRUS IN TEHRAN DURING LAST DECADE

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Abstracts-Invited Speakers

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Abstract

The polled estimated prevalence of HBV infection in the general population of Iran is 2.2 %. However, the estimations are based on heterogeneous studies and specific data about Tehran province are lacking. Prevalence rate among different populations in Tehran had been 1.2%, 1.8%, 34.7%, 153 per 105 female sex-workers, non-IV drug opioid poisoned patients, homeless subjects, blood donors, respectively. Although, the prevalence of HBV among blood donors showed a downward trend over the period of six years. However, there is no overall confirmed prevalence during the last decade in Tehran, particularly among general population. A well-designed study is required to estimate true prevalence and trends after integration of routine vaccination in extended program of immunization in Iran.

DISTRIBUTION AND RISK FACTORS OF HEPATITIS B VIRUS INFECTION IN THE GENERAL POPULATION OF **CENTRAL IRAN (QOM)**

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Abstract

Background: Hepatitis B is the most common chronic viral infection in humans and the most common cause of death among viral hepatitis. As 70% to 80% of chronic hepatitis cases are caused by HBV in Iran, this virus alone is considered the most important cause of liver diseases and the major cause of mortality arising from viral hepatitis cases in Iran.

Objectives: We planned this study to determine the prevalence of hepatitis B in the general population of Qom, central Iran.

Patients and Methods: The present study is a cross-sectional study. A total of 3690 samples were collected from 7 rural clusters and 116 urban clusters. Ten teams, each consisting of 2 trained mem-

bers were assigned to conduct the sampling and fill the questionnaires. The data were analyzed using SPSS.

Results: The prevalence rate of hepatitis B infection in Qom Province was 1.3%. The mean age of the patients with hepatitis B was 44.17 years. The prevalence of hepatitis B was 1.6% in men and 1.1% in women. Moreover, the prevalence of hepatitis B correlated positively with age, tattooing, and literacy level.

Conclusions: The prevalence rate of hepatitis B in Qom is 1.3%. It is possible to prevent the disease by increasing public awareness. Further investigation on clinical presentations and a determination of the genotype of the virus are suggested.

THE STATUS OF VIRAL HEPATITIS **IN HORMOZGAN**

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Abstract

In overall, 509 patients enrolled to this study. The mean age of these patients was 38.87 ± 9.55 years ranging from 1 to 90 years. Routs of transmission were: 238 (46.7%) inject of substance, 149 (29.3%) unknown rout, 62 (12.2%) blood transfusion, 50 (9.8%) sexual contact, and 10 (2%) mother to child. Frequency of HCV genotypes were: 316 (62.1%) 1a, 117 (23%) 1b, and 76 (14.9%) 3a. there was no significant association between HCV genotypes and gender, educational degree, risk factor of Hepatitis C, job, monthly income, HIV infection, Hepatitis B virus (HBV) infection, Intravenous drug injection, and underlying disease (P > 0.05).

THE CURRENT IMPORTANCE OF **HEPATITIS A IN IRAN**

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Abstract

Infection with hepatitis Avirus (HAV) occurs worldwide and is the most important cause of acute viral hepatitis. The highest prevalence of this infection is seen in developing countries, where the low standards of sanitation promote the transmission of the virus. Most of the acute HAV hepatitis cases are asymptomatic or symptomatic without jaundice, so going undetected the disease severity rise up with increasing ages, in older individuals an acute disease can lead to unusual prolonged, recurrent and even fulminant course. There is a mortality rates of above 50%, even after liver transplantation, in fulminant forms. HAV is a health problem in countries where the seroepidemiology is changing from hyperendemicity to intermediate rates. In recent years, because of improving sanitation and hygiene especially in water supply, the disease burden decreased in many parts of our country Iran. The results of researches in Iran revealed a heterogenic pattern of seroprevalence (as low as <30% in urban area of north Iran and Tehran to as high as more than 90% in zabol). These pockets of low prevalence increases the harm of hepatitis outbreaks with more severe forms of disease specially in older adult. Furthermore, hepatitis A is hyperendemic in most of our neighbor countries. In recent years our country experienced several outbreaks of hepatitis An in Karbala pilgrims. Most of the patients were adults and some of them experienced a very sever and prolonged course of the illness and even fulminant form. Result of a meta-analysis in 2013 regarding HAV seroprevalence rate, revealed; HAV infection in Iran may be considered as low or very low. It seems the our country is in a transition phase from hyperendemic to intermediate endemic with frequent pockets of low endemicity and serious harm of outbreaks in older individuals. Therefore, now in the right time to gift HAV vaccine to our people. With regard to low endemicity of hepatitis A infection in recent years in the I.R. Iran, it seems logic that efforts should be made to vaccinate high-risk populations along with more improvement in environmental hygiene and sanitations. This is true especially for travelers to neighboring countries. The I.R. Iran is located in the vicinity of countries of Middle East and south Asia with high endemicity of HAV infection. In Iraq, Syria, Pakistan, Turkey, Egypt, and Lebanon borders more than 90% of subjects tested are reported to be sero-positive with significant infection in children aged less than 10 years of age. Studies from some countries in the

2000s show a lower rate in children, with less than 50% of the 15 years old individuals being immune in studies conducted in Kuwait, Saudi Arabia, and the United Arab Emirates.

EPIDEMIOLOGY OF HEPATITIS E VIRUS INFEC-TION IN IRAN

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Abstract

Hepatitis E Virus (HEV) are the leading cause of acute viral hepatitis worldwide. The virus can be spread by the fecal-oral route or through contaminated water. The predominant mode of transmission in Iran is fecal-oral route, especially feces-contaminated drinking water. Person-to-person transmission is most likely rare in Iran, since no association between the household size and seroprevalence rate of HEV has been reported. Furthermore, HEV can be transmitted through animals to humans from exposure to infectious body fluids of infected animals, transfusion of infected blood products, and vertical (maternal-fetal) transmission. HEV has infected one-third of the world's population. Furthermore, 20 million new cases and 3.5 million acute cases of HEV infection occur globally each year, and HEV-related hepatic failure is responsible for approximately 56000 deaths per year. Most of HEV infections are acquired in late childhood or young adulthood. Caution should be taken in high-risk groups like pregnant women, children, immunocompromised and transplanted recipients, where HEV infection may lead to hazardous transfusion-associated liver disease. Although HEV infection is a self-limited infection, the mortality rate in pregnant women is 10%-25%, it may raise up to 40% in this group. It is noteworthy that the mortality rate is 1%-2% in the general population, but it may rise to 75% in patients with liver disorders. HEV infection is endemic in many developing countries with a prevalence of more than 50%. In non-endemic countries, the prevalence varies between 1% to 20%. Iran is also one of the countries where hepatitis E is endemic and several cases of HEV infection outbreak have occurred so far. The prevalence of HEV infection is very different in Iran. Seroprevalence of HEV in general population of Iran for total HEV antibod-

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ies is ranging from 0 to 14.2 % in different studies. Hepatitis E is also considered as emerging transfusion-transmitted infection. Studies on the seroprevalence of HEV in blood donors in Iran are limited to main cities. The results showed a varies results from 4.5 to 16.7%. Despite, the prevalence of HEV in Iranian blood donors is high, screening of HEV in Iran blood banks is not performed until now. The seroprevalence of HEV among hemophilia and thalassemia patients in Iran is lower than expected and is in the range of that found in the general population of Iran. The seroprevalence of hepatitis E among patients under hemodialysis varies considerably from 4% to 28% in different cities of Iran. In the conducted studies in Iran, we identified various HEV seroprevalence among this patients group. The different ranges of HEV infection among Iranian hemodialysis patients seems to be very controversial and needs more evaluation. We have only two studies regarding the possible effect of HEV seroprevalence in intravenous drug users (IDUs) in Iran. These studies indicated high seroprevalence of HEV infection among IDUs in Iran with more than 20% prevalence. In conclusion, the status of HEV infection in Iran is varies in different geographic region and patient's groups. It varies between 2.3% to more than 40% among Iranian population. This pattern is more likely to the other EMRO and Middle Eastern countries. However, Iran is classified as an endemic region. It is obvious that the prevalence of HEV in general population of Iran increased by age. Unfortunately, due to the little awareness of health workers and also inappropriate diagnosis of HEV infection in Iran, it is still underestimated. Further prospective studies with community based, on prevalence of HEV infection are needed to achieved the better knowledge on the infection in Iran.

DC-BASED IMMUNOTHERAPY: A NEW HORIZON IN TREATMENT OF CHRONIC HEPATITIS B

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Abstract

Persistent hepatitis B infection is a major public health concern because of its propensity to prog-

ress to liver cirrhosis and hepatocellular carcinoma (HCC). Patients with chronic HBV infection who show remission, develop a vigorous CTL and a strong type-1 T helper cell (Th1 cell) cytokine response that is comparable to patients who have a self-limiting disease. Dendritic cells (DC) are the most potent antigen-presenting cells (APC) and are crucial for inducing primary antiviral immune responses. After antigen uptake, DC migrate to lymphoid organs where they mature. While undergoing maturation, DC highly express costimulatory molecules, such as CD80 and CD86, on their cell surface and interact with CD28 receptor on T cells. In addition, DC secrete cytokines, especially IL-12, that additionally contribute to T cell activation. Exposure of T cells to viral antigens in the absence of or inadequate presence of costimulatory molecule expression by APC, may result in tolerance to the virus. In humans, DC generated in response to GM-CSF and IL-4 show characteristic features of typical myeloid DC and produce IL-12 that favors Th1 polarization. In contrast, DC derived from plasmacytoid cells develop in an IL-3 cytokine milieu and promote Th2 differentiation. An imbalance between myeloid and plasmocytoid derived DC in peripheral blood may contribute to alteration of the T cell response leading to impaired induction of CTL. DC propagated from peripheral blood from chronic HBV patients and modulated ex vivo may function as a powerful tool for antigen-specific immunization strategies. However, concerns have been raised regarding the use of immature DCs (iDCs) in clinical trials since antigen presentation by iDCs, in particular antigens representing self-proteins, is known to tolerize T cells rather than immunize hosts. mDCs generated and transfected with HBV associated antigens in vitro, in an environment free of Cytokine inhibitory factors, have evolved potentially as a powerful vaccination tool for Anti HBV immunotherapy. The recent studies showed that using of TLR agonists to regulate specific cytokine production in young mDCs, allowing them to provide appropriate signals for polarization of CD4+ T cell responses in a Th1-direction, to efficiently stimulate CD8+ CTL responses and to activate natural killer cells. In the future, it is predicted that adoptive T cell therapy using TCR-transgenic lymphocytes will be combined with DC- based vaccine strategies to retain the potency of T cell-mediated responses in vivo over longer periods of time. Thus DC vaccine strategies will hopefully find additional application in future combination immunotherapies.

INFECTIONS AS A THREAT FOR

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BLOOD SAFETY

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Abstract

In past century, late of 80s, the incidence of post transfusion hepatitis varied between 2-4% in northern Europe to near 20% in southern Europe, most likely due to what known as Non A-Non-B hepatitis. After decades past, recently the evidences revealed that the risk of post transfusion hepatitis dramatically decreased and reached to 1/ near 200000 for HBV and 1/near 2000000 for HCV. These obvious achievements in transfusion medicine was attributed to the promotion in screening methods like introduction of serological methods and highly sensitive and specific MP-NAT and/or ID-NAT tests, combined to improving the blood donor selection programs and improvement in community's health status by introducing the HBV vaccine in EPI. Nowadays, we are faced to another important achievement about HCV treatment which leads the policy makers to set a goal of HCV elimination till 2030. In addition, regarding the expert opinion a functional cure for HBV would be available in next 5 years. Large scale screening and providing the safe, effective and inexpensive treatment could lead to very fast changes on the epidemiological figures of these two most important viral hepatitis. So that, it would be expected that paradigm shift will occur in the blood safety issue. In the next decades blood transfusion centers will be faced to the threat of EIDs (Emerging Infectious Diseases). Thus, authorities developed a tool kit which is started by EID monitoring sites (horizon scanning) and accompanied by risk assessment tools, a flow diagram to follow as one proceeds to determine whether intervention development and implementation are required in addition to methods to validate and assess the efficacy of any introduced intervention. Each country has to implement its own strategy to predict, found and fight EIDs as threats of blood safety.

TTIS SURVEILLANCE SYSTEM FOR BLOOD SAFETY IN IRAN, 2016

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Abstract

Blood is a biologic product, so it is very important to be sure about safety of blood and its products in every time towards Zero Risks and from Donor vein to recipient vein as well. Two preventive strategies could reduce the risk of transmissibility of transfusion-transmitted agents, one is during Donor Selection Process and the second one is a strong screening system for Transfusion Transmitted Infections. Vigilance of the prevalence of TTIs among blood donors has a critical role in an active Blood Safety Surveillance System. An active surveillance system for safe blood donation has been established since March 2016 in country. The Blood Donation Selection process of each reported positive cases monitored retrospectively during this surveillance system. A technical group evaluates all the process of the selection process, donor called back for confidential counseling and medical counselor evaluated for his/her counseling skills. Then the analytic situation of positive cases of each blood donation center triangulated with the data of Exemption Rate and the Rate of CUE (Confidential Unit Exclusion) monthly as well for each blood donation center. The results of these data triangulations could help the national blood transfusion system for finding the gaps, such as insufficient counseling skills of medical counselors, hot spot located of blood collection center and inappropriate design of counseling room about confidentially of counseling processes. Then technical committee in provincial level decided the best interventions based on the evidences of the monthly report, for filling the gaps. The interventions could be included with conducting a training workshop for scaling up the counseling skills of medical counselors, standardization of counseling room for insurance of confidentiality, even changing the location of the blood collection center for example. The trend of prevalence of the HBsAg and HCVAb in the past decade shows significantly the increase of the speed of the decreasing the slope of TTIs diagram among blood donors in 2016, during 12 months after establishment of this surveillance system.

TREATMENT OF AUTOIMMUNE HEPATITIS

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Abstract

Autoimmune hepatitis (AIH) is a generally unresolving inflammation of the liver of unknown cause. The diagnosis is based on histologic abnormalities, characteristic clinical and laboratory findings, abnormal levels of serum globulins, the presence of one or more characteristic autoantibodies and the exclusion of other conditions that resemble AIH. In patients negative for conventional autoantibodies in whom AIH is suspected, other serological markers including at least anti-SLA and atypical pANCA, should be tested. Diagnosing AIH in patients with underlying NASH may be difficult, especially in the presence of a positive ANA. The conditions most likely to be confused with AIH are Wilson disease and drug-induced hepatitis (DILI). DILI and AIH proposing possible connections with suggested diagnoses and clinical characteristics. Overlap conditions must be considered in unusual cases with increased alkaline phosphatase.IgG4-related AIH is a new entity that is not explained yet fully. Liver biopsy examination at presentation is recommended to establish the diagnosis and to guide the treatment decision. In general, treatment of AIH should be response guided and treatment regimens should be individualized. The aim of treatment in AIH is to obtain complete remission of the disease and to prevent further progression of liver disease. The cornerstone of treatment is immunosuppresion with corticosteroid with or without azathioprine. Treatment should be continued for at least three years and for at least 24 months after complete normalisation of serum transaminases and IgG levels (biochemical remission). Treatment end points are remission, treatment failure, incomplete response and drug toxicity. At least 10–15% of patients seem to be refractory to standard treatment, as a result of non-compliance, partial compliance or true non-response. In difficult cases alternative treatments also is better to be considered. The current choices second line immunosuppressive therapy include mycophenolate mofetil and cyclosporin or tacrolimus Mostly

corticosteroid therapy is favored even in asymptomatic. Treatment at pregnancy and postpartum period is important. Teratogenicity associated with azathioprine therapy is a theoretical consideration, but increased birth defects have not been reported in mothers receiving this treatment and nor there been apparent adverse consequences of breast feeding by treated mothers. Relapse occurs in approximately 80% of patients who enter remission, depending in part on the laboratory and histological findings prior to drug withdrawal. The optimal time to prevent the consequences of repeated relapse and re-treatment is after the first relapse then Autoimmune hepatitis is known as a life-long disease .It is important to note that patients with cirrhosis were equally likely to achieve complete response. Then treatment must be considered even in these patients. As many other chronic hepatitis disorders liver transplantation is the last resort of treatment. Overally 5 year survival is good and around 80 to 90 percent. AIH recurrence is seen in about one third of patients and surveillance liver biopsies may be warranted.

CONTROVERSIES IN THE MANAGE-MENT OF PSC

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Abstract

Primary sclerosing cholangitis (PSC) is a chronic progressive disorder of unknown etiology that is characterized by inflammation, fibrosis, and stricturing of medium and large ducts in the intrahepatic and/or extrahepatic biliary tree. PSC is usually a progressive disorder that ultimately leads to complications of cholestasis and hepatic failure. The majority of patients with PSC have underlying ulcerative colitis (UC). Patients with IBD and PSC may have a different phenotype than patients with IBD alone. Studies suggest that among patients with UC, pancolitis is more common in patients who also have PSC. Patients with primary sclerosing cholangitis (PSC) may be asymptomatic and diagnosed as part of the evaluation of abnormal laboratory tests or they may have symptoms such as fatigue and pruritus. Pruritus is a common symptom of PSC that can be extremely disabling, leading to severe excoriations and a decreased quality of life. Fevers, chills, night sweats, and right i

upper quadrant pain can also be present. Liver biochemical tests usually demonstrate a cholestatic pattern, with elevation of the serum alkaline phosphatase predominating in most patients. Primary sclerosing cholangitis (PSC) needs to be differentiated from secondary causes of sclerosing cholangitis and IgG4-associated cholangitis/autoimmune pancreatitis. In addition, PSC-autoimmune hepatitis overlap syndrome should be considered. IgG4-associated cholangitis is the most frequent extrapancreatic manifestation of type 1 autoimmune pancreatitis (IgG4-related), present in over 70 percent of such patients. It also rarely occurs in the absence of pancreatitis. Whether IgG4-associated cholangitis, autoimmune pancreatitis, and PSC are separate entities or are different manifestations of one disease is unclear. Serum IgG4 should be measured in all newly diagnosed patients with PSC, since treatment of IgG4-associated cholangitis/autoimmune pancreatitis includes glucocorticoids. There are two major goals of treatment in primary sclerosing cholangitis (PSC):

Retardation and reversal of the disease process
Management of progressive disease and its complications

There is no proven treatment that slows progression of the disease. A variety of immunosuppressive and anti-inflammatory agents have been studied in patients with PSC, but none has shown a consistent benefit on overall or transplant-free survival. Thus, a role for any medical therapy is unproven. In patients who are already taking UDCA, we suggest stopping UDCA but reinstituting it at standard doses (13 to 15 mg/kg per day in divided doses) if they develop worsening pruritus or jaundice. However, given the uncertainty regarding its benefits, an alternative approach is to start (or continue) UDCA in patients who want to take it despite the uncertain benefits. After six months, if the alkaline phosphatase normalizes or is decreased by at least 40 percent, or if the patient experiences symptomatic improvement, UDCA can be continued. Otherwise, it is stopped. No studies have demonstrated a long-term benefit from glucocorticoid therapy, either alone or in combination with other agents.cyclosporine, tacrolimus, methotrexate and azathioprine have all been used in clinical trials for management of PSC but none of them had significant effect in endoscopic retrograde cholangiopancreatography (ERCP) findings or histology.Recenty it has been found that oral vancomycin improved liver biochemical tests, symptoms and Mayo Risk Score particularly in those without cirrhosis but more studies are needed for long term follow up. We suggest that patients with a dominant stricture and pruritus

and/or cholangitis undergo endoscopic therapy to dilate and/or stent the stricture. Therapy of asymptomatic dominant strictures should not be undertaken routinely until benefit is demonstrated in controlled trials. Long-term prophylactic antibiotics are indicated for patients with recurrent cholangitis despite efforts to treat a dominant stricture. Given the high incidence of cholangiocarcinoma, we suggest annual screening for cholangiocarcinoma in patients with PSC. Screening consists of either ultrasound or MRI with MRCP, plus measurement of a serum CA 19-9. Other screening examinations include annual ultrasound of the gallbladder to screen for gallbladder cancer and bone density examination at diagnosis and every two to three years thereafter. Patients should also undergo screening for colorectal cancer and, if they have cirrhosis, hepatocellular carcinoma. Liver transplantation is now the treatment of choice for patients with advanced liver disease secondary to PSC.

UPDATE OF INTERVENTIONAL PRO-CEDURES FOR HCC

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Abstract

One of the most frequent primary malignant tumors in the world is hepatocellular carcinoma (HCC). Currently, the optimal treatment methods for HCC are hepatic resection and liver transplantation. Unfortunately, surgical therapies are suitable for 20% of patients and those who are not eligible for surgery should undergo interventional therapies. In the past decade, a variety of interventional procedures have been employed for local control of hepatocellular carcinoma (HCC) including transcatheter arterial chemoembolization (TACE) and many tumor ablation techniques, such as percutaneous ethanol injection (PEI), radio-frequency ablation (RFA), percutaneous microwave coagulation therapy (PMC), laser-induced interstitial thermotherapy (LITT), cryoablation, and acetic acid injection. By development of new technologies in imaging and drug delivery, it is likely that

H C 7 in the future patients with HCC will be treated by combination therapies to improve patient survival. Computed tomography (CT) and magnetic resonance imaging (MRI) have a crucial role in diagnosis and also follow-up of HCC patients treated by interventional procedures, by which the treatment efficacy, recurrence of disease and certain complications are evaluated. In this review article, we discuss the imaging modalities and also tailoring of interventional procedures for HCC patients.

APPLICATION OF EUS IN LIVE DIS-EASE

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Abstract

EUS is not the first option for evaluation of liver disease but it can be helpful some times for better evaluation of left liver lobs especially in patient that is candidate for liver transplantation and suspected to small lesion. The second most frequent cause for performing of EUS in liver disease is FNA of suspected lesion in the left lobe of liver and with low accuracy biopsy from liver for parenchymal disease and some other conditions as it described in below Although the entire liver cannot be seen by EUS, a large portion of the liver can be seen during a radial EUS examination. A significant part of the left lobe of the liver can be imaged from the gastroesophageal junction and from the body of the stomach. The inferior vena cava can be seen as an anechoic structure within the liver parenchyma. The liver appears as a complex solid organ with many vascular and fluid-filled structures (bile ducts). Large parts of the right lobe of the liver can be imaged by transgastric imaging from the antrum and the duodenum, especially from the duodenal bulb EUS for detection biliary lesions: in many reports EUS is superior to ERCP and MRCP for diagnosis of biliary lesions for example stone or sludge and mass lesion EUS technique could be used as the first-line procedure in patients with biliopancreatic diseases in the evaluation of common bile duct (CBD) stones, the sensitivity of EUS ranged from 88% to 100%, with a diagnostic accuracy rate up to 99% In contrast, the sensitivity of endoscopic retrograde cholan-

giopancreatography (ERCP) was somewhat lower at 79-90%, because of the problem of false-negative results caused by small stones located within dilated bile ducts or sludge that could be ignored in ERCP. Thickening (greater than1.5 mm) of the common bile duct wall is seen in patients with PSC but not in those with uncomplicated IBD or CBD stone. For this reason EUS can be used in diagnosis of PSC. Liver lesions or metastases: Endoscopic ultrasound can be used to visualize the left lobe and part of the right lobe of the liver. Endoscopic ultrasound can be used to visualize the left lobe and will have a significant outcome in the management of gastrointestinal tumors. EUS-FNA plays an important role in assessing liver masses that are detected by. EUS sometimes can detected small liver lesion that CT cannot detected and for this fact EUS can be a complementary imaging for better evaluation of liver EUS can detect small focal liver lesions that are not detected on CT scan. EUS could detect small (1.0 cm) hepatic lesions undetected by CT scans and could be used to biopsy deep-seated hepatic lesions. We can performed FNA from all of suspicious lesion in liver without hold of size of liver lesion EUS can detect small hepatic lesions previously undetected by CT scans and could be an important preoperative staging tool for liver involvement in malignancy. Esophageal varices: Endoscopic sclerotherapy (ES) and band ligation are standard treatments for esophageal varices. Unfortunately, recurrence is common and seems to be related to esophageal collateral vessels, easily identified by EUS. Eradication of these vessels might lead to a more durable therapeutic effect. EUS-ES is as safe and effective as ES in variceal eradication. Recurrence tends to be less frequent and occurs later. Persistence of esophageal collateral vessels after sclerotherapy is a risk factor for recurrence Endosonography usually allows detection of fundic varices even in early stage EUS is also able to demonstrate dilation of the azygos vein which occurs in patients with more severe esophageal varices the diameter of azygos vein ranges from 5+-1mm in normal individuals and patients with grade 1 esophageal varices to 7.2+-1mm and in patients with grade2 varices and 8.4+-1mm for grade 3 varices for this reason EUS is a rough orientational guide for assessing the severity of portal hypertension. Endosonography-guided Cholangiopancreatography and drainage: EUS can be helpful in difficult ERCP with not successful cannulation of ampulla and in 2 methods retrograde or integrade puncture of biliary ducts with passing guide wire from this location inserted a stent via the fistula for biliary discharge Puncture and injection of contrast into the bile/pancreatic duct to visualize

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94

the ductal system was first described in the mid 1990's. Harada et al. first reported pancreatography following puncture of the pancreatic duct under ES guidance in 1995. As ESBD is a combination of techniques of ES-guided fine needle puncture and EBS, an echoendoscope, puncture needle, guidewire, stent and stent pusher are necessary. Stent placement is carried out under fluoroscopy. Session, Puncture of the bile duct is achieved with 19 G needles for EUS-FNA These needle sallow passage of a 0.035-inch guidewire through the lumen after removal of the core needle. As a stent is inserted and placed over the guidewire, it is advantageous to use a thicker guidewire. Use of a thinner needle such as 22 G, which only allows access of a 0.018-inch guidewire, implies the risk of dislodgement of the guidewire during the subsequent procedure. After removal of the inner (core) needle and aspiration of bile followed by injection of contrast a slight amount of a guidewire is advanced deep into the intrahepatic duct through the outer (sheath) needle. Following removal of the outer needle while leaving the guidewire, a dilator (tapered catheter or dilator balloon) is fed over the guidewire and advanced to the puncture site, and dilation of the tract is performed. Then, aspiration of bile is repeated, followed by removal of the dilator. Finally, a stent and a pusher are fed over the guidewire and the stent is placed across the sinus tract. EUS is an important new tool for accessing the portal vein: There is a large number of potential uses of EUS-guided portal vein catheterization, and many of them are dependent upon the safety profile of the procedure. EUS used to place a 19-gauge needle into a branch of an intrahepatic portal vein, performeda portogram by using contrast and/or carbon dioxide (CO2) injection, and, after confirmation of the location of the needle in the portal vein, a pressure transducer catheter was placed into the lumen of the portal vein. For 1 hour, continuously monitored the portal vein pressure, demonstrating minimal pressure variation over time. Hepatic venous pressure gradient (HVPG), an indirect measure of the portal vein pressure, is highly predictive of the patient's clinical course. Patients with cirrhosis with HVPG greater than 10 mm Hg have a 90% risk of decompensation within 1 year Furthermore, patients with cirrhosis with resistant HVPG are at risk of variceal hemorrhage. The most obvious advantage is the fact that the EUS approach provides a direct measurement of the portal vein pressure. Although interventional radiologists theoretically may gain access to the portal vein through the percutaneous route, a high rate of bleeding complications precludes the routine use of this approach. Furthermore, the

determination of the HVPG cannot diagnose presinusoidal portal hypertension. The disadvantage of EUS-guided pressure measurements is the need to have endoscopic access to the upper GI tract.

FIBROSCAN ROLE IN FATTY LIVER DISEASE

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Abstract

Non-alcoholic fatty liver disease has been considered as one of the main etiology of chronic liver disease globally (1, 2). Non-alcoholic fatty liver disease (NAFLD) has two main subgroups including non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). NAFL and NASH are different spectrum of the same histological disease. The gold standard tool to diagnose NAFLD is liver biopsy and histological study and various stages are clarified according to histopathological investigations. There are some limitations for liver biopsy like invasive nature, complications, low level of individuals' satisfaction and sampling variation. There were many investigations which tried to find methods to identify NASH including imaging evaluations and blood tests. In this regard, application of Fibroscan (transient elastometer) (Echo Sens, Paris, France) is a device that can examine liver stiffness. Serial evaluation of liver stiffness can provide evidence about the progression of liver diseases like NASH. In our study using TE in detecting level of fibrosis in NAFLD cases has high accuracy and can be a good alternative for liver biopsy in patients who cannot undergo invasive procedures. TE is an easy method to evaluate liver fibrosis, noninvasive, needing short time to obtain results appreciated by patients. Although further longitudinal investigations are needed to confirm the outcomes.

FIBROSCAN: PRINCIPLE AND IN-TERPRETATION, THE ASSESSMENT OF LIVER FIBROSIS REPRESENTS A CRITICAL COMPONENT IN THE

EVALUATION OF CHRONIC LIVER DISORDERS

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Abstract

Liver biopsy represents the gold standard diagnostic tool for liver fibrosis assessment since the first description of the percutaneous liver biopsy in 1923. However, liver biopsy has intrinsic limitations that dampen the enthusiasm of patients and clinicians for their routineincorporation in clinical practice including, pain, risk of bleeding and hospitalization. Furthermore, liver biopsy is subject to sampling error and both intraobserver and inter-observer variability in interpretation, and is difficult to repeat for serial assessments over several points in time. Several no invasive methods to evaluate liver fibrosis proposed including direct and indirect serum markers of liver fibrosis and several imaging-based methods, such as transient elastography. Vibration-controlled transient elastography (VCTE) is the most commonly used imaging-based fibrosis assessment method in the United States. It can be performed at bedside in an ambulatory office setting, is rapid to perform, has a wide range of scores (2.5_75 kPa), is associated with acceptable intra-observer and inter-observer reproducibility and has been validated in large cohorts worldwide in a spectrum of liver diseases. Recently American Gastroenterological Association Institute revealed a guideline on the role of Elastography in the evaluation of liver fibrosis. In this guideline in patients with chronic hepatitis C and B, the AGA recommends VCTE, if available, rather than other nonproprietary, noninvasive serum tests (APRI, FIB-4) to detect cirrhosis. The cutoff point to detect cirrhosis is 12.5 kpa and 11 kps for HCV and HBV respectively. In HCV subjects cutoff point of 9.5 kpa is defined as severe fibrosis and cutoff point of 17.0 kPa to detect clinically significant portal hypertension to inform preoperative care. The AGA makes no recommendation regarding the role of VCTE in the diagnosis of cirrhosis in adults with NAFLD. In adults with NAFLD and a higher risk of cirrhosis, the AGA suggest using MRE, rather than VCTE, for detection of cirrhosis. In patients with chronic alcoholic liver

disease, the AGA suggests a VCTE cutoff of 12.5 kPa to detect cirrhosis. In summary; the assessment of liver fibrosis in patients with chronic liver disease remains an important component of clinical management. Although liver biopsy continues to have a vital role in the care of patients, noninvasive serum and imaging based fibrosis assessment tools are also helpful in routine clinical practice. Pooled analyses of diagnostic performance studies suggest that VCTE can be used to accurately diagnose cirrhosis in patients with chronic liver disease, particularly those with chronic hepatitis B or C infection. Of course VCTE has several limitations, including some limitation for performance, variable diagnostic performance across liver conditions with differing cutoffs to establish significant or advanced liver fibrosis or cirrhosis, inaccurate readings in patients with acute hepatitis, alcohol abuse, food intake within 2-3 hours, congestive heart failure, and extrahepatic cholestasis which need to take in consideration when applying for a patient.

MONITORING AND EVALUATION OF HCV ELIMINATION PROGRAM IN AUSTRALIA

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Abstract

Australia has had an active HCV screening program, leading to an estimated 82% of the HCV-infected population being diagnosed. A Government-funded interferon-free direct acting antiviral (DAA) treatment program for chronic hepatitis C virus (HCV) infection has been available in Australia since March 2016. Monitoring and evaluation of HCV elimination program in Australia require data on treatment uptake, outcomes and population-level impact on HCV prevalence, incidence, and disease burden. There are several key areas of DAA treatment program evidence-gathering that are underway in Australia. The Pharmaceutical Benefits Scheme (PBS), an Australian Government program subsidizing prescription medicines, receives the administrative records of dispensed prescriptions from pharmacies across Australia. i

Data on dispensed DAA prescriptions for a longitudinal cohort of individuals, representing a 10% random sample of the PBS database are used to monitor DAA treatment uptake. Real world Efficacy of Antiviral therapy in Chronic Hepatitis C (REACH-C Study) is an observational cohort from a national network of diverse clinical services, including tertiary clinics, general practice, drug and alcohol centers, and prison-based clinics. The REACH-C data are used to evaluate the real-world DAA treatment outcomes. Ongoing surveillance through the annual Needle and Syringe Program (NSP), including HCV RNA testing will enable evaluation of the impact of DAA treatment uptake on HCV RNA prevalence among people who currently inject drugs. Data linkage studies are underway that link notified HCV cases (mandatory in all Australian jurisdictions since the early 1990s) with several administrative datasets, which record individual-level PBS DAA treatment, hospitalization, cancer diagnoses and death. These studies will characterize the population-level DAA treatment impact on key markers of decompensated cirrhosis, HCC, and liver-related mortality.

ELIMINATING HEPATITIS C IN IRA-NIAN PRISONERS AS PART OF THE NATION-WIDE HEPATITIS C ELIMI-NATION PROGRAM – A PILOT STUDY

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Abstract

Introduction: In order to eliminate hepatitis C virus (HCV) infection in Iran by 2030 it has been calculated that we should treat 24,000 subjects each year for the next 13 years with a treatment modality effective in at least 80% of cases. A large number of these patients are Persons Who Inject Drugs (PWID) who also serve as a major pool for dissemination of the disease. A main prevalent area for hepatitis C infection is prisons where Iranian studies report an HCV prevalence between 10 and 80%. Many of these patients are infected in the prison through inmate interactions including unsafe tattooing and needle sharing between PWID. Considering the turnover of prisons in Iran,

targeting prisons provides a unique opportunity for both treating patients and preventing disease spread and would be enough to eliminate hepatitis C by 2030. The problem with prisoners is the lack of compliance and follow-up even when all these services are provided for free. The logistics of testing prisoners is also an area of concern. Methods: In order to identify the obstacles and the best procedures to treat HCV in prisons a pilot study will be carried out in 2 prisons in Iran. The study will start in June 2017 and preliminary results will be available by the time of the summit. We will be using a fixed dose combination pill containing 400 mg sofosbuvir and 60 mg daclatasvir (Sovodak, RojanPharma, Tehran, Iran). One pill a day for 12 weeks for all patients, weather cirrhotic or not. This medicine is produced in Iran and is very cheap. Most importantly it is a pangenotypic treatment and thus alleviates the need for genotype testing making it even cheaper to use. Important adverse events are extremely rare. In the pilot phase, only prisoners remaining in the prison for 6 months or more will be included. This allows us to see the response rate of our treatment. During the main elimination phase though, no follow-up is required as we know the response rate is above 95% and we are not planning retreatment for resistant subjects. The prisons will be visited in regular intervals and new inmates will be tested for hepatitis C infection. In the pilot phase, rapid tests, dried blood spots (DBS) and serum will be collected for both HCV antibody and if positive, HCV RNA. The sensitivity and specificity of these methods will be compared and the most suitable will be used for the main elimination phase. Medicine will be provided by Directly Observed Treatment (DOT). The patients will be called each day and observed swallowing their pills. The prison health system is already accustomed to DOT as it is being used for treating tuberculosis in prisoners for years. Subjects will be tested again for HCV RNA 12 weeks after the end of treatment to determine response rate.

Conclusion: We expect that after refining our procedures, we will be able to screen all prisoners for hepatitis C antibody at point of care using rapid tests. DBS will be collected from positive cases and taken to a central laboratory to confirm active infection by PCR methods. We expect this method to be extremely effective in eliminating hepatitis C in Iran by 2030.

ELIMINATION OF HEPATITIS C IN HEMOPHILIA, THALASSEMIA AND

PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Hepatitis C virus infection is the main cause for morbidity and mortality of liver disease in special patients. Hepatitis C virus (HCV) infection is a common cause of chronic hepatitis in patients with Hemophilia and thalassemia. Most patients acquired the infection through transfusion of blood and its products. The burden of HCV infection mandates us for screening and start of therapy as soon as possible. It seems that at least 50% of hemophilia and 20% of thalassemia patients were infected with HCV infection and the most common genotypes were 1a, 3a and 1b, respectively. Hepatitis C virus (HCV) infection is a significant cause of morbidity and mortality in hemodialysis (HD) patients. The reported prevalence of HCV among the HD population has varied greatly from 1.9 to 84.6% in different countries in recent years. During 10 years with support of scientists, Hemophilia centers, thalassemia foundation, Iran Hepatitis Network, and Ministry of Health more than 10000 of thalassemia and hemophilia patients treated as a national program and Peginterferon alpha-2a in combination with weight-based ribavirin has SVR rate of 50% for genotype 1 and 70% for genotype non-1 infections. Hepatitis C infection elimination is an ultimate goal until 2030, but before that we can eliminate it in some special patients such as hemophilia, thalassemia and patients on hemodialysis. The micro-elimination of HCV is the complete reduction of HCV infection to zero in targeted populations (e.g. hemophilia, thalassemia, patients on hemodialysis, PLHIV, and prisoners), settings (e.g. hospitals), or limited geographic areas (e.g. Birjand). Substantial steps toward micro-elimination have already been undertaken in most high-income countries, typically focused on those with advanced liver disease. Ireland, for example, has effectively eradicated HCV in its hemophilia-patient population. Really we can do micro elimination in our hemophilia, thalassemia and patients on hemodialysis. We started it 10 years ago and focused to screen and treat with old drugs. In thalassemia and dialysis centers nosocomial transmission of HCV is possible and decrease the burden of HCV with therapy will stop this rout of transmission. The efforts will focus on all provinces with collaboration of NGos, Universities, research centers in a high "Province Committee". The most applied approach would be to break down national elimination goals into smaller goals for individual population segments, for which treatment and prevention interventions can be delivered more quickly and efficiently. The micro-elimination approach encourages policymakers and other stakeholders to set extend national goal, and motivated the people for testing and motivation the patients to adhere to therapy. Our ultimate goal is elimination of HCV infection in hemophilia, thalassemia and patients on hemodialysis until 2020.

HEPATITIS C IN LEPROSY: BABA BAGHI STUDY

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Abstract

With availability of direct-acting antiviral agents (DAAs), there is great effort to eliminate HCV by 2030 globally. The case-finding is one of the main challenges in elimination of viral hepatitis C. One of the neglected groups for screening of hepatitis C is the patients with history of Leprosy. We conducted a multi-phase, multi-center study for evaluation of hepatitis C epidemiology, molecular epidemiology, natural history, risk factors and treatment response in patients with leprosy in different locations in Iran. The study showed high prevalence of hepatitis C in patients with leprosy with overall 47.3% HCV Ab seropositivity in all 239 cases studied in Baba Baghi village (main study location), villages of East Azerbaijan, villages of West Azerbaijan and Behkadeh Razavi in North Khorasan with prevalence of 61.5%, 9.1%, 6.7% and 25.5%, respectively. Moreover, in Baba Baghi village, the family members living with leprosy cases were tested for HCV Ab as well. The seropositivity rate of HCV in the latter group was 1.4%.

Assessment of HCV transmission risk factors showed that living in Baba Baghi, living with a HCV-infected spouse and having surgery are the main risk factors of HCV transmission in patients with leprosy history. Among 113 patients with his97

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tory of leprosy, 38 (33.6%) had negative result for detection of HCV RNA and presumed to had spontaneous clearance of HCV. The observed rate for HCV spontaneous clearance was compatible with previous reports in other HCV-infected patients in Iran. In this ongoing study, the HCV genotype of 69 patients was evaluated with predominance of HCV-1b in 68 (98.5%) patients. The HCV genotype of the two family members of these patients were HCV-1b as well. It is very important to remind that the most prevalent isolate of HCV in Iran is HCV-1a followed by HCV-3a and a 10% fraction of patients with HCV-1b. On the other hand, the most prevalent HCV genotype in Azerbaijan (the northern neighbor of Iran) is HCV-1b. Currently, we have a plan to assess the molecular epidemiology of the HCV isolates from patients with leprosy to find the probable source of infection.

In this prospective study, we have started to treat the patients with HCV RNA with Fixed-dose combination of Sofosbuvir/Ledipasvir or combination of Sofosbuvir+Daclatasvir for 12 weeks. The rapid virologic response and early virologic response rates were both 100% however, one patients relapsed by now resulting in 96% rate of sustained virologic response.

In conclusion, with the current evidences there is great interest to recommend screening of HCV in patients with history of leprosy in Iran and other countries.

TREATMENT OF HCV/HIV CO-INFEC-TION WITH DAAS, IRANIAN EXPERI-ENCE

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Abstract

We expect our approximately 3 to 5 percent of patients with chronic hepatitis c (HCV) infection are co infected with HIV. coinfection with HIV accelerate the progression of hepatic fibrosis and cirrhosis .HIV/HCV coinfected patients suffer from more liver related morbidity and mortality than HCV mono infected patients. Unfortunately patients coinfected with HCV /HIV have decrease accessed to liver transplantation. For all these reasons treatment of HCV in this patients should have a high priority and effective treatment in this patients remain an unmet medical need.

Method: In this study, was single site open label trial, 56 patients with HCV /HIV coinfected treatment. These patients were naïve and the other non-responder to Peg and Ribavirin .Patients were genotype 1a, 1b and 3a, that received Sofosbiovir with Ledipasvir for genotype 1 and daclatasvir+Sofosbuvir for 12 week and in patients with cirrhosis we added ribavirin to mention earlier.

Result: Out of 57 patients enroll, 6 were female and 51were male. 29 patients were genotype 1a and 1b, 27 were genotype 3 and 1patient was 1a and 3a most common adverse event were headache, fatigue, vomiting. All patients tolerate mention treatment and they have not serious adverse reaction.

Conclusion: Responded treatment for all patients were 100%, even after 3 months end of treatment patients had SVR .With advent of all oral regimens that include new direct acting antiviral agents (DAAs) that are safe highly effective and have fewer drug interactions that older regimens.

A REVIEW ON SOCIAL INTERVEN-TIONS FOR PREVENTION AND CON-TROL OF VIRAL HEPATITIS

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Abstract

Viral hepatitis is a global public health problem affecting millions of people every year, causing disability, death and the high costs of treatment of liver failure and chronic liver disease. Nowadays, it is expected viral hepatitis become a silent epidemic in entire worldwide. Due to differences in the geographic distribution, tailored prevention strategies are required. Till now, several programs were known as affordable solution including: raising awareness, high risk groups vaccination, safe blood supply, voluntary blood donations, safe injections, safer sex practices, harm reduction practices, and safe food, as well as Early diagnosis and improvement in current therapies, better provide

in access to treatment especially in low income countries. Further new prevention programs which conducted in various countries were suggested such as increase in awareness among the general population, develop more and effective data registry and surveillance system, intensive infant immunization program, lowering the cost of screening, correctional settings prevention strategies, implementing special services for drugs user, motivating behavior change, as well as integrating viral hepatitis prevention, screening, treatment into HIV/AIDS programs. However, the eradication of viral hepatitis will require governmental financial investment and substantial effort.

A REVIEW ON THE LAST IRANIAN SCHEDULE AND GUIDELINE OF HBV IMMUNIZATION (2015)

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Abstract

Hepatitis B vaccine is known as the most effective measure for prevention of Hepatitis B virus (HBV) infection. The strategy includes vaccination of all newborns as well as immunization of high-risk population. In Iran, vaccination of infants against HBV infection has been included in the national Expanded Program on Immunization since 1993. Following the advice of National Committee of Hepatitis in 2002, Iran's Ministry of Health and Education planned to apply a mass program for vaccination of individuals born during 1989-1992. This review summarized the HBV related issues mentioned in the last version (8th Edition) of "Schedule and Guideline of Immunization Approved by National Immunization Technical Advisory Group" published in 2015. In this edition, pentavalent vaccine was first introduced and hepatitis B vaccine was consequently permitted to be administered in four doses; HBV vaccine at the birth and then pentavalent vaccine at 2, 4 and 6 months old. Major topics of the review are: how to prescribe hepatitis B vaccine and its doses in children and adults, HBV immunization program in infants and the program in children who refer for vaccination with a delay, high risk groups for whom HBV vaccine prescribing is strongly recommended, indications of repeat a dose of HBV vaccine and/or checking serological response after vaccination. This guideline is also comprised some suggestions for immunization against HBV in special groups such as infants born from mothers with a seropositivity for hepatitis B surface antigen, people with a bleeding disorder, transplant recipients, etc.

INTRAFAMILIAL SEROPOSITIVITY OF HEPATITIS IN PATIENTS WITH HEPATITIS B AND C VIRUS

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Abstract

Hepatitis B virus (HBV) and Hepatitis C virus (HCV infection) are considered important public health problems. Hence, knowing the routes of transmission impacts the design of interventions to reduce the burden of disease. There are some common ways of spreading hepatitis including blood, sexual contacts and vertical (from infected mothers to offspring). In addition, Intrafamilial transmission of hepatitis considered as horizontal (between the spouses or children) transmission draw researchers' attention to itself in recent decades and still debated. That is, many studies show that HCV and HBV infections might cluster in families or households. Household behaviors, which involve a risk of transmission of hepatitis, include the sharing of personal hygiene items. Further, inasmuch as different studies show various results, It seems that more study are needed in this field to come to a definite conclusion especially concerning temporal association between intrafamilial exposure and infection.

EVALUATION OF SCIENTIFIC EVI-DENCES OF SYSTEMATIC REVIEWS AND META-ANALYSES ON HEPATI-TIS IN IRAN

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Abstract

Physicians, policy maker need to be informed about the effectiveness of the treatments, drugs, methods and accuracy of the tests that they use. The Evidence-Based Medicine Pyramid is simply a diagram that was created to help us understand how to weigh different levels of evidence in order to make health-related decisions. Systematic reviews are at the top of the pyramid, meaning they are both the highest level. Hepatitis viruses, such as HAV, HBV, HCV, HDV and HEV cause potentially life-threatening inflammation of the liver, which is characterized by acute and chronic forms of liver disease. According to 2013 World Health Organization global health impact report of viral hepatitis. The aim of this study was to determine quality of the systematic review and meta-analysis of published studies on hepatitis in Iran.

Methods: We searched international databases such; ISI Web of Sciences, Medline via Ovid, PubMed, Embase, Scopus and Iranian databases; MagIran, SID and Iran doc to July 2015. We examined sensitivity analysis, cumulative-analysis, regression, quality of studies and publication bias for assessing of the studies.

Results: Overall, 165 articles were obtained and after omitting the repeated studies, 81 articles were left. Based on analysis, the titles and summaries of 27 articles were selected and their texts were completely analyzed. In addition, after the evaluation of all articles, 55 of the articles were selected. A sensitivity analysis performed to determine the effect of each study on the effect size by sequentially omitting each data set, in the studies, 12% have done sensitivity analysis. The sources of heterogeneity in included studies, 5% have done regression. To assess publication bias in systematic review and meta-analysis, 74% have done. Cumulative meta-analysis to examine the changes of target indicator over time can be which needs that 7% have done in studies. For Quality assessments of included studies based some check-lists such PRIS-MA, CONSORT, JADA, only 36% have done. Also to assess publication bias in systematic reviews and meta-analysis, we observed that 48% have done in included studies.

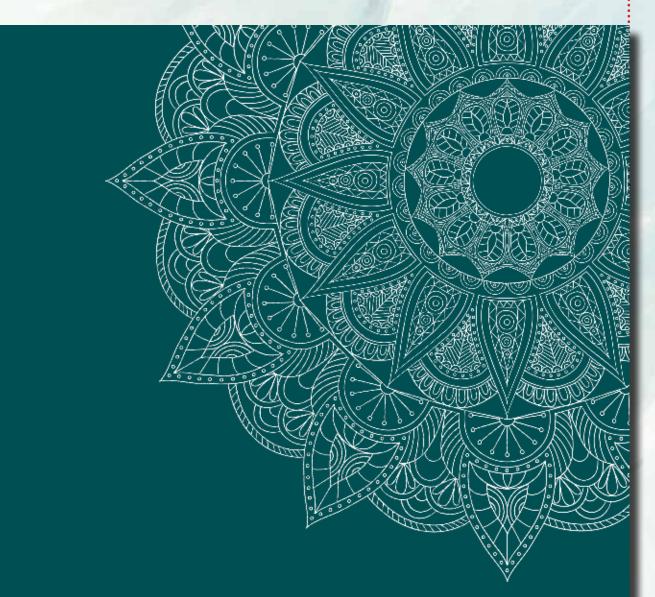
Conclusion: Based on results, systematic reviews and meta-analysis about hepatitis should use from suitable criteria. Authors and editorial journals are not considered adequately. To use the results of review studies, their results should be highly accurate.











The First Drawing & Illustration Contest with the Theme of Eliminating Viral Hepatitis



The First Drawing & Illustration Contest with the Theme of Eliminating Viral <u>Hepatitis</u>

The 7th International Tehran HepatitisConference



Organized by: Iran Hepatitis Network







ELIMINATE HEPATITIS







With Special Thanks To Mehrdad Amirfakhri, Our Unrelenting Support and All staff of Iran Hepatitis Network





"Finding infected patients and preventing the transmission are two important steps in viral hepatitis elimination"

"NOhep" is a global movement to eliminate viral hepatitis from the world by 2030 and Iran Hepatitis Network as a member of World Hepatitis Alliance (WHA) follows the NOhep activities in Iran. Fortunately, Iran has the lowest prevalence rate of viral hepatitis compared to the other Middle East countries. This low prevalence gave us the opportunity of eliminating viral hepatitis from Iran sooner than other countries of

our region. But one of the main problems is finding infected patients. Most of viral hepatitis infected cases are asymptomatic and unknown. We need to find infected patients and link them to the treatment. Therefore, all people should know about hepatitis to prevent them and help eliminating these diseases.

In this regard, Iran Hepatitis Network held the 1st Drawing & Illustration Contest with the theme of eliminating viral hepatitis to take more effective steps to create a culture of hepatitis awareness. This awareness will help finding unknown infected cases and preventing the transmission of viral hepatitis. So, it could facilitate removing of viral hepatitis from our community.

Seyed Moayed Alavian MD

Professor in Gastroenterology and Liver Diseases Director of Iran Hepatitis Network

1. www.worldhepatitisalliance.org/member/iran-hepatitis-network-ihn

2. http://hep.ir/

3. Hesamizadeh, K., Sharafi, H., Rezaee-Zavareh, M. S., Behnava, B., & Alavian, S. M. (2016). Next steps toward eradication of hepatitis C in the era of direct acting antivirals. Hepatitis monthly, 4)16).

4. Alavian, S. M., & Rezaee-Zavareh, M. S. (2016). The Middle East and hepatitis C virus infection: does it need special attention? The Lancet Infectious Diseases, 1007-1006 ,(9)16.





"Removing one of the main barriers for viral hepatitis elimination programs in Iran; lack of enough knowledge"

The World Health Organization sets the goal of viral hepatitis elimination by year 2030. Reaching this important goal seems to be impossible without raising the knowledge of general population about viral hepatitis. Unfortunately, our studies showed a lack of enough knowledge regarding viral hepatitis in Iran. All people should know about the transmission routs of viral hepatitis to prevent transmission, their symptoms and

risk factors to find unknown infected cases, and the importance of viral hepatitis elimination programs to facilitate reaching this goal.

Holding such festivals and campaigns can raise the general concern about this important issue, help people to know more about viral hepatitis, and facilitate the viral hepatitis elimination programs.

Hamidreza Karimi-Sari MD

Executive manager of hepatitis awareness campaigns Head of Young Investigators' Department Iran Hepatitis Network

1. Karimi-Sari, H., Tajik, M., Bayatpoor, M. E., & Alavian, S. M. (2017). Increasing the awareness of the general population: an important step in elimination programs of viral hepatitis. The American Journal of Gastroenterology, 395-393 ,(2)112. Available at: https://www.nature.com/ajg/journal/v112/n2/abs/ajg2016534a.html

2. Karimi-Sari, H., Bayatpoor, M. E., & Alavian, S. M. (2017). Awareness Campaign in (bio) Medical Students in Iran: a model for increasing the knowledge regarding hepatitis B and C. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 418 ,(6)23. Available at: http://dx.doi.org/10.1016/j.cmi.2016.11.022

3. Karimi-Sari H, Tajik M, Bayatpoor M E, et al. (2017). Public Awareness Campaign and Knowledge of Iranian (Bio)Medical Students Regarding Hepatitis B and C Infections. Hepatitis Monthly. 17;2017:e45929. Available at: http://hepatmon.com/en/articles/13512.html

4. Karimi-Sari H, et al. (2017). Knowledge, attitude, and practice of Iranian health sciences students regarding hepatitis B and C virus infections: A national survey. American Journal of Infection Control, in press. Available at: http://dx.doi.org/10.1016/j.ajic.2017.07.012





"Art and artists can help viral hepatitis elimination programs"

Over the last decades, one of the most important health problems which has affected the health of millions of people annually and has led to their morbidity and mortality has been viral hepatitis. Since one of the main causes of viral hepatitis is related to the lack of awareness about their transmission ways, a decision based upon holding the 1st Drawing and Illustration Contest with the theme of eliminating hepatitis was made in order to take more effective steps to create a

culture of hepatitis awareness. This contest is aimed at making people aware of transmission, prevention, and treatment of viral hepatitis.

Therefore viral hepatitis could not be eliminated without raising the concern about them among general population. We know art and artists can be effective regarding this important issue in our community. It is hoped that holding such festivals can help improving the level of community awareness and concern about these diseases.

Such festivals could also remove the stigma and false believes about viral hepatitis as the barriers for their elimination programs.

Maryam Nima

Director of 1st Drawing & Illustration Contest with the theme of Eliminating Viral Hepatitis

Iran Hepatitis Network



Ramin Mehdinezhad Dorosti MA in painting

رامین مهدی نژاد درستی کارشناسی ارشد رشته نقاشی

- ۱ رییس کمیته هنر همایش بین المللی بزرگذاشت حکیم ابوالقاسم فردوسی
 - ۲ عضو هیات مدیره انجمن نقاشان ایران(تامرداد ۱۳۹۲)
 - ۳– معاون گروه نقاشی از تاریخ ۱۳۸۰تا ۱۳۸۳
- ۴- مدیر گروه نقاشی دانشکده هنر و معماری تهران مرکز از تاریخ ۱۳۸۶ تا خرداد۱۳۹۲
 - و مدیر گروه نقاشی ااز نیمسال دوم ۹۵ تا کنون
 - ۵– عضو موسسہ توسعہ هنر های تجسمی
 - ۶- شرکت در بیش از ۵۰ نمایشگاه نقاشی در داخل و خارج از کشور
- ۷- عضوشورای سیاست گذاری ربع قرن دانشگاه آزاد اسلامی جهت بر پایی مسابقات هنری
 - ۸– تدریس در دانشگاه هنر تبریز . اصفهان . یزد
 - ۹ عضو هیات علمی دانشکده هنر و معماری دانشگاه آزاد واحد تهران مرکز
 - ه۱ داور بیست و یکم جشنواره ادبیات دینی ... کشور در همدان
 - ۱۱ دبیر انجمن هنرمندان نقاش ایر ان

افتخار ات:

- لوح تقدیر در دومین دوسالانه دیوار نگاری شهر تهران در بخش کارگاه نقاشی سه بعدی ثبت طر منعتی کشور به شماره ۳۷ه۸–۸۳۷۲/۹/۲۸ کسب رتبه اول تا سوم بین اساتید با توجه به ارزیابی دانشجویان در ترم های مختلف
 - شرکت در بیش از ۵۰ نمایشگاه نقاشی در داخل و خارج از کشور





Melika Sharifinia Painter, Graphist, Cinema and Television Actress ملیکا شریفی نیا نقاش و بازیگر سینما و تلویزیون و هنرآموخته رشته گرافیک

- ۱. متخصص ماسک سازی و نقاشی و تصویرگری
- ۲. دارنده مدرک مربی گری هنر کودک
- ۳. برنده جایزه خوارزمی در رشته های عکاسی و نقاشی سالهای ۸۱ و ۸۲
- ۴. شـرکت در ورک شـاپ هـای اسـاتيد مختلـف همچـون کريـم نصـر و فرشـيد مثقالـی و بنـی اسـدی و
 - گلدوزیان و میر اسـدللّه و...
 - ۵. شاگردی آیدین آغداشلو در ۹سالگی
 - ۶. تصویر سازی کتاب کودکان در سال ۹۲
 - ۷. تصویر سازی در کتاب تصویر گر ان سال ۸۵
 - ۸. شرکت در نمایشگاه های گروهی عکس و نقاشی در سالهای۸۵ و ۸۷
 - ۹. شرکت در جشنواره بنیاد کودک
 - ه ۱ . شرکت در جشنواره ی صلح
 - ۱۱. بازیگر تئاتر، سینما و تلویزیون





Niyosha Khatib BA in Graphic, Painter, Photographer

نیوشا خطیب کارشناسی گرافیک ، نقاش و عکاس خبری و هنری

۱. نمایشگاه گروهی ۵تاه ۱ تیر ۱۳۸۹ گالری شیث/تهر ان۲

۲. نمایشگاه گروهی نقاشی و عکاسی/ ۵تا ۱۰ آذر ۱۳۹۰/ گالری کمال الدین بهزاد / تهران

۳. نمایشگاه انفرادی / ۲تا ۸ دی ۱۳۹۰ /گالری شیث /تهران

۴. جزو ۱۲ برگزیده آثار ورک شاپ برج میلاد ۲/ مهر ۱۳۹۱ / برج میلاد / تهران

۵. نمایشگاه انفرادی با عنوان مردانگی <mark>های یک زن / ۷ تا ۱۳</mark> تیر ۹۴ / گالری شیث/ تهران

۶. نمایشگاه انفرادی با عنوان پایان ناتمام یک زن / ۲تا ۱۳ شهریور ۹۳ / گالری سبحان / تهران

۷. نمایشـگاه انفـرادی با عنوان زنان کافـه پـوش / ۲۵ دی تـا ۲۰ بهمـن ۳۳ / کافـه شیرازبا مدیریـت سجاد افشاریان / تهـران

۸. نمایشگاه انفرادی عکس / ۲۱ اسفند ۹۳ / کافه گالر<mark>ی مجموعه فرهنگی هنری سرنا / تهران</mark> ۹. برگـزاری و نمایشـگاه گردانـی نمایشـگاه گروهـی نقاشـی و عکاسـی روزمرگـی/ ۸ تـا ۲۶ خـرداد۹۳ / گالـری رج / تهـران

ه ۱ . مقاله نویسی بر ای مجله تیر اژه با عنوان یادداشت ها و نقاشی های یک نقاش

۱۱. نمایشگاه گروهی عکس با عنوان سی در سی / آذر ماه ۹۴ / گالری ایده پارسی

۱۲. نمایشگاه گروهی عکاسی و نقاشی با عنوان دیوار ۴۷ / تهران / اسفند ۹۴

۱۸. نمایشگاه گروهی عکس و نقاشی با عنوان سی نما ، کیارستمی / مهر ۹۵ / پردیس چارسو

۱۳. نمایشگاه گروهی / مهر ۹۵ / گالری ثالث

۱۴. نمایشگاه گروهی نقاشی / اسفند ۹۵/ گالری بیان / اصفهان

۵۱۰ و ۰۰۰





Mahdi Safiabadi ,MD

مهدی صفی آبادی پزشک پژوهشگر

مسئول آموز ش كميته تحقيقات دانشگاه علوم پز شكى بقية الله (عج)

۲. عضو بنیاد ملی نخبگان

۳. عضو مرکز گوارش و کبد دانشگاه علوم پزشکی بقیة اللّه (عج)

۴. عضو شبکه هپاتیت کل کشور

۵. مترجم کتاب Decision Making in Medicine- An Algorithmic Approach

۶. حضور به عنوان داور علمی در کنگره بین المللی هپاتیت ۶

۷. حضور به عنوان داور علمی در کنگره بین المللی هپاتیت ۷

۸. حضور به عنوان داور علمی در بخش دانشجویی اولین کنگره بین المللی ارولوژی–نفرولوژی ۹. حضور به عنوان داور علمی در بخش دانشجویی دومین کنگره بین المللی ارولوژی–نفرولوژی

۱۰. حضور به عنوان داور علمی در بخش دانشجویی کنگره بین المللی گوش و حلق و بینی ۱۱. حضـور بـه عنـوان داور علمـی و مـدرس در بخـش دانشـجویی اولیـن کنگـره پزشـکی اجتماعـی ایـران

۱۲ . ار ائه مقاله در بخـش دانشـجویی ۲۷ میـن کنگـره بیـن المللـی دانشـجویان پزشـکی اروپـا، آلمـان برلیـن(ESC)

۱۳ . ار ائـه مقالـه در بخـش دانشـجویی۲۸ میـن کنگـره بیـن المللـی دانشـجویان پزشـکی اروپـا، آلمـان برلیـن(ESC)

۱۴ اراًئه مقاله در بخش دانشجویی کنگره بین المللی هلند، خرونینگن (ISCOMS)

۱۵. ار ائه مقاله در بخش دانشجویی کنگره بین المللی هپاتیت ۴

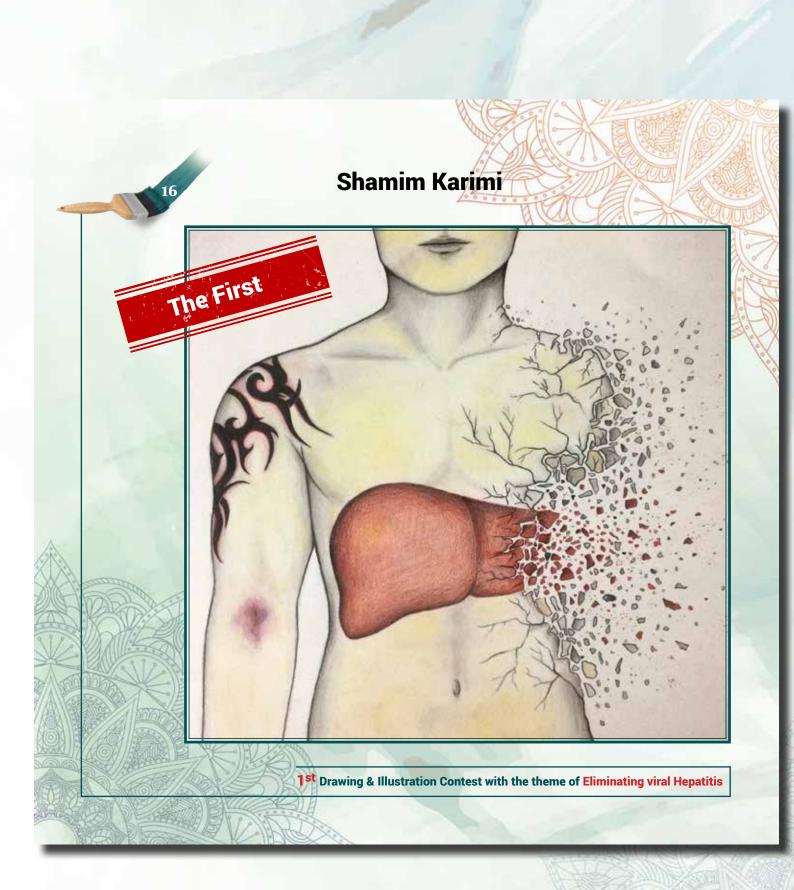
۱۶. انتشار بیش از ۱۵ مقاله پ<mark>ژوهشی</mark> در زمینه علوم پزشکی



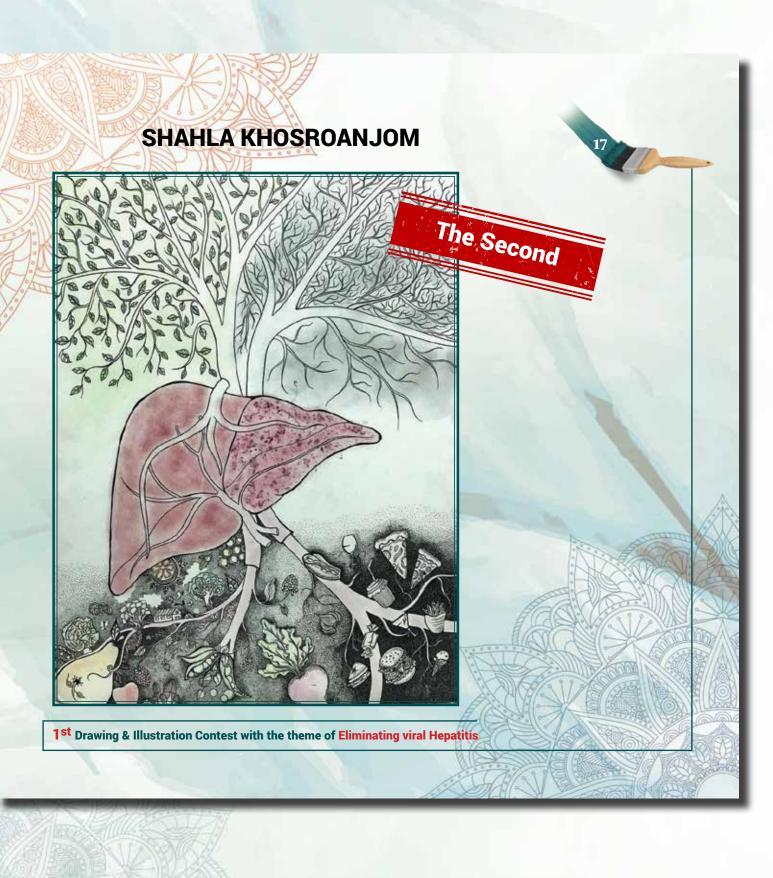


Drawing









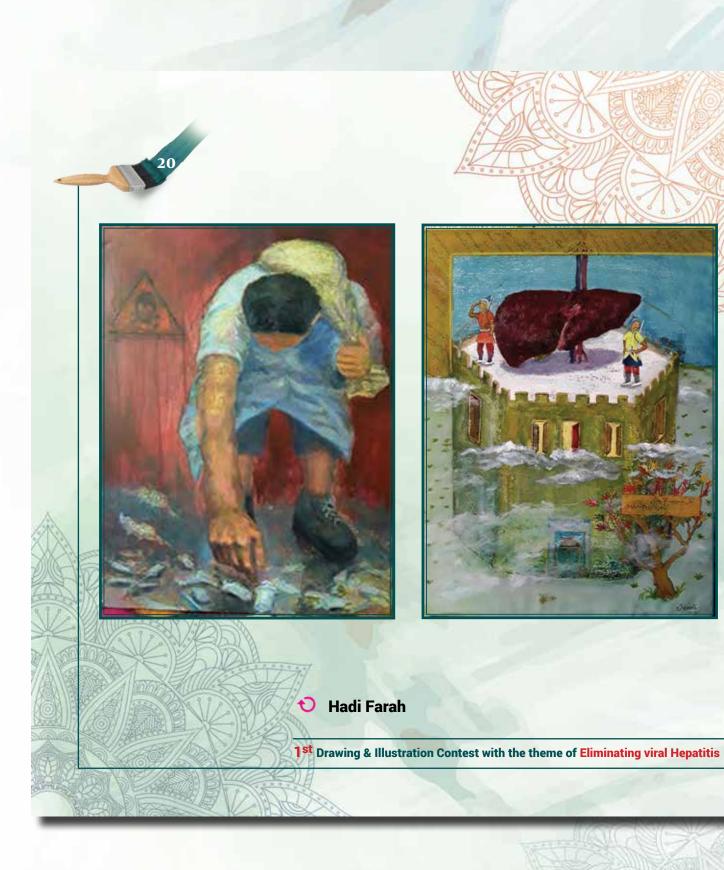




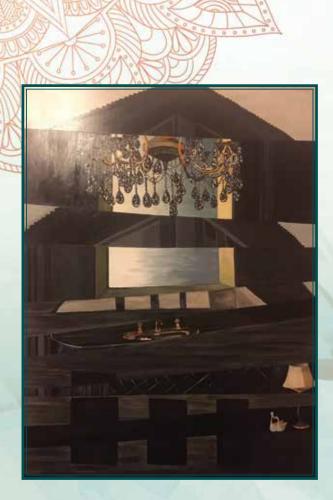










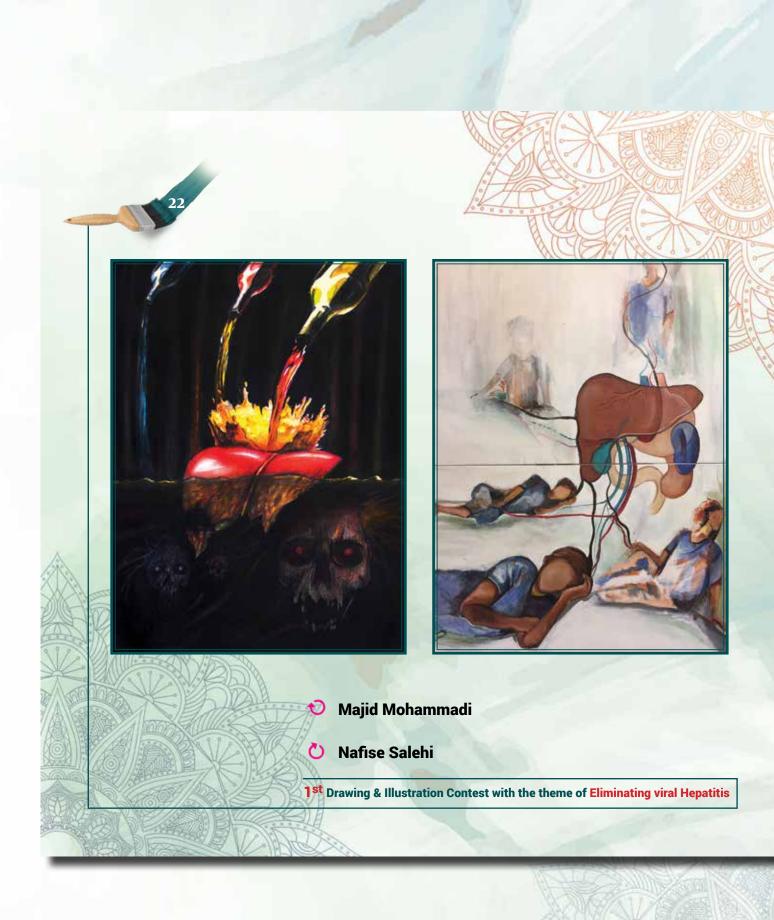




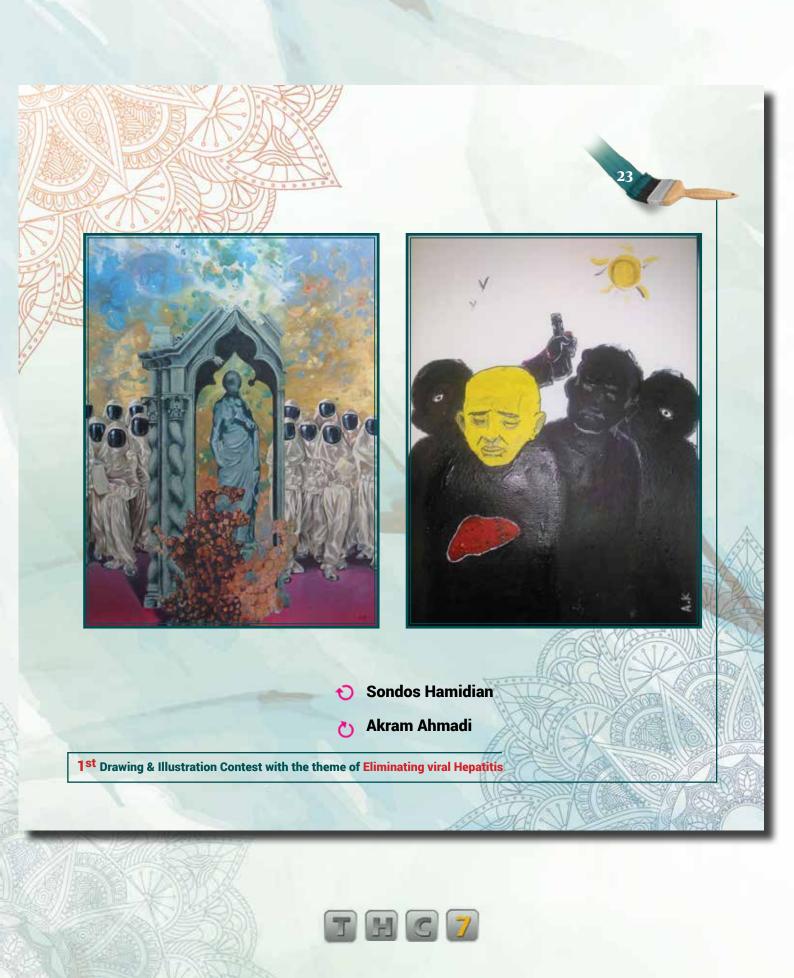
🕤 Maryam Bigdeli

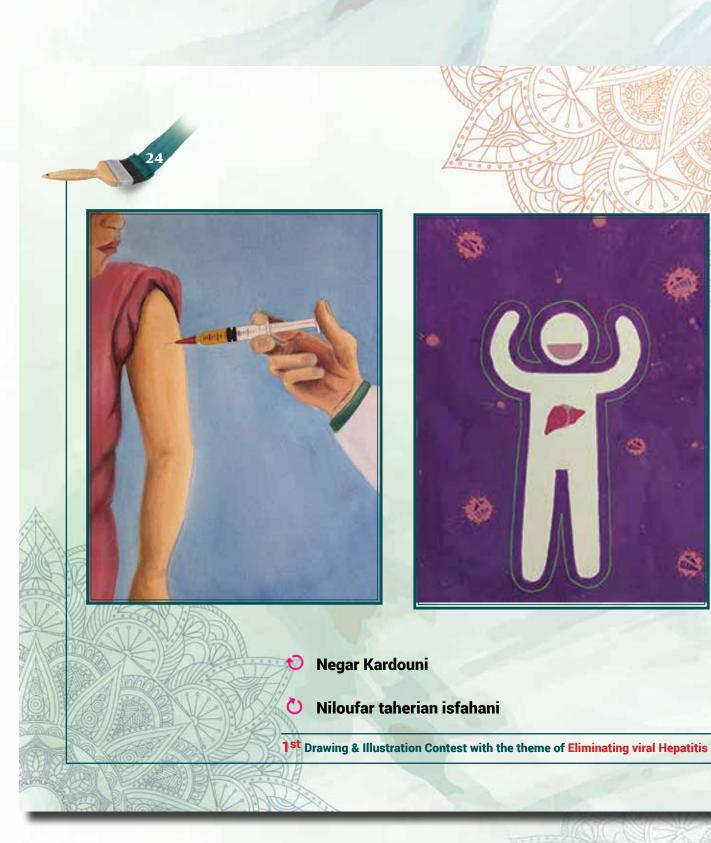
1st Drawing & Illustration Contest with the theme of Eliminating viral Hepatitis



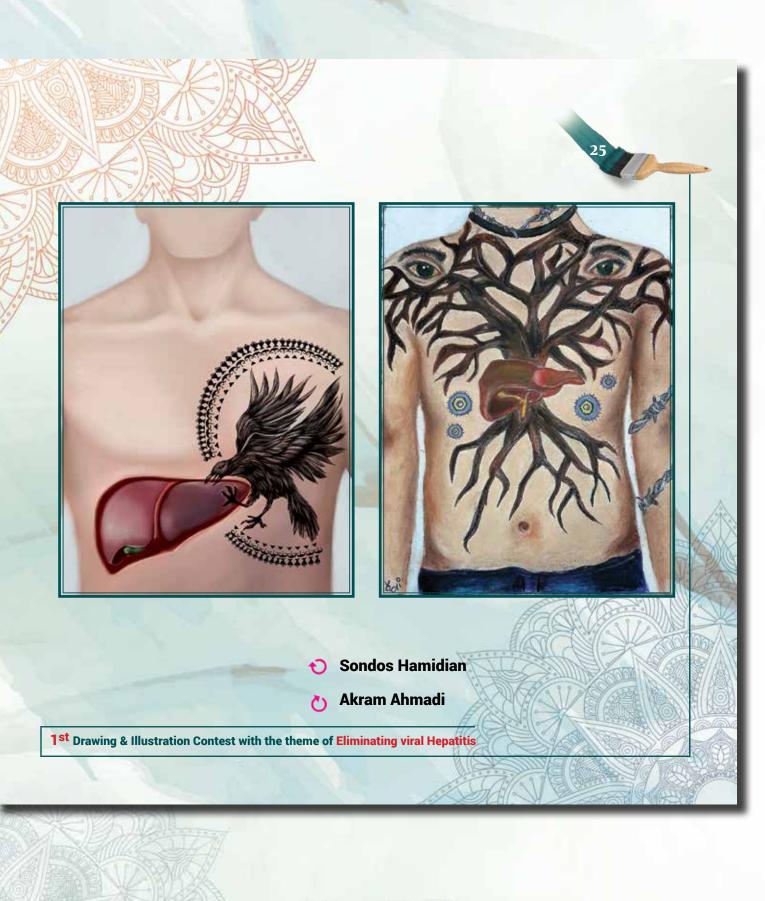




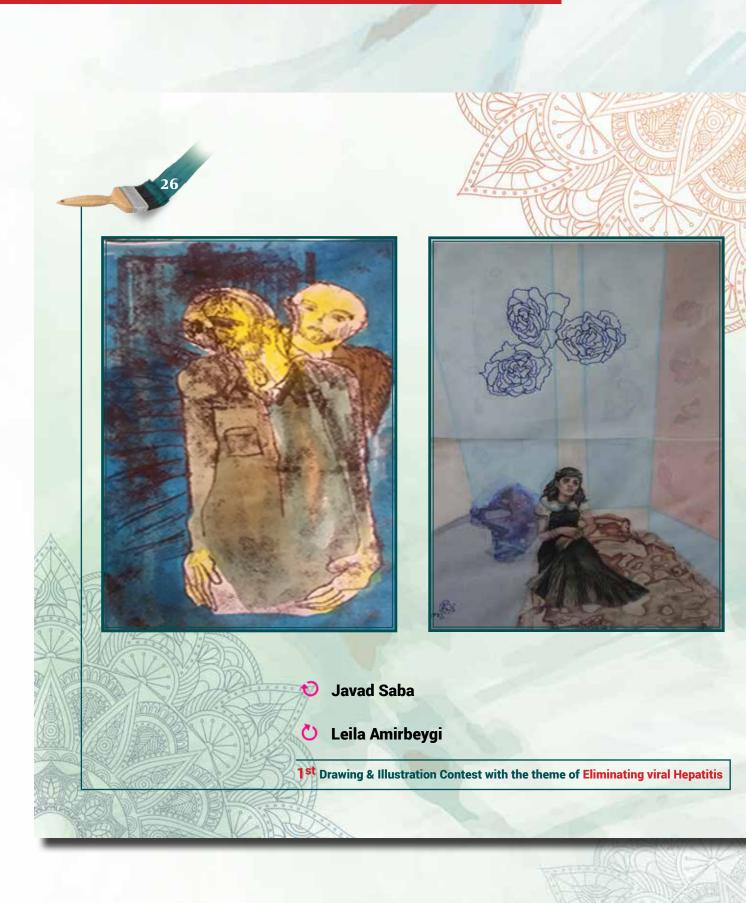






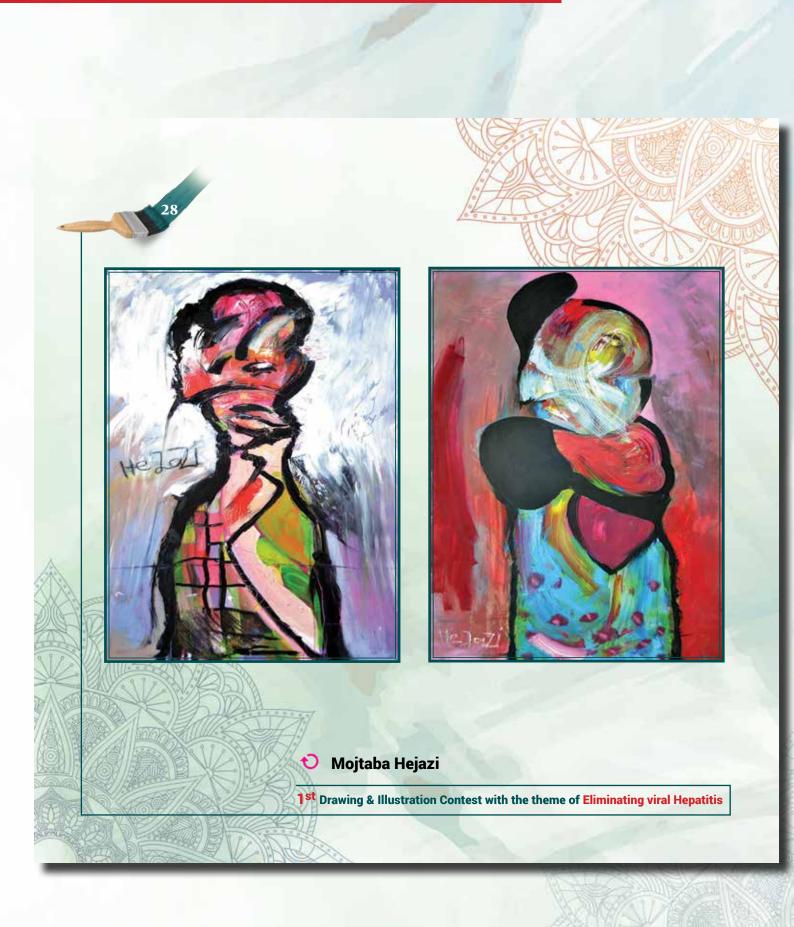




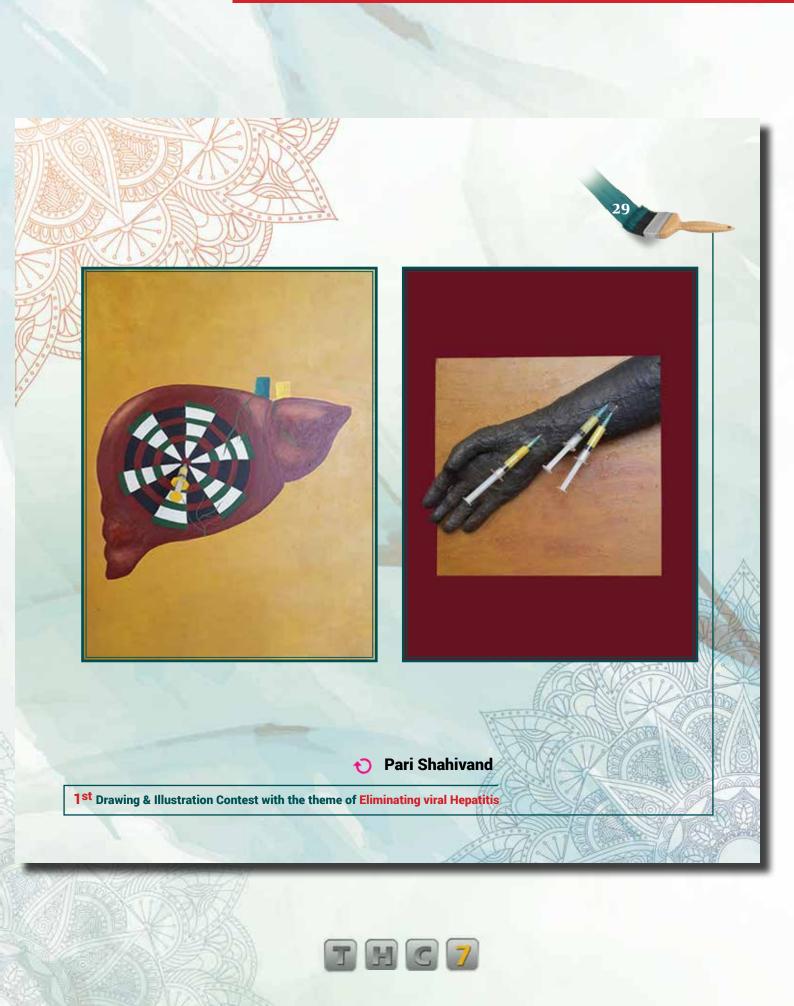


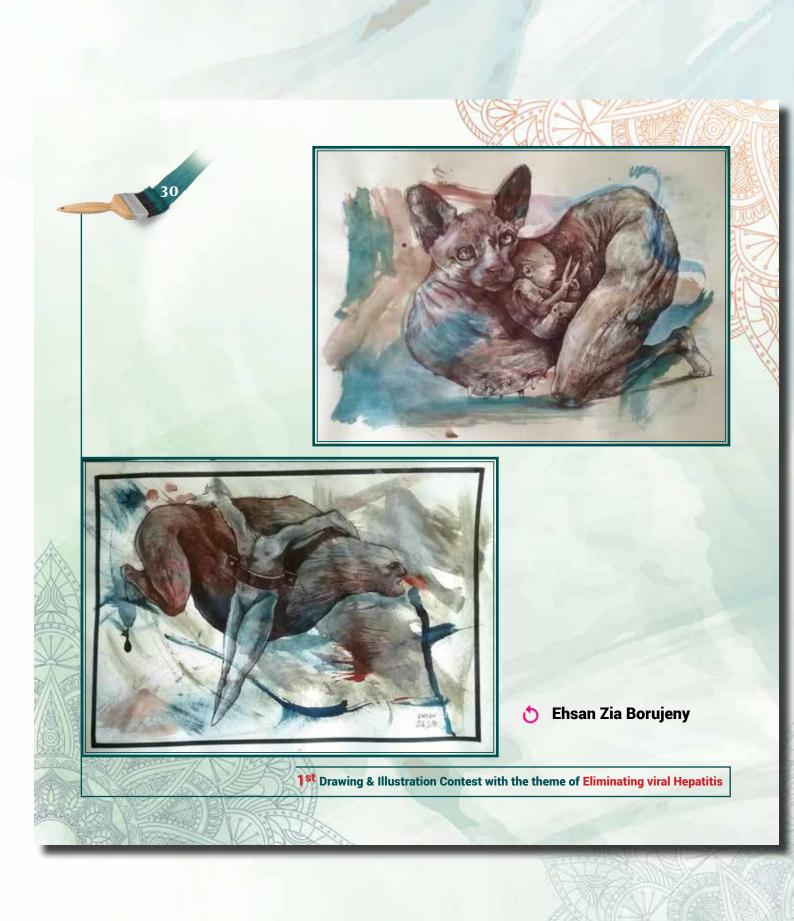














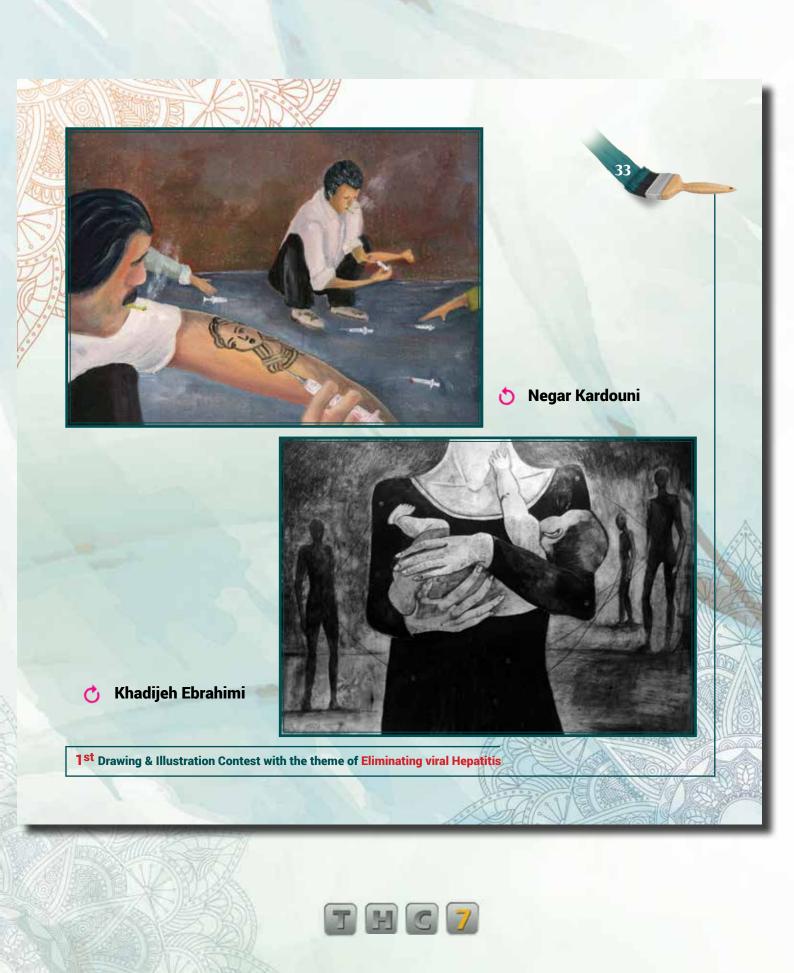


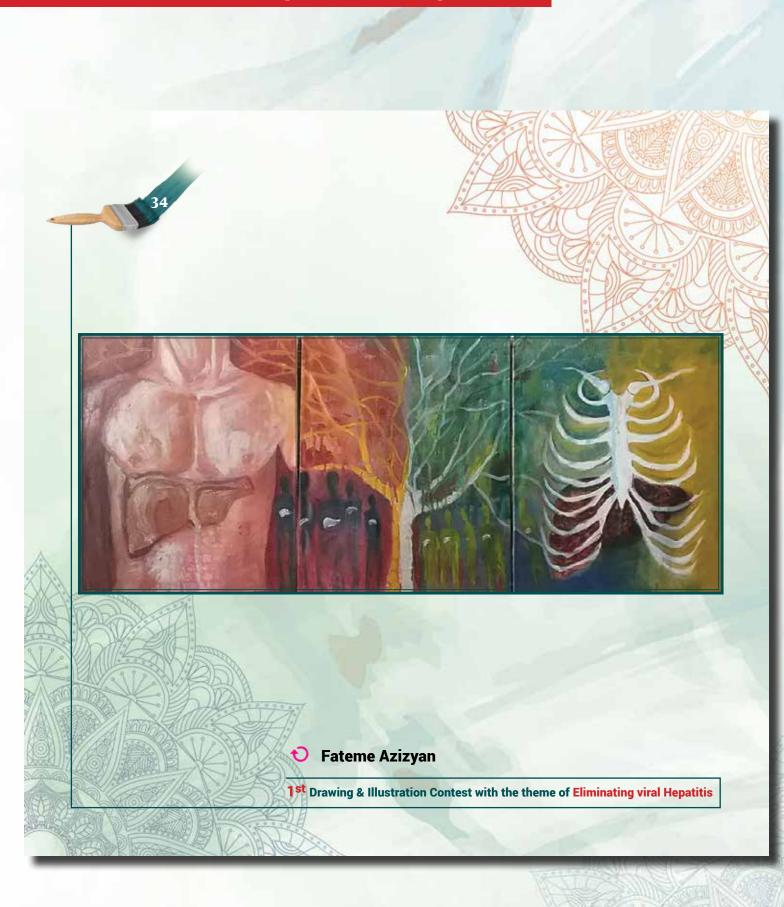




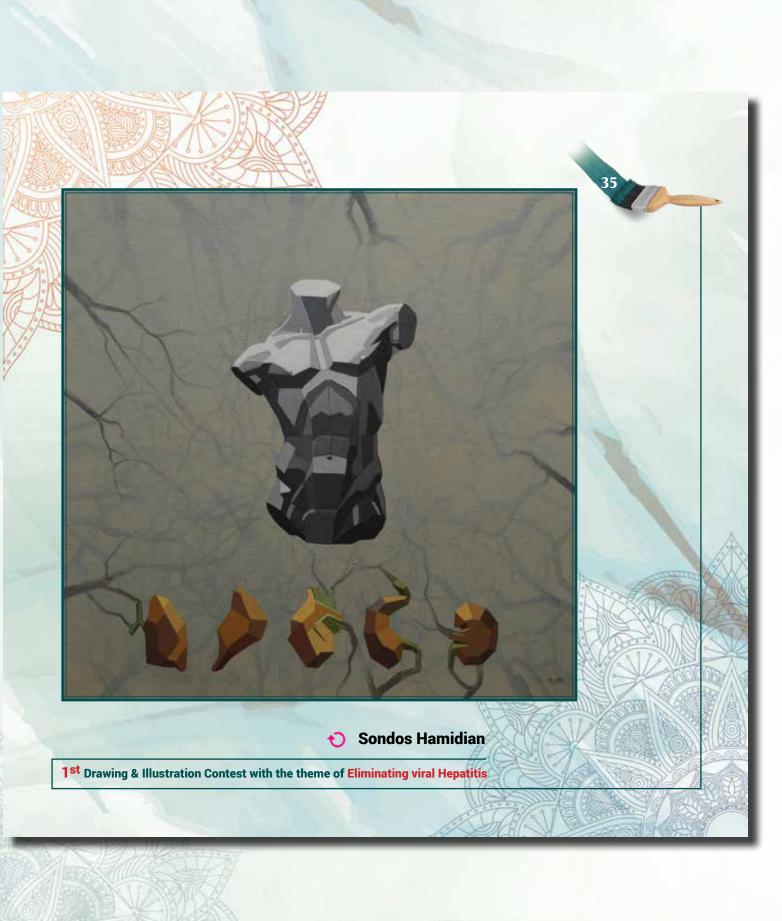
















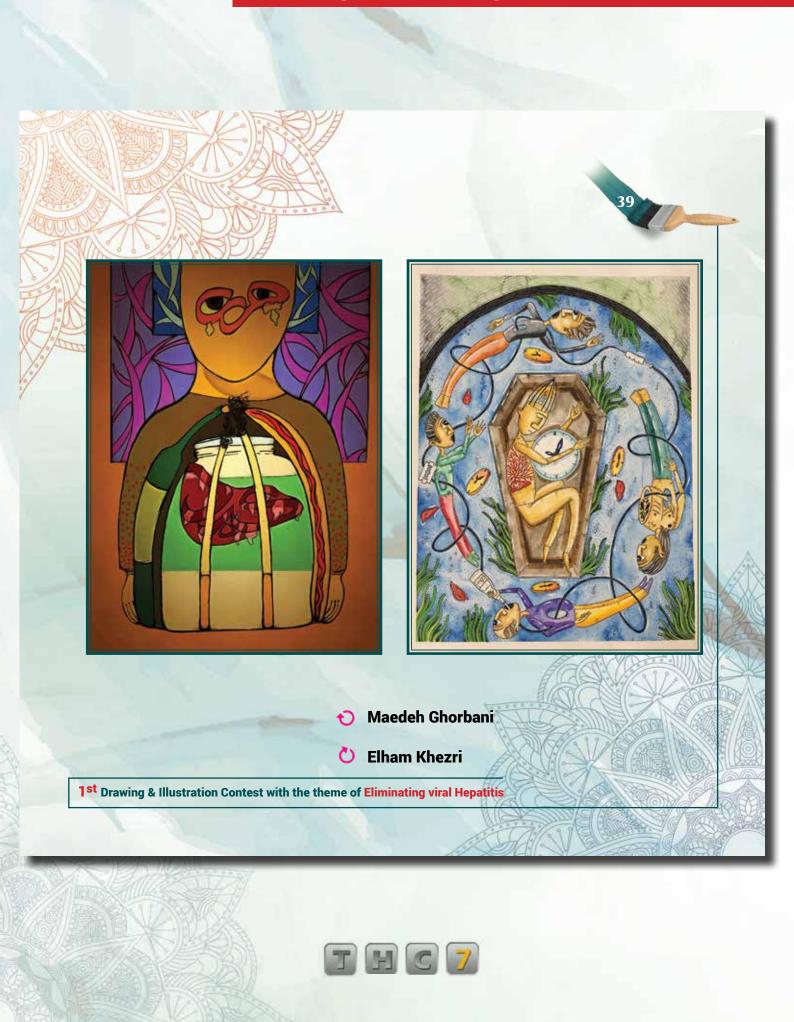


Illustration

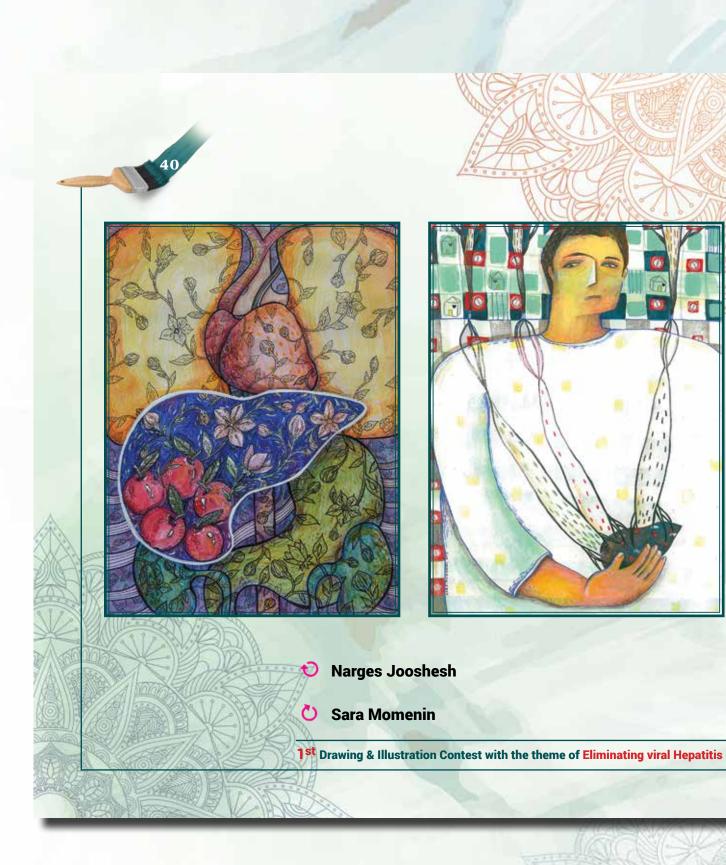








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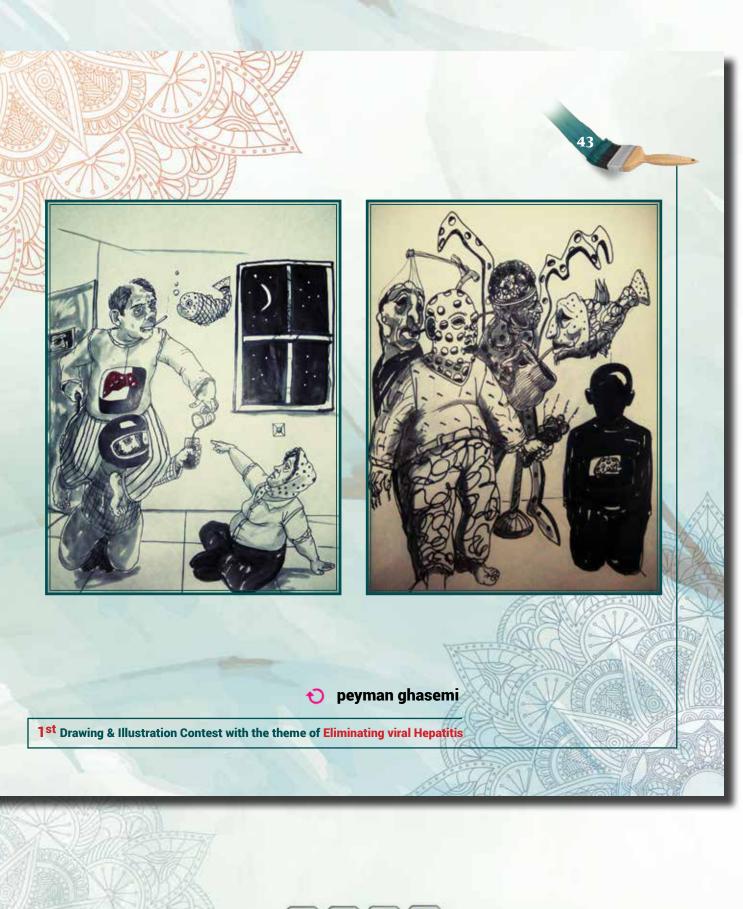




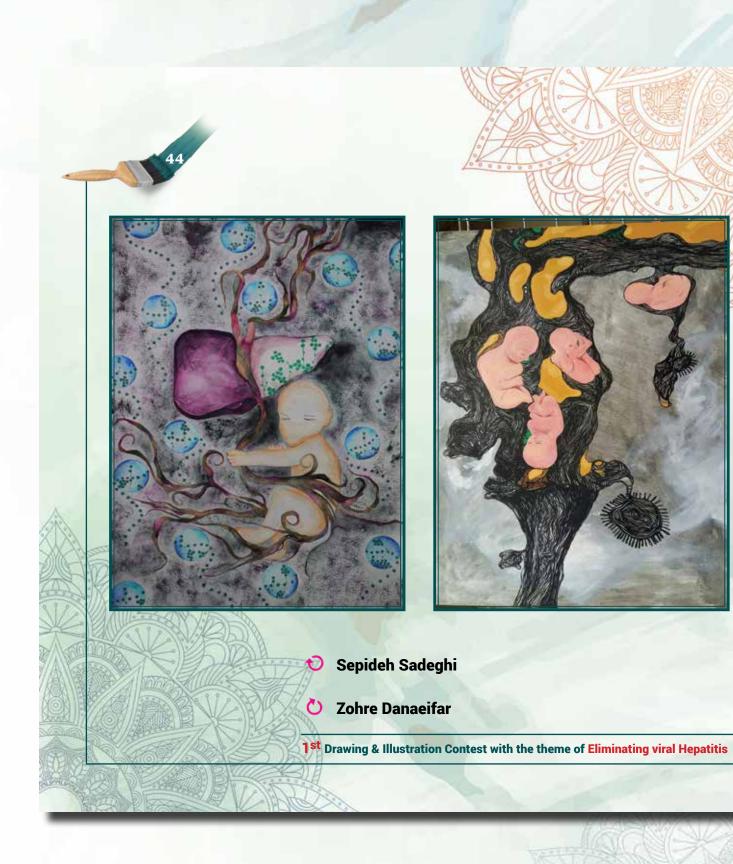




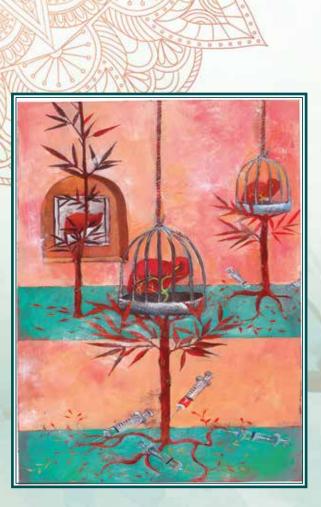










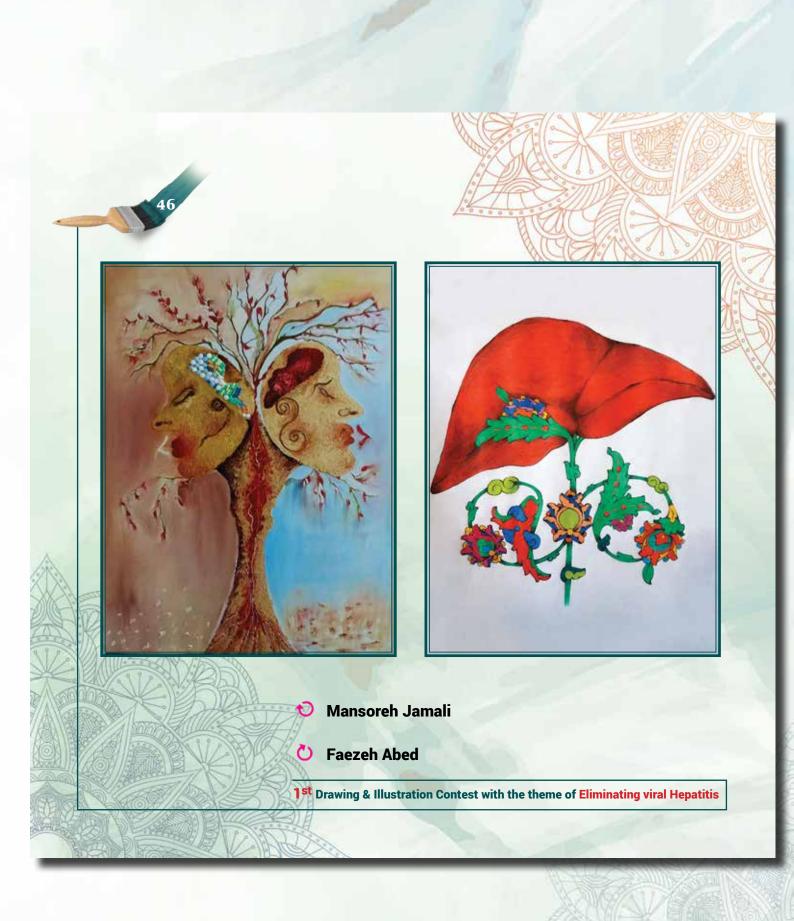




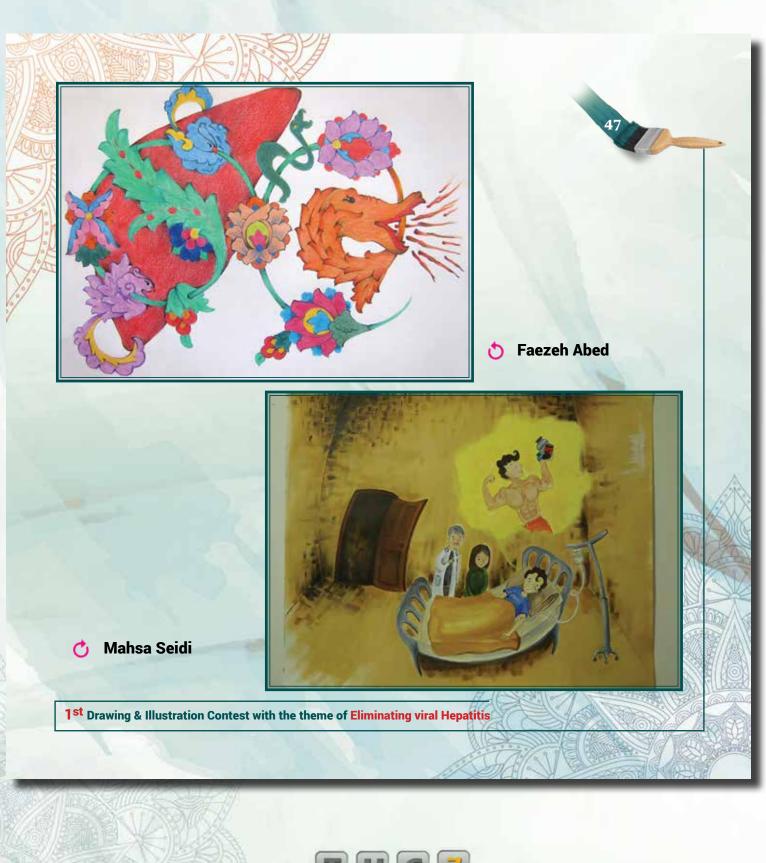
- 🕤 Zohre Mohammadi Moein
- ど Sanaz Daemi Langerodi

1st Drawing & Illustration Contest with the theme of Eliminating viral Hepatitis

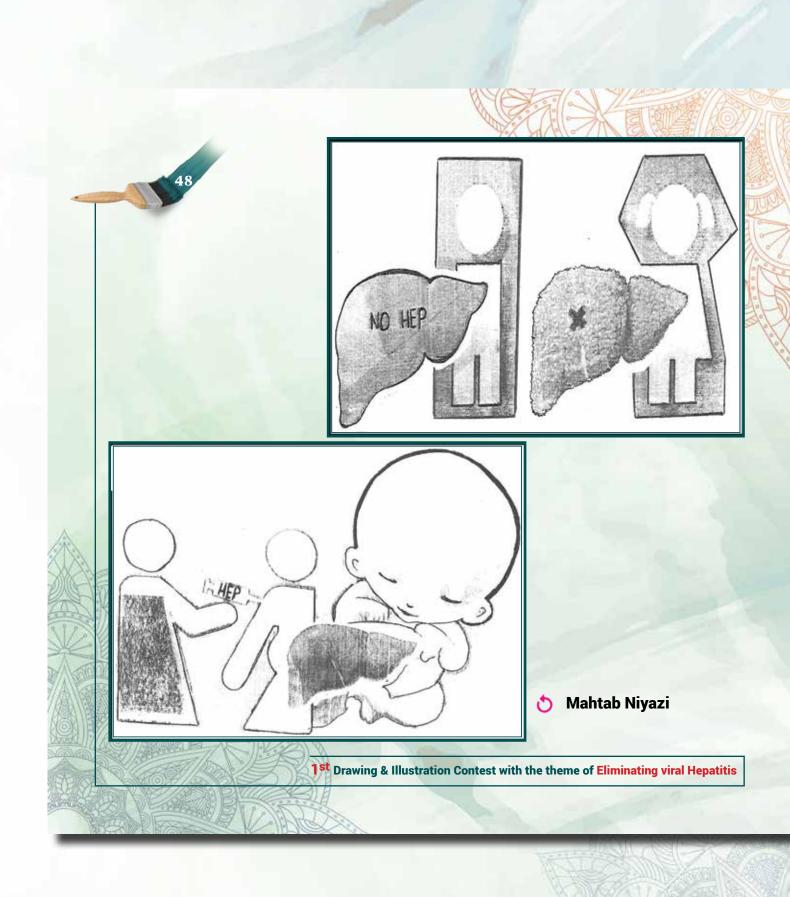
















👌 Vahid Shanaki

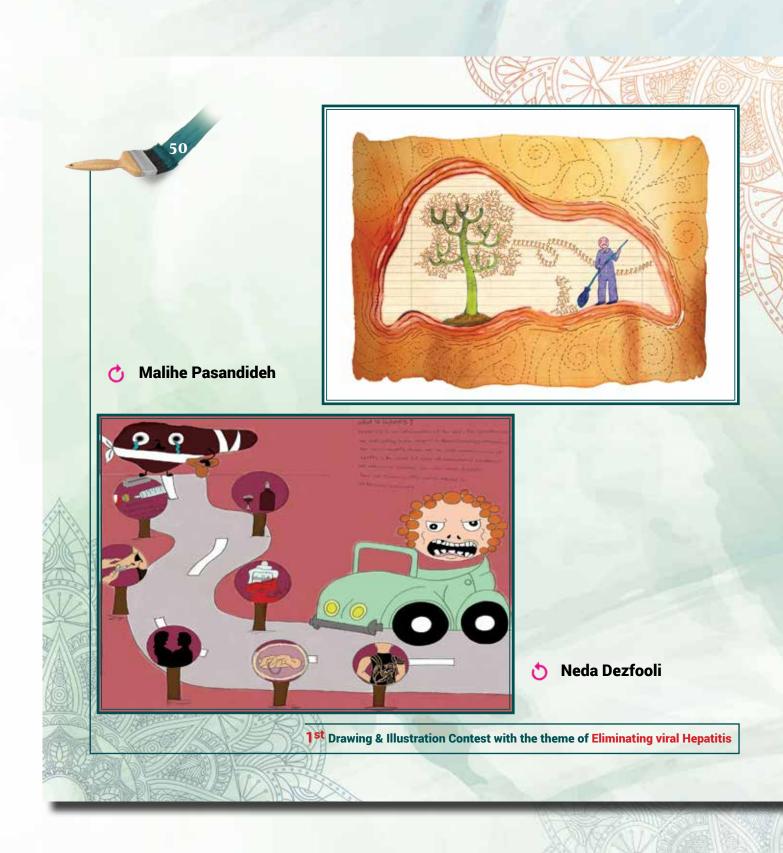
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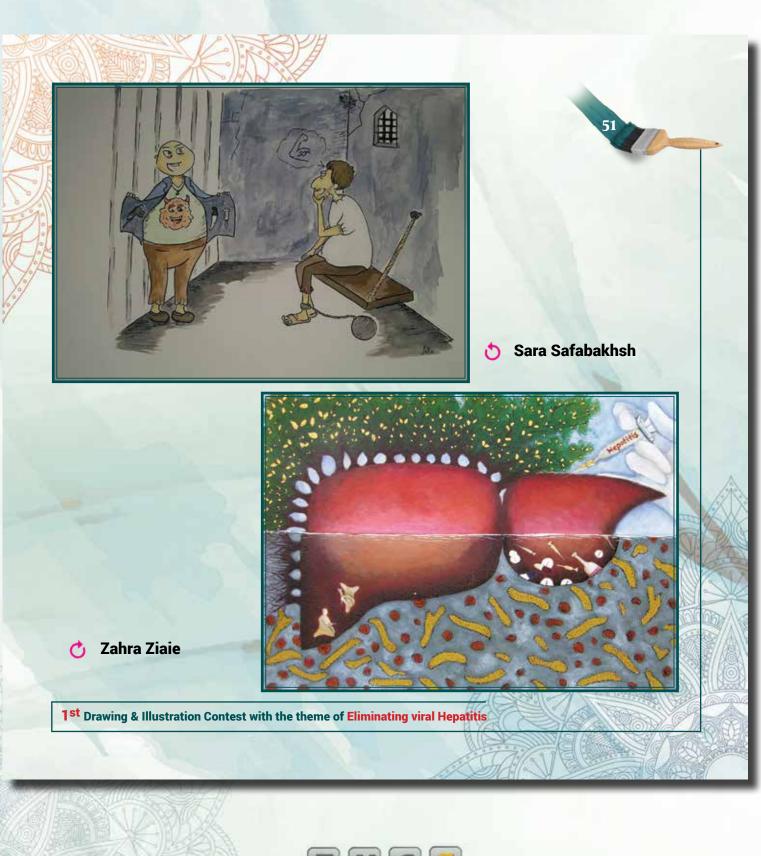
🖒 Fateme Behzadi

1st Drawing & Illustration Contest with the theme of Eliminating viral Hepatitis

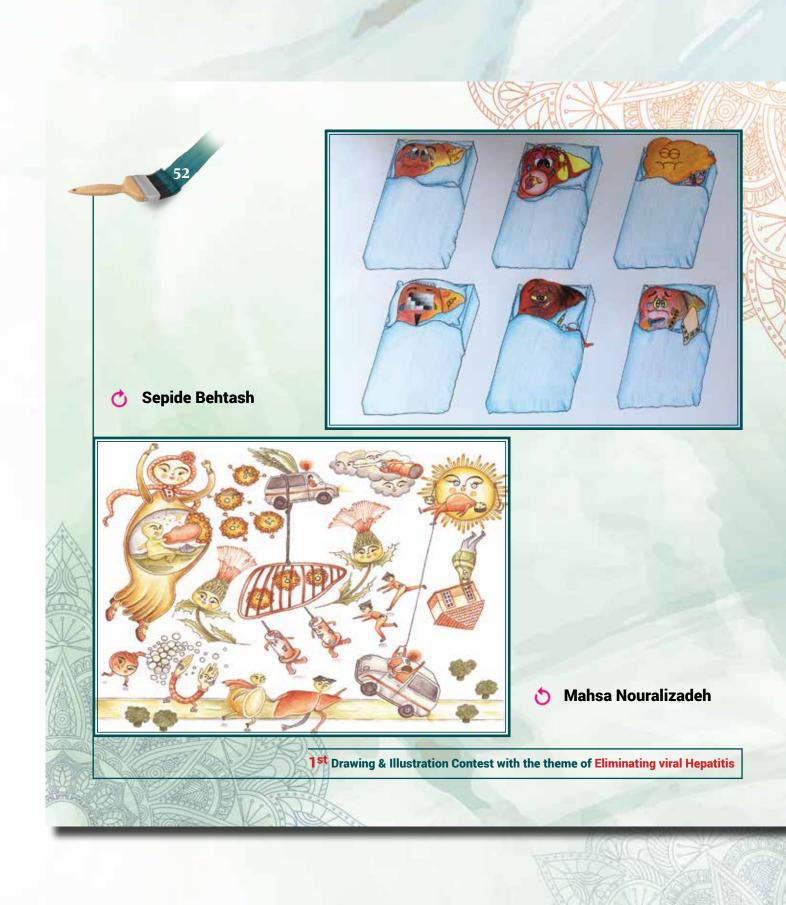




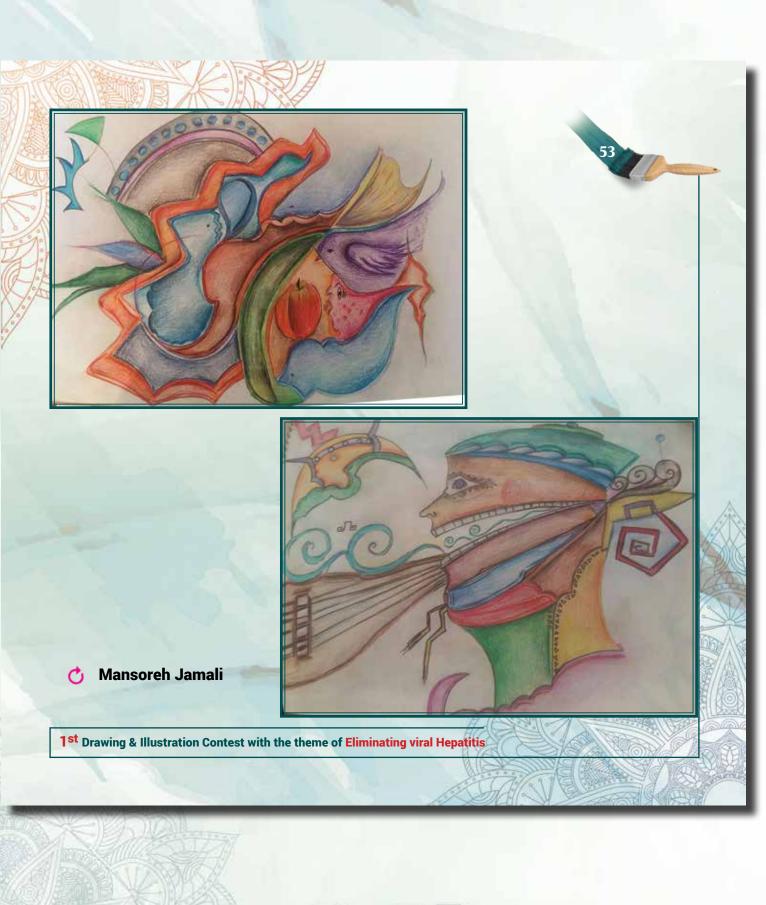




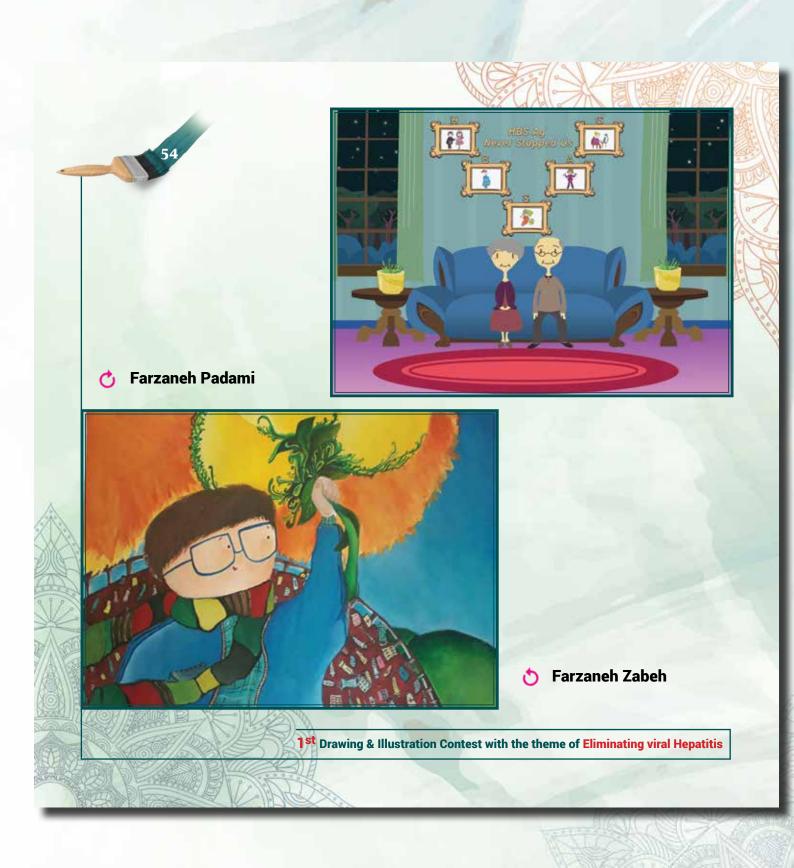




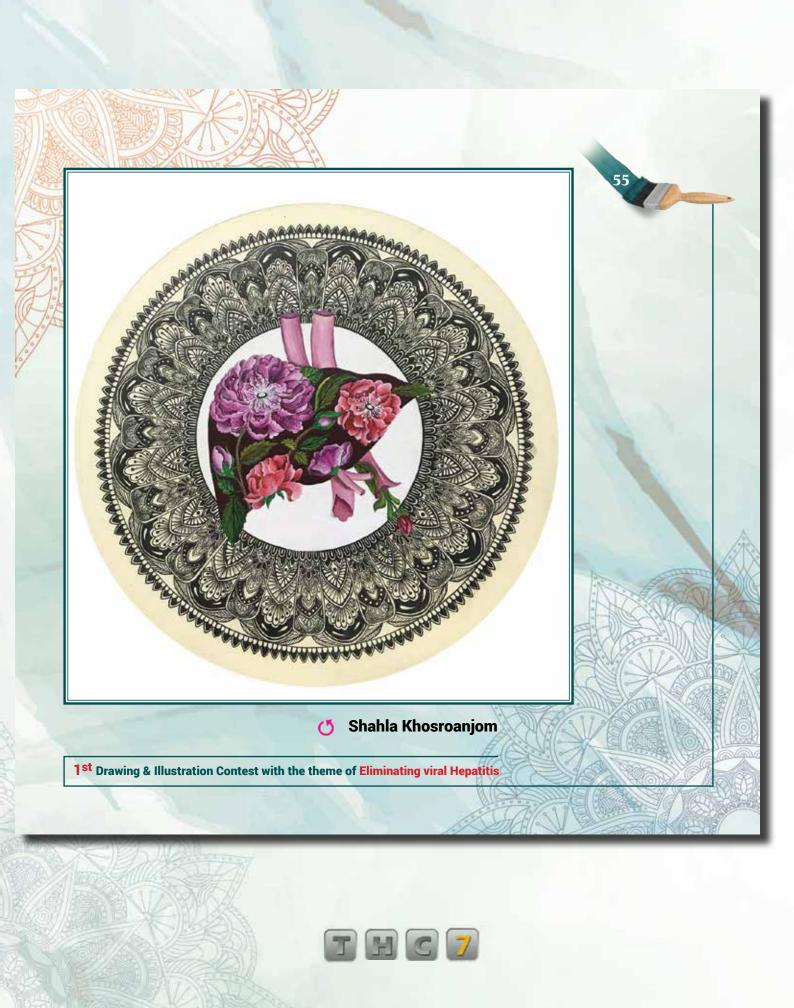


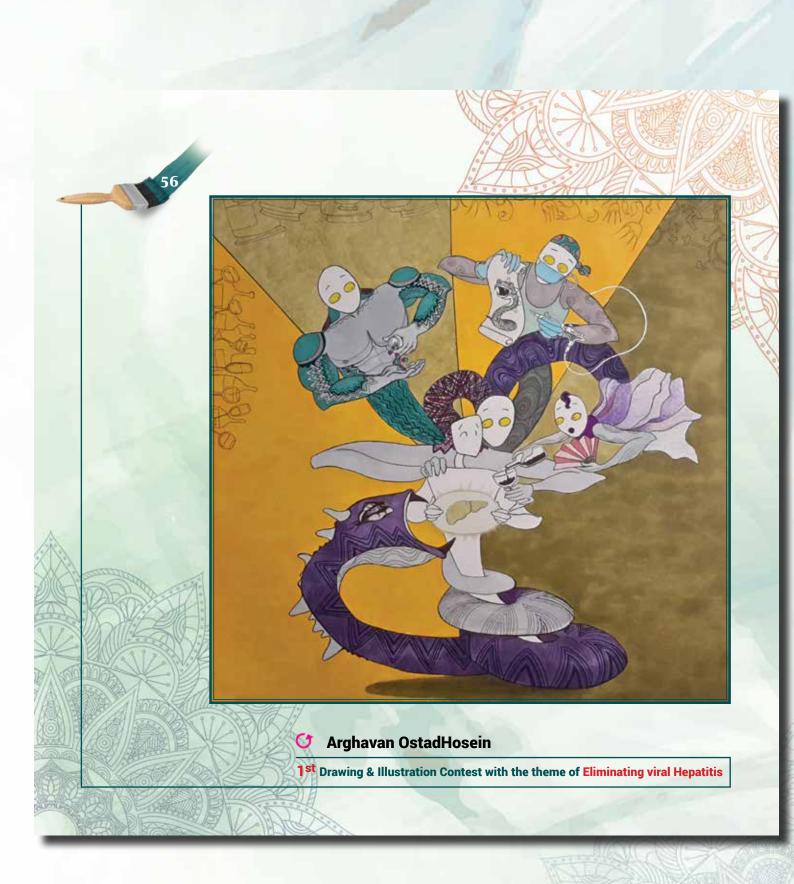




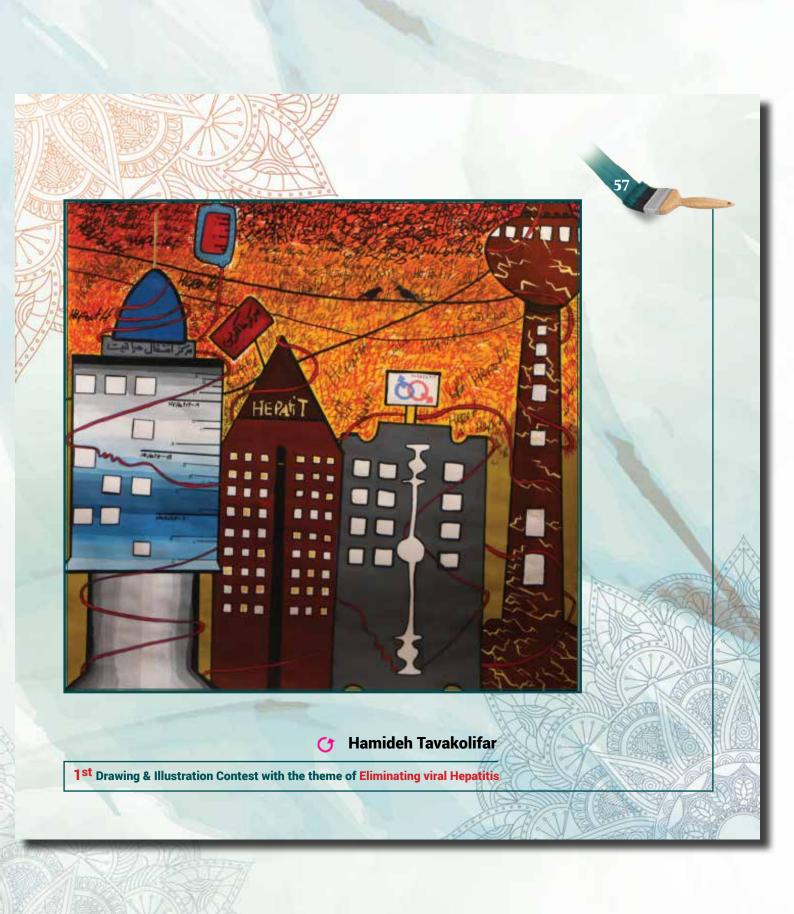




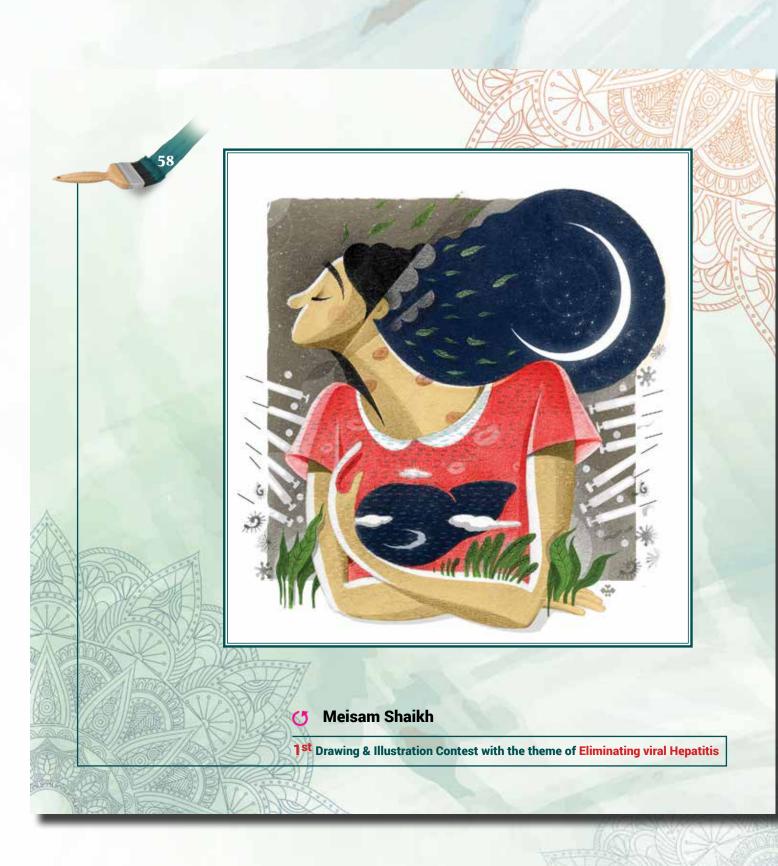




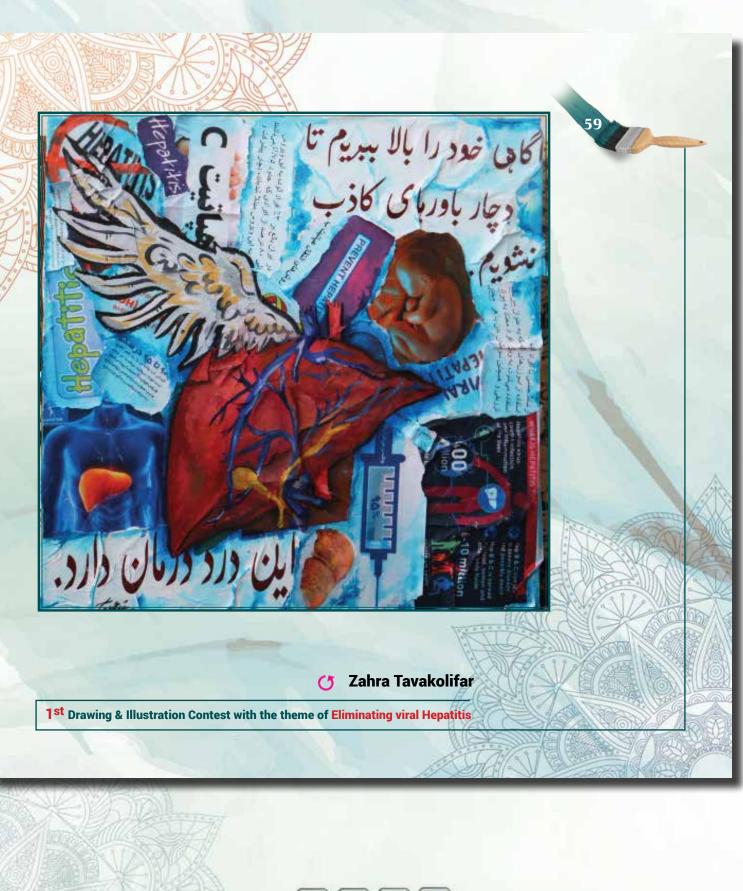




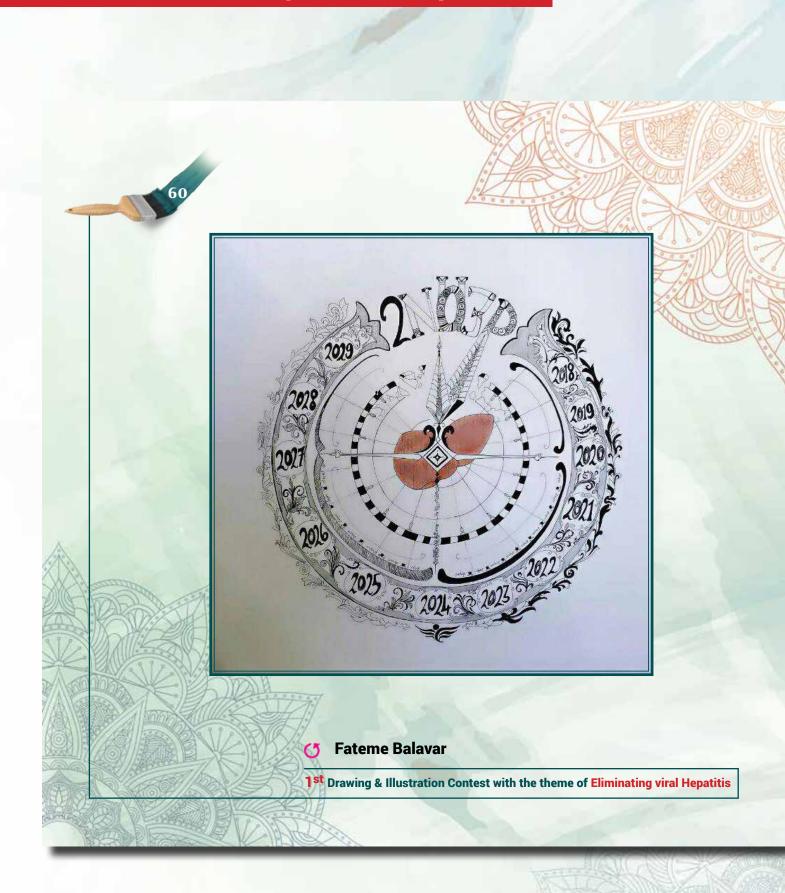




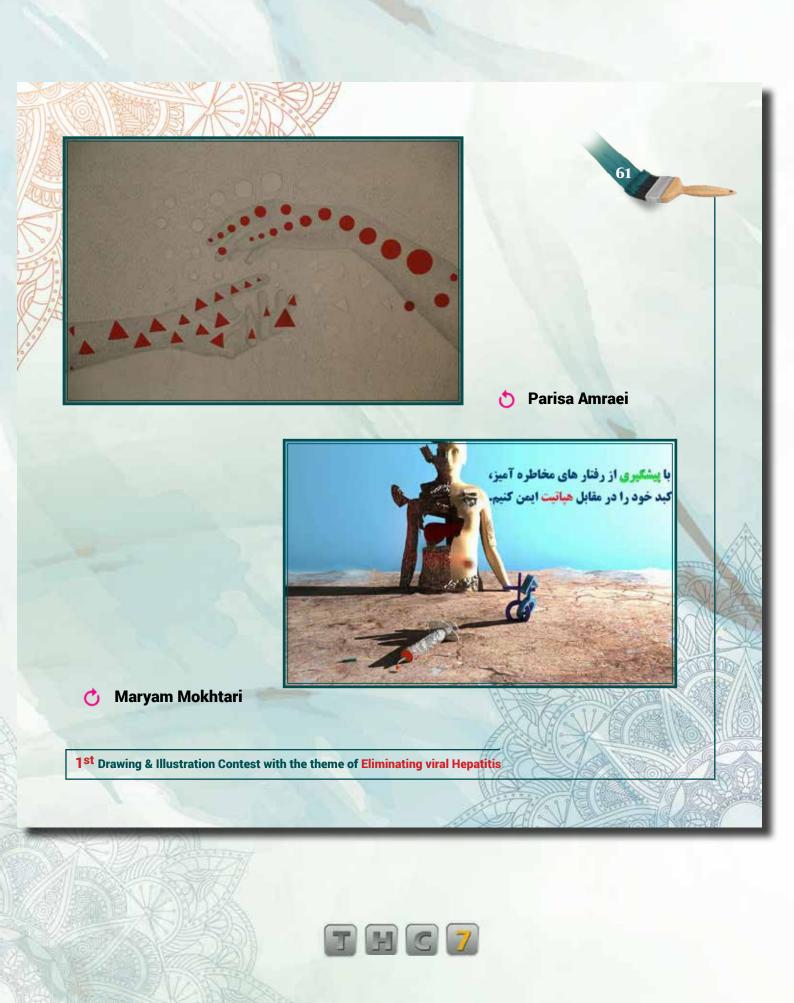






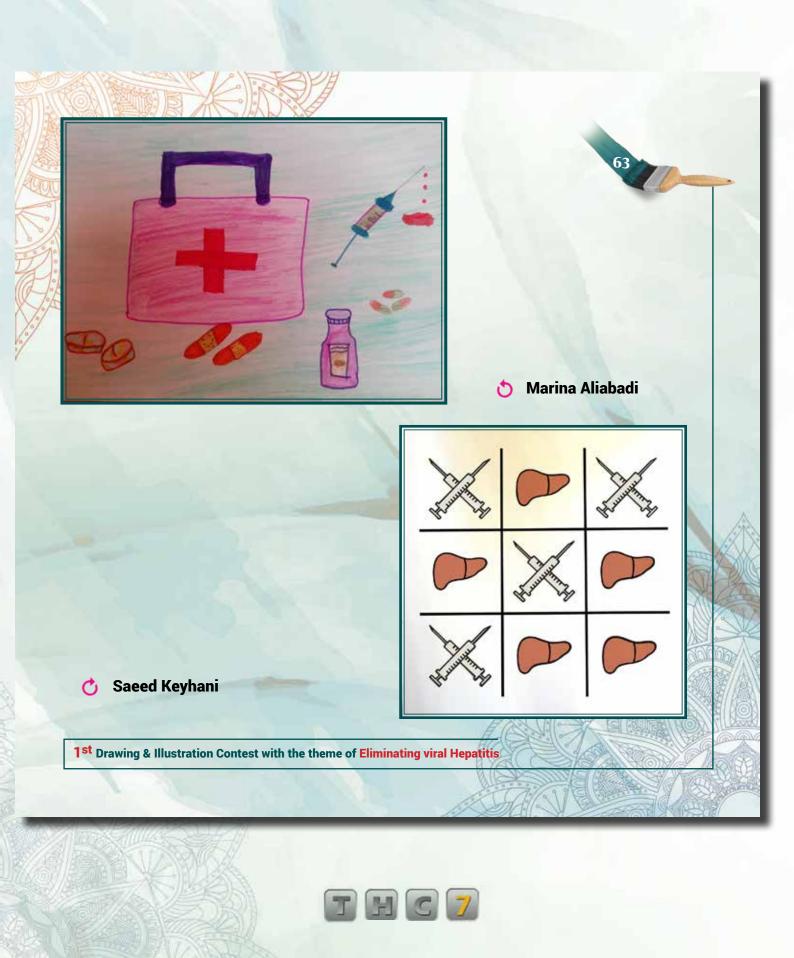


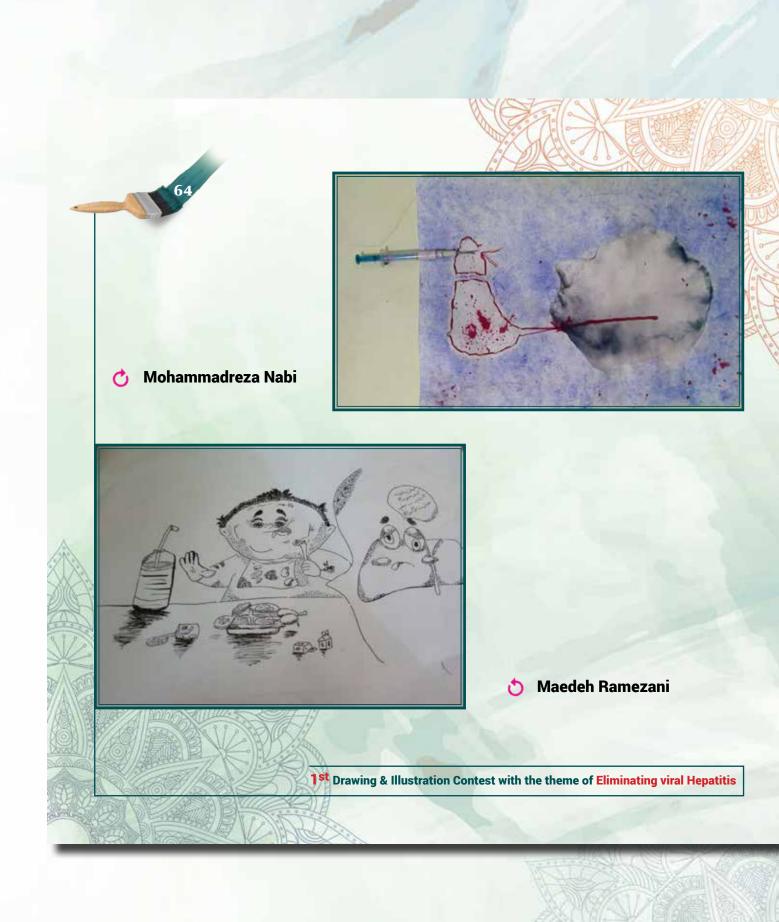




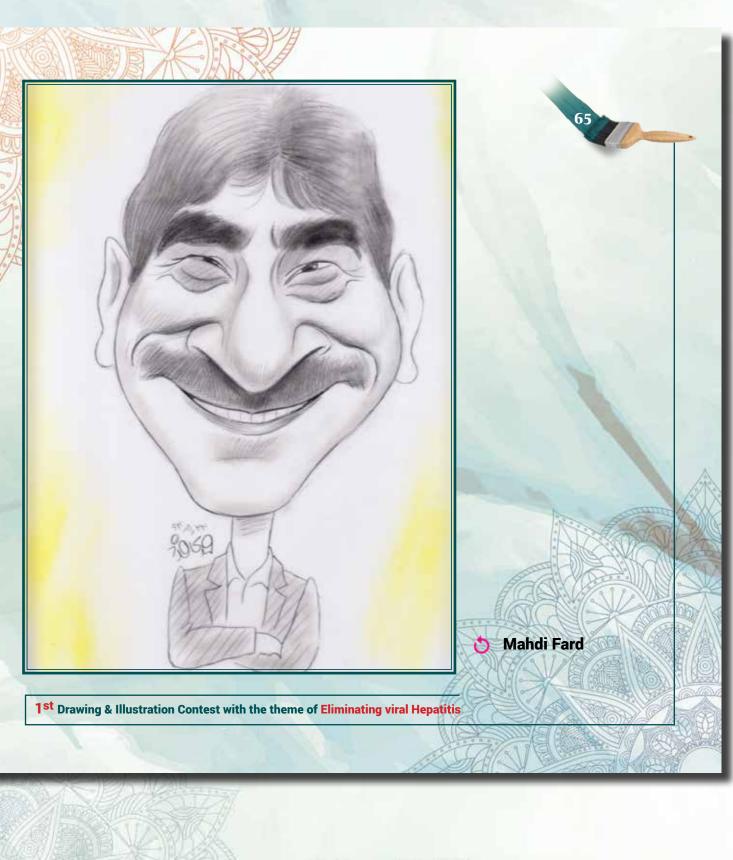


















Hope Health Club



Hope Health Club is a non-governmental organization (NGO) which seeks a healthy lifestyle for people all over the world. The main goal of this foundation is to promote liver health and reduce the burden of liver diseases by providing support for research and education into the causes, diagnoses, prevention and treatment of liver diseases. This foundation was founded by Prof. Seyed-Moayed Alavian, Professor of Gastroenterology and liver disease and editor-in-chief of the hepatitis monthly journal, the only specialized journal pertaining to liver disease in the Middle East and central Asia in 2015.

This foundation tries to supply comprehensive educational materials covering the signs, symptoms and treatment of many of the prevalent forms of the liver disease as well as variety of helpful tips on precautions or healthy choices that can help people to preserve from liver diseases. The information provided here is profitable for those living with or at the risk of liver diseases and the health care professionals who care for them.

High public awareness occurs when a significant proportion of society agrees that the having a healthy lifestyle is an issue that is of great importance to all citizens. Low public awareness occurs when a majority of people do not know or do not care about their healthy. Therefore, one of the purposes of Hope Health Club is to raise public awareness about health issues in general and liver diseases in particular.

In order to reach this goal, Hope Health Club attempts to hold public conferences by the name of "Omid" and with the cooperation of other organisms and NGOs. It is notable that thanks to the people's warm reception, 9 Omid conferences have been held up to now. Among this foundation's activities, the election of 8 Health Ambassadors among prominent faces like actors, directors, doctors and those who care about health issue is noteworthy. For instance, Mr. Jamshid Mashayekhi as a prominent Iranian actor received the statue and certificate of Health Ambassador this year. These ambassadors attempt to motivate people to exercise more, eat less unhealthy foods and forbid young people from starting smoking.



Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL)





ELIMINATE HEPATITIS

The 7th International Tehran HepatitisConference

Organized by: Iran Hepatitis Network

