7th Congress of the Polish Association for Study of Liver

9-11 June 2016
Serock

Programme and abstracts

Programme of events

9 June, Thursday	
15.00–15.45	**OPENING OF THE CONGRESS** Robert Flisiak
15.00–15.15	**Report on the activity of the Association over the past year and term of office** Robert Flisiak, Jerzy Jaroszewicz, Alicja Kalinowska
15.15–15.20	**Presentation of award in the Prof. Piotr Boroń Hepatology Contest** Jacek Juszczyk
15.20–15.25	**Presentation of awards for the best papers submitted for the 7th Congress** Robert Flisiak
15.25–15.35	**Liver Specialist Certificates** Robert Flisiak
15.35–16.25	**INAUGURATION SESSION** Chairs of the Session: Robert Flisiak, Piotr Małkowski
15.35–15.55	**Results of treatment and prevention of HBV recurrence after LTx** Patrizia Burra
15.55–16.15	**Is hepatitis E virus infection an exotic problem?** Piotr Grabarczyk
16.15–16.25	**Increased frequencies of Th-17 CD4-T-cells and decreased of T-regulatory cells in non-alcoholic fatty liver disease** Magdalena Świderska, Kamil Grubczak, Jerzy Jaroszewicz, Anna Parfieniuk-Kowerda, Joanna Pogorzelska, Tadeusz Wojciech Łapiński, Marcin Moniuszko, Robert Flisiak
16.25–16.40	Coffee break
16.40–19.10	**1ST PLENARY SESSION** **HEPATOCELLULAR CARCINOMA** Chairs of the Session: Piotr Małkowski, Tadeusz Wróblewski
16.40–16.55	**Epidemiology of HCC in Poland** **In the light of the LIVER study** – Anatol Panasiuk **In the light of data collected by Cancer Treatment Centres and National Health Fund** – Piotr Małkowski
16.55–17.15	**Diagnosis of HCC based on imaging examinations** **Computed tomography (CT)** – Ryszard Pacho **NMR and other examinations** – Edyta Szurowska
17.15–17.30	**Strategy for the treatment of HCC patients based on "HCC Banacha" Project** Tadeusz Wróblewski
17.30–17.50	**Surgical treatment of HCC patients** **Liver resection** – Tadeusz Wróblewski **Liver transplantation** – Paweł Nyckowski
17.50–18.10	**Treatment based on interventional radiology methods** **TACE** – Mikołaj Wojtaszek **RFA** – Krzysztof Milczarek
18.10–18.25	**Chemotherapy – eligibility and variants of treatment** Andrzej Deptała
18.25–18.40	**Most common reasons for the unsuccessful diagnosis and treatment of HCC** Krzysztof Zieniewicz
18.40–18.50	**Hepatocellular carcinoma treatment by liver transplantation in patients with liver cirrhosis** Beata Łągiewska, Dariusz Wasiak, Marek Pacholczyk, Wojciech Lisik, Maurycy Jonas, Agnieszka Perkowska-Ptasińska, Olga Tronina, Janusz Trzebicki, Magdalena Durlik, Piotr Małkowski, Maciej Kosieradzki
18.50–19.10	**Discussion panel with speakers**

10 June, Friday	
8.00–9.30	**2ND PLENARY SESSION** **CYSTIC HEPATIC LESIONS** Chairs of the Session: Irena Jankowska, Tadeusz Łapiński
8.00–8.20	**Choledochal cysts in children** Adam Kowalski
8.20–8.40	**Polycystic disease of the liver and kidneys – a task for a nephrologist or hepatologist?** Ryszard Grenda, Irena Jankowska
8.40–9.00	**Liver cysts – a task for a surgeon or hepatologist?** Dorota Broniszczak, Piotr Socha
9.00–9.20	**Parasitic liver cysts** Tadeusz Łapiński
9.20–9.30	**Alveococcal hepatic tumors in the Department of Infectious and Tropical Diseases and Hepatology, Medical University of Warsaw, in 2011-2016** Maria Olszynska-Krowicka, Piotr Karol Borkowski, Małgorzata Polońska-Płachta, Alicja Wiercińska-Drapało
9.30–9.45	**Coffee break**
9.45–10.45	abbvie **SPONSORED SESSION** Chair of the Session: Waldemar Halota
10.45–12.05	**3RD PLENARY SESSION** **INCREASING THE POOL OF ORGANS AVAILABLE FOR LTx BY ORGANS FROM HBV-INFECTED DONORS** Chairs of the Session: Piotr Małkowski, Krzysztof Zieniewicz
10.45–11.05	**Experiences of the Szczecin centre** Marta Wawrzynowicz-Syczewska
11.05–11.25	**Experiences of the Warsaw centers** Krzysztof Zieniewicz, Marek Pacholczyk
11.25–11.35	**Costs** Piotr Małkowski
11.35–11.45	**Legal aspects** Jarosław Czerwiński, Roman Danielewicz
11.45–11.55	**Discussion**
11.55–12.05	**Individualization of immunosuppression treatment with tacrolimus during antiviral therapy based on 3D regimen in patients after liver transplantation with hepatitis C reactivation** Joanna Musialik, Henryk Karkoszka, Aureliusz Kolonko, Andrzej Więcek
12.05–13.15	**4TH PLENARY SESSION** **ANALYSIS OF CLINICAL CASES – INTERACTIVE SESSION** Chairs of the Session: Joanna Pawłowska, Marek Woynarowski, Andrzej Habior
13.15–14.15	GILEAD **SPONSORED SESSION** Chairs of the Session: Anna Piekarska, Marta Wawrzynowicz-Syczewska, Krzysztof Simon
14.15–15.30	**Lunch break**
15.30–17.00	**5TH PLENARY SESSION** **HCV INFECTIONS** Chairs of the Session: Robert Flisiak, Waldemar Halota
15.30–15.50	**Is the treatment of G1a HCV infected patients a Polish problem?** Anna Piekarska
15.50–16.10	**HCV infections – an attempt to verify risks** Waldemar Halota
16.10–16.30	**Ways to improve drug programs for the treatment of hepatitis** Andrzej Horban

16.30–16.50	**Interferon-free therapy in the "real world"** Robert Flisiak
16.50–17.00	**Interferon lambda polymorphisms associate with body iron indices and hepatic expression of interferon-responsive long non-coding RNA in chronic hepatitis C** Anna Wróblewska, Agnieszka Bernat, Anna Woziwodzka, Joanna Markiewicz, Tomasz Romanowski, Krzysztof Piotr Bielawski, Tomasz Smiatacz, Katarzyna Sikorska
17.00–17.20	MSD **SPONSORED SESSION** Chair of the Session: Waldemar Halota
17.20–17.35	**Coffee break**
17.35–19.05	**GENERAL MEETING OF THE POLISH ASSOCIATION FOR STUDY OF LIVER**
	11 June, Saturday
8.30–10.40	**6TH PLENARY SESSION** **HBV INFECTIONS** Chairs of the Session: Małgorzata Pawłowska, Jerzy Jaroszewicz
8.30–8.45	**A new look at the immunopathogenesis of HBV infection** Iwona Mozer-Lisewska
8.45–9.00	**What's new in the "old" HBV?** Jacek Juszczyk
9.00–9.15	**HBV infection in patients with hematooncologic patients** Małgorzata Pawłowska
9.15–9.30	**Serological markers of HDV infection in the population of Polish patients** Krzysztof Tomasiewicz
9.30–9.45	**Treatment of HBV infections: how to eliminate cccDNA** Jerzy Jaroszewicz
9.45–10.00	**Current challenges in anti-HBV immunization** Anna Boroń-Kaczmarska
10.00–10.10	**Distribution of HBV genotypes and HBsAg serum concentrations in Poland: results of multicenter EpiGeneS study** Jerzy Jaroszewicz, Małgorzata Pawłowska, Anna Piekarska, Krzysztof Tomasiewicz, Krzysztof Simon, Włodzimierz Mazur, Dorota Zarębska-Michaluk, Arleta Kowala-Piaskowska, Marta Wawrzynowicz-Syczewska, Magdalena Świderska, Paweł Rajewski, Dorota Dybowska, Anna Pniewska, Marta Strycharz, Elżbieta Murias-Bryłowska, Monika Pazgan-Simon, Ewelina Zasik, Wiesław Kryczka, Iwona Mozer-Lisewska, Waldemar Halota, Robert Flisiak
10.10–10.40	Bristol-Myers Squibb **SPONSORED SESSION**
10.40–11.00	**Coffee break**
11.00–12.30	**7TH PLENARY SESSION** **AUTOIMMUNE LIVER DISEASES** Chairs of the Session: Krzysztof Simon, Krzysztof Tomasiewicz
11.00–11.20	**Autoimmunization and HCV infection** Tadeusz Łapiński
11.20–11.40	**AIH/PBC overlap syndrome – diagnostic and therapeutic problems** Krzysztof Simon
11.40–12.00	**Monitoring of patients with AIH** Krzysztof Tomasiewicz
12.00–12.20	**Long-term care of patients with AIH** Małgorzata Woźniak
12.20–12.30	**Long term follow up of AIH children who completed at least 6 months course of budesonide and azathioprine therapy** Marek Woynarowski, Małgorzata Woźniak, Beata Oralewska
12.30–12.45	**SUMMARY AND CLOSURE OF THE CONGRESS** Robert Flisiak, Piotr Małkowski

ORAL PRESENTATIONS

The abstracts are printed in the form sent by authors, accepted by the Scientific Programme Committee.

INAUGURATION SESSION

Is hepatitis E virus infection an exotic problem?

Piotr Grabarczyk

Instytut Hematologii i Transfuzjologii w Warszawie

Hepatitis E virus (HEV) was identified in 1983 with an outbreak of hepatitis caused by unknown human unenveloped virus transmitted by contaminated food and water. Up till now four blood borne HEV genotypes have been identified. In hyperendemic areas HEV epidemiology is associated mainly with drinking water contaminated by HEV genotypes 1 and 2, while in industrialized countries the main cause is zoonotic infection via consumption of different kinds of meat contaminated with genotype 3. Irrespective of genotype vertical and perinatal transmission of HEV has also been observed.

Mostly, genotype 3 is responsible for acute infections with no significant symptoms or progression to chronic infections, however in some immunocompromised patients it may be responsible for symptomatic chronic infections.

During the last several years, the incidence rate for non-travel-associated HEV infections in Europe has increased. Depending on the age, region, exposure risk, and diagnostic assay used the prevalence of anti-HEV IgG in European healthy individuals ranges from 5% to 52.5%. A recent study revealed anti-HEV IgG and IgM in 44% and 1.2% Polish blood donors respectively. The frequency of RNA HEV was estimated at 1/2.109 donations. IgG frequency increased from 25% in the youngest donors to over 65% in donors aged 47-58 and was observed to be higher in males than in females. Differences in IgG frequency were observed between regions: from 30% in Podlasie to 65% in Pomorze and Wielkopolska.

Due to epidemiological situation in Poland there is an urgent need to investigate the clinical relevance of HEV.

Increased frequencies of Th-17 CD4-T-cells and decreased of T-regulatory cells in non-alcoholic fatty liver disease

Magdalena Świderska[1], Kamil Grubczak[2], Jerzy Jaroszewicz[1], Anna Parfieniuk-Kowerda[1], Joanna Pogorzelska[1], Tadeusz Wojciech Łapiński[1], Marcin Moniuszko[1], Robert Flisiak[1]

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Introduction: Deregulation of immune responses may influence progression of NAFLD to non-alcoholic steatohepatitis (NASH). Our recent data suggest the role of Th17-related cytokines in fibrosis advancement in NAFLD. We aimed to analyze T-regulatory and Th17-producing T-lymphocytes by flow-cytometry with respect to NAFLD activity.

Material and methods: Extensive immunophenotyping was performed in a subset of 22-patients with NAFLD and 10-healthy volunteers. *Ex-vivo* surface (CD4, CD25, CD127) and intracellular cytokine expressions (IL-10, IL-17, FoxP3, RORgt) were analyzed by flow-cytometry (BD FACS-Calibur). Plasma concentrations of Th-17 and regulatory cytokines were measured by Bio-Plex™ Cytokine Assay (Bio-Rad).

Results: The percentage of IL-17-producing cells among CD4(+) T-lymphocytes was twofold more frequent in NAFLD (1.75 vs. 0.82%), while of T-regulatory cells (CD4+CD25+FoxP3+, T-regs) lower (3.7 vs. 9.4%) compared to healthy subjects. This resulted in aberrated ratio of Th-17 to T-regs in NAFLD ($p = 0.004$). In 14/22 (64%) of NAFLD patients ALT-activity was elevated suggesting the diagnosis of NASH. In NASH, percentage of T-regs was markedly lower than in NAFLD (0.16 vs. 0.23%). ALT activity and serum triglycerides correlated positively with frequency of Fox-P3-positive T-regs. Importantly, IL-22 serum level shown a positive association with frequency T-regs ($R = 0.45$, $p = 0.01$) while IL-21 with IL-10 producing CD4-T cells.

Conclusions: The disbalance between Th-17 and T-regulatory immune responses is present not only on cytokine but also cellular level in NAFLD. Especially in NASH higher percentage of IL-17 producing T-cells is coupled by lower of T-regulatory cells. These results underline the importance of Th17-respones in pathogenesis of NAFLD but also implicate potential usefulness of anti-Th17 therapies.

PLENARY SESSION 1
HEPATOCELLULAR CARCINOMA

Epidemiology of hepatocellular carcinoma in Poland (LIVER project)

Anatol Panasiuk[1], Krzysztof Simon[2], Krzysztof Krzemieniecki[3], Krzysztof Zieniewicz[4], Paweł Pęciło[5]

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[5]Bayer

Multi-center epidemiological and clinical examinations LIVER were performed in patients diagnosed with HCC in 2012-2015. There were 1371 HCC patients included in the study (LIVER 1 – 618 pts, LIVER 2 – 753 pts). Mean age was 62.0 ± 11.2 years (the range 20-96). HCC was most frequently diagnosed by infectious diseases consultants (29.2%), surgeons (28.3%), hepatologists (22%) and oncologists (13.4%). HCC was diagnosed based on imaging examinations (CT 87%, USG 60%, histopathology 79%) and laboratory tests (94%), including AFP. Patients with HCC showed HCV infection (44%), HBV infection (22.5%) while alcohol abuse was observed in 22% of patients. No apparent cause of the neoplasm was determined in 22% of patients. While HCC diagnosis, 61% of patients showed local advancement or spread of the disease. The advancement according to BCLC scale was determined: stadium A – 32%, stadium B – 40.5%, stadium C – 27.8% of patients. Further epidemiological and clinical data are still to be worked out.

Epidemiology of HCC in Poland – data from NFZ and Center of Oncology (CO)

Piotr Małkowski, Dariusz Wasiak

Warszawski Uniwersytet Medyczny

Statistical epidemiologic data is not precise. According to NFZ, the number of new cases increases each year, reaching 1851 in 2013. The incidence rate raises as well, equaling 3.1 in 2008 and 4.8 in 2013. CO data diverge in total numbers and incidence rates. The latter varies by province and ranges from 0.75 (świętokrzyskie) to 8.92 (mazowieckie). The number of HCC-related deaths fluctuates around 2000 yearly. The death ratio alters around 5 and is higher for men (M – 5.7; W – 4.7). Morbidity and mortality rates increase after the age of 50. The total number of HCC-related deaths constantly increases too. The percentage of LTx due to HCC in 2005 equaled 4.27% and increased to 21.68% in 2015. 60% of recipients with HCC had a post-hepatitis C liver cirrhosis.

Hepatocellular carcinoma (HCC) diagnosis based on imagining techniques – computed tomography

Ryszard Pacho

Wojskowy Instytut Medycyny Lotniczej, Warszawski Uniwersytet Medyczny

Computed tomography (CT) of the abdomen was introduced into medical practice 41 years ago. Examining the liver has been and still is one of the main purposes of application of the method. In the past 40 years this imagining technique has significantly developed – the area of acquisition of data has grown from 1 to 16 cm, the time of acquisition has shortened to 0.2-0.4 s and the data-processing programmes are much better. The concomitant introduction of iteration techniques in image development allowed a lowering of the dosage of radiation in abdominal exams by 80%.

In comparison with other non-invasive imagining techniques, such as magnetic resonance imagining (MRI), ultrasonography (USG) and in minor percentage nuclear medicine techniques (including positron emission tomography), the advantages of CT are the shortest time of the exam, a very good spatial definition and a high level of independence of the resulting image from the person performing the exam.

The disadvantage of CT-scanning is the application of X-rays and a slightly lower sensitivity in identification of very small focal lesions (< 1 cm), in comparison with MRI and the lack of hepatotropic contrast agents.

Diagnosis of hepatocellular carcinoma in CT, similarly as in MRI, is based on the difference between the enhancement of healthy liver parenchyma and liver affected by the disease. HCC has a rarely encountered distinctive feature: it washes contrast out from the tumour. Computed tomography, in comparison with

other imagining techniques, allows a better imagining of blood vessels involved in the tumour.

CT is the method of choice because of its availability, precision in evaluation of HCC and metastases and the relatively low cost of the technique.

Diagnostic imaging of HCC – MRI and US

Edyta Szurowska

Gdański Uniwersytet Medyczny

Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world and the third most common cause of cancer-related mortality. It is strongly associated with cirrhosis. Carcinogenesis of HCC occurs in a stepwise approach comprising the following steps: regenerative nodule, dysplastic low and high grade nodules, early HCC and large HCC. All patients with cirrhosis should be screened with ultrasound examinations every 6 months. Ultrasounds (US) have a limited role in the characterization of HCC – there is not a characteristic appearance at US, but focal liver lesions identified during ultrasonographic surveillance in patients with cirrhosis require further investigation, and lesions larger than 1 cm should be assessed with multiphasic computed tomography (CT) or magnetic resonance imaging (MRI). Non-invasive CT and MR imaging has become the standard for HCC diagnosis in cirrhotic livers. In this lecture, the basics of MR imaging in livers with cirrhosis will be discussed. Typical imaging features of HCC, including increased arterial phase enhancement and either delayed or portal venous phase washout, provide very high specificity and acceptable sensitivity in recognition of nodules larger than 10 mm. Diagnostic limitations apply to detecting hypo- or isovascular HCCs and differentiating dysplastic/regenerative nodules, perfusion defects, intrahepatic vascular shunts, focal steatosis from early HCCs. New techniques such as diffusion-weighted images and hepatocyte-specific contrast enhancement magnetic resonance imaging can improve detection and characterization of HCC.

Strategy of treatment of HCC patients according to "HCC Banacha" project

Tadeusz Wróblewski, Wacław Hołówko

Department of General, Liver & Transplant Surgery,
Medical University of Warsaw

HCC Banacha project is the largest one in Poland concerning complex treatment of patients with HCC. It is based on BCLC scale and Milano criteria. It was introduced to our Department in 2013 year and till the end of 2015 565 patients have been treated by one of the following method: (1) 18 liver resections, (2) 60 OLTx, (3) 1115 TACE: a) in 52 patients as a tumor stabilization or downstaging tumor therapy for potential OLTx candidates, b) 1063 palliative TACE procedures in 420 patients with or not additional percutaneous RFA, (4) 42 patients after TACE and 15 without any earlier treatment were qualified for chemiotherapy with Sorafenib. Results of TACE therapy have been evaluated by multidisciplinary team consisted of liver surgeon, hepatologist, interventional radiologist and oncologist according to the mRECIST scale based on CT or MR scans. In all patients these imaging scans are performed 1.5 months, each 3 months and finally each 6 six months after the last TACE procedures. Preliminary data indicate that combined treatment (TACE, OLTx, Sorafenib) enable to cure primary and recurrent tumors and should be considered in all non-resectable HCC.

Liver transplant for hepatocellular carcinoma (HCC)

Paweł Nyckowski

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Warszawski Uniwersytet Medyczny

Since the start of liver transplantation, treatment of HCC has played a central role. As liver transplantation progressed in an experimental environment, the high mortality procedure was frequently reserved for patients with advanced liver malignancy. As the procedure and immunosuppression were refined, patients and allografts survivals improved to the point that oncologic recurrence and survival rates could be determined. The initial experience clearly showed that in the immunosuppressed state following liver transplantation, patients with advanced stage HCC had extraor-

dinarily high recurrence rates. As more experience was gained and allograft outcomes continued to improve, non-oncological indications for liver transplantation were expanded and, appropriately, oncological indications were constricted. In 1989, a moratorium on liver transplantation for HCC was put in place. Following this, enthusiasm waned and few guidelines directed the listing and transplantation of patients with HCC until the publication of the Milan criteria. The Milan experience, with an identified subset of early HCC patients who had both excellent allograft and oncologic outcomes, rekindled interest in liver transplantation for malignant disease. The re-expansion of liver transplantation into the HCC recipient pool was temporally correlated with two other shifts in liver transplantation practice. First, in Western countries with significant rates of hepatitis C virus infections and obesity, the acute rise in the incidence of HCC cases has made the hepatology and transplant community focus on the problems of effective treatments. Second, in 2002 the UNOS implemented the model for end-stage liver disease (MELD) waitlist rank system and created MELD exception algorithms that advantage waitlisted patients with UNOS T2-3 criteria HCC. Currently, liver transplantation stands as the best treatment modality for early-stage HCC in patients with decompensated cirrhosis giving patients the opportunity to be free from potentially lethal complications of both cancer and their underlying liver disease. In settings where the number of patients with HCC and cirrhosis exceeds the availability of cadaveric liver allografts, alternative strategies were required. These include more liberal use of liver resection, interventional and systemic treatments, public health campaigns for organ donation awareness, and living-related liver transplantation.

Transarterial chemoembolization (TACE) in the treatment of intermediate stage hepatocellular carcinoma (HCC)

Mikolaj Wojtaszek

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Transarterial chemoembolization (TACE) was introduced into clinical practice in 1977, but found its place in the BCLC official guidelines for HCC treatment in 2008, taking its place in between radical forms of therapy and palliation chemotherapy with sorafenib.

Conventional TACE is the selective administration of a chemotherapy agent into the tumor feeding vessels combined with an oil-based liquid embolic such as lipiodol. The main limitation of lipiodol, or conventional embolization is the fact, that it is impossible to form a long lasting stable emulsion which would release the chemotherapy agent gradually along time. In order to overcome these limitations, DEB-TACE (Drug Eluting Bead Transarterial Chemoembolization) was introduced in which microparticles are saturated with a chemotherapy agent (ie. Doxyrubicin). This allows for the stable and continuous release of high concentrations of the agent around the tumor itself, while limiting high systemic concentrations and hence potential complications of chemotherapy.

Until now, there is no set number of TACE procedures that should be performed. Most centers perform 1 to 4 treatment sessions, but it is generally know that qualification for treatment should be individually based and should take into account factors such as the number of lesions, liver function and patient status.

The most widely used prognostic score for TACE is currently the HAP Score in which the liver function is assessed in relation to the tumor size. Imaging scores for treatment are usually based on the mRECIST as well as the Choi classification systems.

Radiofrequency ablation of hepatocellular carcinoma

Krzysztof Milczarek, Dariusz Konecki, Grzegorz Rosiak

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Radiofrequency ablation (RFA) is one of interventional oncology procedures and is widely accepted as a method of treatment of hepatocellular carcinoma (HCC). Because only under 40% of patients are qualified for surgery, many of the remaining patients can be treated with interventional oncology procedures. According to Barcelona Clinic Liver Cancer classification RFA belongs to curative procedures along with surgery and transplantation.

RFA is typically indicated in patients that are disqualified from surgery, have three or less lesions with diameter of 5 cm or less. A single lesion with diameter < 3 cm can be cured in 85%, while in 4 cm lesions the success rate goes down to 60%.

Contraindications include bile duct or major vessel invasion, lesions larger than 5 cm, multiple (> 3) lesions.

The ablation is a minimally invasive procedure, performed percutaneously. Small volume of the liver

sacrificed during the procedure is especially important in patient with liver cirrhosis. The procedure is usually performed under ultrasound and/or computed tomography guidance.

Serious complications are very rare and include: infection, bleeding, thermal injury of diaphragm, bowel, biliary tree or gallbladder. Minor complications are more frequent and include post-ablation syndrome (flu-like symptoms) and shoulder pain for a few days after the procedure.

We report one institution experience after 100 radiofrequency ablations.

Conclusion: Radiofrequency ablation is a very effective and safe procedure in treatment of small HCCs. Strict follow-up regimen is mandatory.

Chemotherapy – eligibility and variants of treatment

Andrzej Deptała

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Zakład Profilaktyki Onkologicznej, Warszawski Uniwersytet Medyczny

Hepatocellular carcinoma (HCC) is a cancer that usually develops in the cirrhotic liver. The coexistence of the two diseases – cirrhosis of the liver and cancer – making treatment of HCC complicated, because of the risk of liver failure due to therapy. Systemic therapy is reserved for the treatment of advanced HCC cases where it was not possible to perform either surgical resection and allogeneic liver transplantation or chemoembolization – i.e. for the stage C according to the BCLC staging system. The current gold standard used for this purpose is sorafenib. Sorafenib (BAY43-9006) belongs to a group of small molecule multikinase inhibitors, and inhibits C-RAF and B-RAF, VEGFR-2, VEGFR-3, PDGFR-β, c-KIT, FLT3. Therefore, sorafenib is the example of a drug combining antiproliferative activity and inhibition of angiogenesis. Two multicenter, prospective and randomized placebo controlled phase III trials – SHARP and the Asia-Pacific – confirmed a statistically significant prolongation of overall survival (OS) in patients with advanced HCC, with acceptable side effects associated with this drug. Sorafenib consistently improves median OS and median disease control rate (DCR) in patients with advanced HCC, irrespective of: cancer etiology, initial tumor size, performance status, the severity of the HCC and prior treatment. So far, there are no published results of prospective, randomized trials that have shown greater effectiveness of other molecularly targeted drugs compared to sorafenib in the treatment of advanced HCC. Chemotherapy may be considered in the case of sorafenib intolerance or when it comes to the progression of HCC after sorafenib.

Common problems and pitfalls in the diagnosis and treatment of the patients with HCC

Krzysztof Zieniewicz

Katedra i Klinika Chirurgii Ogólnej, Transplantacyjnej i Wątroby, Samodzielny Publiczny Szpital Kliniczny w Warszawie

Hepatocellular carcinoma (HCC) is responsible for approximately 600 000-700 000 deaths worldwide. It is highly prevalent in the Asia-Pacific, Africa, and is increasing in Europe and USA. Persistent HBV and HCV infections are the most important risk factors for hepatocarcinogenesis. Both, the incidence and mortality rates have increased in recent decades. The majority of patients are still diagnosed in advanced stage of the disease. The diagnosis should be based on clinical findings together with radiologic imaging and microscopic examination. Resection is the preferred treatment for patients with the disease confined to 1-2 liver segments and preserved hepatic function with no evidence of portal hypertension. Liver transplantation is the best option for the patients with strictly defined clinico-pathiological criteria (Milan, UCSF, up-to-7). There are limited reports on the incidence of mixed hepato-cholangiocarcinoma in patients undergoing liver transplantation. The main reason is the radiological misdiagnosis or an inability to differentiate this tumor from HCC preoperatively. The most common problems and pitfalls in radiological differential diagnosis (ultrasound, CT and MRI), treatment strategy, including multidisciplinary approach and follow-up of the patients are discussed. Transarterial chemoembolization, radiofrequency and microwave ablation and alcoholization as palliative modalities and/or downstaging methods are critically reviewed. Systemic chemotherapy is proved to be of marginal value, whereas sorafenib – small molecule angiogenesis inhibitor – may prolong survival in well-selected patients. The value of clinico-pathological and biological factors (biomarkers) influencing survival is in broad outline presented.

Hepatocellular carcinoma treatment by liver transplantation in patients with liver cirrhosis

Beata Łągiewska[1], Dariusz Wasiak[2], Marek Pacholczyk[1], Wojciech Lisik[1], Maurycy Jonas[1], Agnieszka Perkowska-Ptasińska[3], Olga Tronina[3], Janusz Trzebicki[4], Magdalena Durlik[3], Piotr Małkowski[2], Maciej Kosieradzki[1]

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[2]Department of Surgical and Transplant Nursing, Warsaw Medical University
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Introduction: Over the last 10 years there has been a substantial increase in liver transplantations (OLTx) due to hepatocellular carcinoma (HCC) worldwide. In our clinic the percentage of patients after liver transplantation due to HCC is 21.4% in the last 5 years.

Material and methods: In the years 2000-2015 541 liver transplants were performed. In 75 patients (13.86%) HCC was diagnosed within the cirrhosis of the liver. 66 patients (88%) fit the Milan criteria at the moment of the transplantation. The number of tumor nodules in the removed liver ranged from 1 to 4. Only one patient was diagnosed with multifocal HCC (> 5 foci). The average diameter of the HCC foci was 27.63 mm, and the largest tumor was 10 cm in diameter. Such large neoplasms weren't present in pre-OLTx liver imaging. Microscopic examination of the liver with cirrhosis showed, that well-differentiated HCC (G1) was present in 11 patients (17.18%), poorly-differentiated (G3) in 7 (10.9%), and vaso-invasion within the tumors periphery was present in 17 patients (26.56%).

Results: 55 patients (73.33%) live to this day. 6 patients died due to complications other than HCC in the early period after liver transplantation. HCC relapsed in 11 patients (14.66%), and within those 11, 8 died because of it. 5 patients died in the late period after transplantation due to other reasons.

Conclusions: Long-term results justify liver transplantation in patients with HCC present within the cirrhosis of the liver as a form of treatment.

PLENARY SESSION 2
CYSTIC HEPATIC LESIONS

Choledochal cysts in children

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Congenital choledochal cyst (CC) is a rare disease characterized by extrahepatic or/and intrahepatic bile ducts dilatation. Choledochal cysts more often occur in Asian population compared with Western population with female preponderance 3-4 : 1. Classifacation proposed by Alonso-Lej modified by Todani is based on localization of dilatation on biliary tract and consist of 5 types of malformation. The most probable etiology is described by Babitts theory. Abnormal panceratobiliary duct junction (APBDJ) occurs outside duodenum wall and leads to reflux of pancreatic juice to biliary tree. Digestive influence of pancreatic enzymes on biliary epithelium results in inflammation, wall weakening and further cyst formation. If untreated, choledochal cysts may be complicated by cholangitis, pancreatitis, cholelithiasis, liver abscess formation, hepatic cirrhosis and malignant malformation. Symptoms occur in childhood in ca. 80% of patients. Classic triad of symptoms consist of pain, abdominal mass and jaundice. Diagnosis is based on ultrasonography, magnetic resonance, computed tomography and scintigraphy. Endoscopic retrograde cholangiopancreatography (ERCP) has diagnostic value but as definitive procedure is limited to choledochocele and when acute cyst decopmresion is required. Historically cyst enterostomies were performed but severe complications and malignant tranformations were observed. The only accepted treatment of choledochal cysts is total cyst excision followed by Roux-en-Y hepaticojejunostomy. Due to possibility of postoperative long term complications constant follow-up is necessary.

Experience of Department of Pediatric Surgery and Organ Transplantation in the treatment of children with CC will be presented.

Kidney and liver cystic disease – who's is the patient, nephrologist's or hepatologist's? Part I

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Cystic kidney disease (CKD) is a member of ciliopathies family, where specific genetic error is an underlying cause of cilia malfunction. The clinical effect is forming multiple renal cysts, which then increase their volume and cause the effect of large abdominal mass, hypertension, hematuria and renal failure. Recessive form (Autosomal Recessive PKD; ARPKD; gene PKHD1) is rare disease (1 : 10-40 000), predominantly seen in small children, while dominant form (Autosomal Dominant PKD; ADPKD; genes PKD 1 and 2) is more common disease (1 : 500-1000), which affects both children and adults. Patients with ADPKD typically develop renal failure much later – about 5th decade of life. The management of ARPKD includes substitution of renal function and replacing dysfunction of other organs (including mechanical ventilation in newborns). Renal replacement therapy is introduced once renal failure develops or large kidneys must be removed to decompress the lungs. The treatment of ADPKD includes manipulation of underlying molecular patomechanism of the disease with different drugs, aimed to slow the ongoing growth of the cysts and overall kidney volume, as well as to stop the progression of renal failure. Several drugs, including mTOR inhibitors, ACE inhibitors, V2 (vasopressin) receptor and cAMP blockers have been tested in clinical trials. There is moderate evidence on proven efficacy and safety of these therapies, as the effect on cysts growth was not always accompanied by slowing the progression of renal failure or the therapy was accompanied by significant adverse events. PKD is a challenge for nephrologists.

Liver cysts – surgeon's or hepatologist's patient?

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Liver cysts in children are uncommon. Liver cysts can be present at birth or can develop at a later time. They usually grow slowly and may not be detected until adulthood. Most liver cysts do not cause any symptoms. If cysts become large, they can cause bloating and pain in the upper right part of abdomen. Congenital hepatic cysts occur in approximately 2.5-5% of the general population. Cystic liver lesions may pose diagnostic and therapeutic dilemmas. Since most liver cysts do not cause any symptoms, they usually are detected only on ultrasounds or computerized tomography (CT) scans. Many are simple and solitary and do not require intervention. However, there is a wide range of potential cyst pathologies, some of which may be even life-threatening. Therapy in patients with echinococcal disease is aimed at sterilization and complete excision of hydatid tissue. Abscesses should be treated at the time of identification, but percutaneous drainage and antibiotics are usually adequate treatment. If cysts on imaging studies show abnormalities suggestive of cystic tumors, resection is indicated.

Parasitic cysts of the liver

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w Białymstoku

In Poland, as in most European countries parasitic cysts of the liver caused by *Echinococcus granulosus* and *E. multilocularis*. The incidence of parasitic cysts growing in the last four years. Increasingly, there are reports of European countries cyst caused by cestodes imported from subtropical and tropical: *E. ortleppi*, *E. equines*, equines *E. vögeli* and *E. shiquicus*.

The process of infections is well known. According to recommendations CDC best examinations to confirming infection are imaging (USG, CT, MR).

Treatment of patients infected with the particular type of agent threatening. It is now possible to puncture the cyst, chemotherapy and surgery to remove the cyst.

For each action invasive (puncture surgical removal) before and after surgery is necessary to use the appropriate chemotherapy.

Alveococcal hepatic tumors in Infectious and Tropical Diseases and Hepatology Department of Medical University of Warsaw in years 2011-2016

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Introduction: Alveolar echinococcosis (AE) is emerging disease in Poland. Untreated or inadequately treated AE mortality is over 90% within 10-15 years of diagnosis.

Purpose: To summarize our experience concerning this disease.

Material and methods: Retrospective case series. Subject: 16 patients with the AE, 14 woman, 2 man, age 18-77 years, admitted to our hospital since 2011. All patients were treated with albendazole 2 × 400 mg continuously or with short repeated breaks. A 5 of them also had a surgery.

Results: Almost half cases was accidental findings with no patients complaints. All patients were lived in Poland, one man was from Podkarpackie Voivodeship, the rest were from North-Eastern part and have positive ELISA Em2+ test. Changes in the imaging studies presented themselves as solid, irregularly shaped tumors 5-24 cm, often containing tiny calcifications and rarely containing very small, irregular fluid spaces. 19% patients had metastasis, 6% enlargement liver, no one did not present the signs of hepatic failure. The biggest problem was the mechanical compression of the vessels with the associated thrombosis and the obstructive jaundice. During the treatment with albendazole we did not observe new foci. Most of the tumors slightly decreased in size and in the central part the necrosis appeared.

Conclusions: Treatment with albendazole is effective, to controls growth of the tumor. The necrosis with the secondary liquefaction of large tumors, that appeared approximately after 3 years of treatment, was life threatening. Thus they need surgical interventions even against WHO Informal Working Group on Echinococcosis recommendation.

PLENARY SESSION 3
INCREASING THE POOL OF ORGANS AVAILABLE FOR LTx BY ORGANS FROM HBV-INFECTED DONORS

Increasing the pool of organs for OLX by coming from HBV donors – single-center experience (Szczecin)

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Organ harvesting is not allowed from HBsAg(+) donors in Poland. Due to the possibility of the occult HBV infection in anti-HBc-positive subjects, a careful cross-match between donors and recipients in respect to the HBV serological status is highly recommended. The following organs can be harvested from anti-HBc(+) donors irrespectively of the serological status of the recipient: marrow, lungs, heart, pancreas, cornea. Livers and kidneys can be harvested only if recipients are HBsAg(+) or anti-HBc(+) and/or anti-HBs(+). Livers from anti-HBc(+) donors can be transplanted to the seronegative recipients only in case of emergency and when reactivation prophylaxis is available.

In years 2005-2015 (since 2005 anti-HBc status is checked in every donor in Poland) 421 OLTx were performed in our center with the following D/R serological cross-match: D–/R+ in 309 cases, D+/R– in 16 cases, D+/R+ in 10 cases (including 3 chronic HBV carriers), D–/R+ in 86 cases (including 28 chronic HBV carriers). Five HBV reactivations were noted and all of them concerned seronegative recipients who received anti-HBc(+) livers. In all these cases reactivation prophylaxis with nucleoside analogue was given up due to temporary lack of reimbursement. There were no cases of reactivation in seropositive recipients despite lack of prophylaxis in some anti-HBc(+) recipients.

Transplantation of anti-HBc(+) livers to anti-HBc and or anti-HBs negative recipients should be avoided.

Increasing the pool of organs for OLX by coming from HBV donors – experience of Warsaw's Centers

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The growing discrepancy between the number of patients listed for liver transplantation and the availability of cadaveric organs is one of the most important problems facing potential liver transplant candidates. For this reason transplant professionals and Poltransplant (organ procurement coordinating agency) are attempting to expand the donor pool through developing novel strategies for increasing the availability of donor livers.

There are several ways to expand the donor liver pool. First, increasing knowledge and awareness about organ donation after death and organ transplantation, to increase the proportion of consent for organ donation and number of cadaveric livers. Second, way to expand the liver pool is through advances in medical practice such as split-liver transplantation, living donor liver transplantation, domino transplantation. The third, increase the proportion of harvested livers (multiorgan donors) that are used for transplantation (actual liver donors). Marginal livers, i.e. livers from older donors, donors with history of alcohol abuse, fatty livers, and hepatitis B-infected grafts, previously had been discarded.

But recent studies have shown that many of these livers can be successfully transplanted. The use of liver from cadaveric donors with HBV infection markers, strategies in protecting the donor against recurrence of infection and local center experience on this field is going to be discussed.

Costs of treatment/prophylaxis of post LTx HBV recurrence

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The results of LTx in HBV patients improve, in addition, prophylaxis and treatment of HBV recurrence post LTx still creates a big financial and therapeutic challenge. Classical prophylaxis involving high doses of HBIG and LAM is expensive and sometimes ineffective. The cost of yearly prophylaxis in Poland equals to nearly 160 thousands PLN. Up to date literature divides recurrence likelihood into two groups – high and low risk, concerning both – recipients and donors. New proposals recommend high-dose HBiG during the anhepatic phase and the first week post LTX followed by low-dose HBiG simultaneous with TDF or ETV, including possible HBiG withdrawal in the low-risk recurrence group. HBiG withdrawal in the high-risk recurrence group is not recommended. These proposals may reduce the overall cost of prophylaxis more than fivefold.

Legal aspects of liver transplantation from HBV donors

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Centrum Poltransplant

Organ transplantation is related to the risk of transmission of infection, including hepatitis B. This issue should be seen in several areas: 1) the use of organs from an infected donor of unexplored and unknown HBV status; 2) the use of organs from infected donors with known and negative at the time of transplantation HBV status (infection during the window period); 3) conscious utilisation of organs from an infected donor and transplanted to properly selected recipient with the respect of principles of organ allocation; 4) conscious use of organs from an infected donor and transplanted to any recipient without respect of principles of organ allocation. After the query and analysis of Polish and European legislation and recommendations we summarized that situations mentioned above is characterized by relativism, and may be as follows: 1) the use of organs from a donor with incomplete characterization is unintentional criminal act, exposing health or life of the donor (Polish Penal Code) but it may be defended by EU Directive 53/2010: "if according to a risk-benefit analysis in a particular case, including in life-threatening emergencies, the expected benefits for the recipient outweigh the risks posed by incomplete data, an organ may be considered for transplantation"; 2) situation fully corresponds to the definition of serious adverse event; 3) proceedings fully justified on the basis of the risk-benefit analysis and prediction of the results of transplantation; 4) situation is rather clear, which is a medical mistake and crime against life and health (Polish Penal Code).

Individualization of immunosuppression treatment with tacrolimus during antiviral therapy based on 3D regimen in patients after liver transplantation with hepatitis C reactivation

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Introduction: Interferon-free regimens are now considered as a treatment of choice for patients with hepatitis C (HCV) reactivation after liver transplantation (LTx). The combination of paritaprevir/ritonavir/ombitasvir (3D regimen) cures more than 90% of patients but its known influence on tacrolimus (Tc) metabolism may induce several side effects.

Purpose: The aim of the study was to analyze the Tc dose adjustment based on Tc blood trough level (Tc0) during first three months of 3D therapy in LTx patients with HCV reactivation and its effect on kidney function.

Material and methods: 15 liver graft recipients infected with HCV 1b genotype without liver cirrhosis were included into 3D therapy. On the first treatment day, the recommended, reduced dose of Tc was launched (0.5 mg every 7 days). On day 3, 7, 10, 14, 28, 56, and 84 – Tc0 was determined and the interval of 0.5 mg of Tc administration in order to achieve a therapeutic blood concentration was evaluated.

Results: At 14th day of 3D therapy,Tc0 was significantly increased in 8 patients (mean 41.29 ± 20.72%

higher than initial level, $p < 0.001$), in 5 of them it exceeded the upper limit of therapeutic blood concentration. In the remained patients Tc0 did not change significantly. After 2 months of therapy, the reasonable rate of Tc dosing was adjusted (mean interval between doses was 8.9 days; range 7-14 days). In this time, no significant increase in mean serum creatinine concentration was observed (from 87.7 ± 23.4 to 86.7 ± 17.9 μmol/l).

Conclusions: Close monitoring of Tc0 during antiviral therapy with 3D regimen is necessary and frequency of doses should be individualized.

PLENARY SESSION 5
HCV INFECTIONS

Genotype 1A HCV – is it a Polish problem?

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G1A HCV was rarely recognized in Poland, while in European researches represent about 60% of the population infected 1AHCV. In a recent study published in Poland in 2013 we estimated that 1A is approximately 5% of patients infected by G1 HCV. Currently, we analyze closely subtypes of HCV due to DAA treatment and resistance of 1A to some molecules, induced by the RAV's. In the last year, we analysed patients qualified for treatment in Lodz in 2015 and the study revealed that G1A represent 17% of patients infected by G1 HCV. Patients 1A were born between 1986-1994 and were statistically younger than infected 1B. They also presented mild fibrosis in the liver.

The cause and possible treatment of infected G1A in Poland will be discussed in the lecture.

Interferon-free therapy in the real world

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Virologic and safety outcomes of interferon (IFN)-free regimens were investigated in a number of pre-registration studies showing high sustained virologic response rates and good tolerability in patients with chronic HCV infection. Ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV) and sofosbuvir/ledipasvir ± ribavirin (SOF/LDV ± RBV) were recently tested in numerous "real-world" studies showing efficacy and safety on the level similar to clinical trials. On treatment decompensation in cirrhotics was highlighted by regulatory authorities as an issue related to protease inhibitors. However based on real-world data and some clinical trials without this class of drugs, hepatic functional impairment can in patients with advanced liver disease. The most prevalent in Poland population of patients infected with genotype 1b can be treated with both mentioned regimens for 12 weeks without RBV, with exception of cirrhotics on SOF/LDV who should receive either RBV or treatment extended to 24 weeks. Shortening of treatment to 8 weeks is atractive, but eligible population is still not defined and it should probably be limited to non-cirrhotics with low baseline viral load, particularly those clearing the virus after 4 weeks of treatment. Drug-drug interactions does not seem to be as important issue as it was expected before registration, but special attention for concomitant medication should be paid to anti-retroviral or immunosuppresive drugs before OBV/PTV/r ± DSV ± RBV and to amiodarone or proton pump inhibitors before SOF/LDV ± RBV.

Interferon lambda polymorphisms associate with body iron indices and hepatic expression of interferon-responsive long non-coding RNA in chronic hepatitis C

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Purpose: Single-nucleotide polymorphisms (SNPs) within DNA region containing interferon lambda 3 (IFNL3) and IFNL4 genes are prognostic factors of treatment response in chronic hepatitis C (CHC). Iron overload, frequent in CHC, is associated with unfavorable course and a risk of carcinogenesis. Its etiology and causal relationship to the model of the immune response in CHC are not fully explained. Our aim was to determine if IFNL polymorphisms in CHC patients associate with body iron indices, and if they are linked with hepatic expression of genes involved in iron homeostasis and IFN signaling.

Material and methods: For 192 CHC patients four SNPs within IFNL3-IFNL4 region (rs12979860,

rs368234815, rs8099917, rs12980275) were genotyped. In 185 liver biopsies histopathological analyses were performed. Expression of 5 mRNAs and 3 IFN-responsive long non-coding RNAs was determined with qRT-PCR in 105 liver samples.

Results: Rs12979860 TT or rs8099917 GG genotypes as well as markers of serum and hepatocyte iron overload associated with higher activity of gamma-glutamyl transpeptidase and liver steatosis. The presence of two minor alleles in any of the tested SNPs predisposed to abnormally high serum iron concentration, and correlated with higher hepatic expression of lncRNA NRIR. Homozygosity in any major allele associated with higher viral load. Patients bearing rs12979860 CC genotype had lower hepatic expression of hepcidin (HAMP) (p = 0.03). HAMP mRNA level positively correlated with serum iron indices and degree of hepatocyte iron deposits.

Conclusions: IFNL polymorphisms influence regulatory pathways of cellular response to IFN, and affect body iron balance in chronic HCV infection.

PLENARY SESSION 6
HBV INFECTIONS

Novel facts in immunopathogenesis of viral hepatitis B

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Traditionally innate immunity is viewed as responsible for rapid control of viral replication, whereas adaptive branch is determining the course of disease more slowly, but precisely and effectively. HBV-specific T lymphocytes seem to be the key to cure chronic hepatitis B, since they can both eliminate infected liver cells and destroy the virus in non-cytholitic way, possibly even eliminating cccDNA. Unfortunately, their persistent exposure to high antigen loads causes functional exhaustion and inhibits their actions. Exploration of HBV pathogenesis leads us to conclusion, that probably we should locate our hopes in unappreciated innate response.

Previously, HBV was considered as able to evade innate immune system. Recent studies have shown, that non-specific cells not only recognize the virus, but also cause many complex reactions inside the infected liver environment. Their action is not limited to acute infection, but continues to play various roles throughout the course of chronic hepatitis B. Innate immunity seem to have sophisticated control over the adaptive one, and new methods of this maneuvering in HBV infection are still being discovered. Monocytes, NK-cells, or newly described cells like MAIT or MDSC seem to have great potential, due to their big amount in liver. Current investigations focused on cure of chronic HBV consider harnessing innate immunity for its direct antiviral effects as well as beneficial modulation of HBV-specific T lymphocytes.

What is new in "old" HBV?

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prof. emer. (Poznan University of Medical Sciences)

The treatment goal for chronic hepatitis B is eradication of the HBV. This is rarely achieved because of an inability to eradicate covalently closed circular DNA (cccDNA HBV). The median cccDNA levels is low in acute hepatitis B and in HBeAg negative-phase, and high in immunotolerant and immune-clearance phases. In HBe antigen-positive patients after 48 weeks of treatment with entecavir HBV cccDNA was decreased significantely in serum and liver in patients undergoing HBeAg seroconvertion.

Modern drug development focuses on strategies targeting cccDNA in several ways: 1) entry inhibitor Myrcludex B (targets NTCP receptor to inhibit virus entry), phase 2a of clinical trial [PCT]; 2) cccDNA degrader, silencer, or eliminator (example: lymphotoxin-β receptor, Zinc finger nucleases), 1 PCT/preclinical(P); 3) RNA interference or gene silencer (RNA molecules inhibiting gene expression and relase of new virions; 8 different compunds) 2 PCT/P; 4) assembly effector (inhibits HBV replicating by destabilization of viral nucleocapsid (e.g. heteroaryldihydropyrimidines, HAPs), phenylpropenamide) 1 PCT/P; 5) HBsAg relase inhibitor (5 compounds) 2 PCT/P; 6) new nucleos(t)ide DNA polymerase inhibitor (e.g. tenofovir alafenamide and besifovir: 3 CT, lagociclovir valactate: P); 7) cyclophilin inhibitor (alisporivir and 2 compounds), P); 8) immunomodulators: boost immune response (e.g. peginterferon lambda, cytokines [interleukins 7, 12, 18, 21]; stimulators of interferon genes agonist), P; 9) therapeutic vaccines (induce and stimulate CD4+ and CD8+ T-cell response: Tarmogen and another one) preventing cccDNA formation, eliminating cccDNA or silencing cccDNA transcription.

References: Brahmania M, et al.: Lancet Infect Dis 2016, 16: e10-e21.

HBV infection in patients with lymphoproliferative disorders

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The prevalence of HBV infection in patients with lymphoproliferative disorders is comparable to or higher than in local population. Patients with active or inactive disease or resolved HBV infection are at risk for reactivation with immunosuppressive therapy use. HBV has been associated with the development of non-Hodgkin lymphoma and can be reactivated in pa-

tients being treated for NHL. B-cell depleting therapy such as anti-CD20 monoclonal antibodies, especially when combined with conventional chemotherapy, significantly increases the risk of HBV reactivation, even in patients with resolved HBV infection. HBV reactivation varies from a clinically asymptomatic to associated with acute liver failure. Risk factors for reactivation are characterized as patients factors, viral factors, underlying diseases, type of transplantation as well as the type and intensity of immunosuppression. Risk calculation should be determined through HBV screening and assessment of immunosuppressive therapy potency. Prophylactic antiviral treatment is needed for all HBsAg carriers and selected patients who have anti-HBc without HBsAg and is critical for preventing viral reactivation and improving outcomes.

Treatment of persistent HBV infection – how to eliminate cccDNA?

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Hepatitis B virus (HBV) infection due to its unique features including formation of stable replicative form (cccDNA) and ability of integration cannot be eliminated from infected cells by current therapies. Commonly used inhibitors of HBV-polymerase are very effective in suppressing viral replication thus reducing the risk of liver cirrhosis and hepatocellular carcinoma although HBsAg-loss is rare. In the recent years several studies tested the efficacy of combination nucleos(t)ide analques and pegylated interferon. Preliminary data suggest that this approach shows benefit in obtaining HBsAg-loss and seroconversion compared to monotherapy, though exact therapeutic schedules have to be yet established. Importantly novel therapies aimed at various steps of HBV-lifec cycle (DAA – direct acting antivirals) are underway. Among most promising class of new antivirals are entry (Myrcludex), core (NVR 3-778) and HBsAg-release (REP-2139) inhibitors. Particularly core inhibitors are promising since they might also affect the content and stability of cccDNA. In order to reach definitive cure of HBV cccDNA has to be aimed. Currently siRNA's targeting cccDNA products (for example ARC-520) are tested in phase II clinical studies. Novel concepts of cccDNA disruption including CRISP/Cas9 system and lymphotoxin beta receptor (LTbR) agonists are evaluated in animal studies. In conclusion numerous novel anti-HBV therapies aiming at HBV-eradication are extensively studied suggesting the revolution in anti-HBV therapy strategies in upcoming years.

Hepatitis B vaccination – current challenging

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The major steps towards the global control of HBV infection and its complications include improvement in sanitation and living condition, implementation of hepatitis B vaccination, and the introduction of effective antiviral agents to treat chronic hepatitis B patients. Similar to other infectious agents, successful HBV infection is composed of three components, an infectious source, a susceptible host and an established route of infection. Therefore the most cost-effective method to control hepatitis B is to prevent susceptible persons from infection, rather than treating those who are already infected. In this regard there are two major measures. The first opportunity is to interrupt the route of infection and the second is to immunize the susceptible hosts. Among them, vaccination and public education are the most important.

Following a complete course of vaccination seroprotective rates in healthy children and adults are reached more than 90%. Based on the current scientific evidence there are no need to administer booster vaccine to sustain long-term protection. But booster vaccine dosis should be provided to non-responders and to the persons from risk groups.

The knowledge on HBV infection and transmission ways as well as prevalence of anty-HBcAg total and anty-HBsAg in selected population in Poland will be presented.

Distribution of HBV genotypes and HBsAg serum concentrations in Poland: results of multicenter EpiGeneS study

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Introduction: National multicenter network (EpiGeneS) was established in 2013 for the follow-up of chronic hepatitis B in Poland. The aim of current analysis is to describe distribution of HBV-genotypes and its associations with HBsAg levels.

Material and methods: In this study 400 treatment-naïve individuals with persistent HBV-infection were included in 9 centers in Poland. HBV-genotyping was performed with Inno-Lipa (n = 388) and HBsAg quantification by Roche-Elecsys (n = 393).

Results: The majority of treatment naïve-patients were young (median 35 yo, IQR: 26-44) and HBeAg-negative (95%). The most prevalent genotype in Poland was HBV-A (n = 73%) followed by HBV-D (18%). Interestingly, third most common was HBV-H (4%) and mixed genotypes were detected in 4%. Prevalence of genotype D (24%) and H (7%) is significantly higher in eastern Poland compared to the rest of country (15% and 2% respectively, $p < 0.001$). Median HBsAg levels were higher in HBV-A vs. non-A genotype (14 346 vs. 3768 IU/ml, $p < 0.001$), although comparable HBV-DNA. The lowest qHBsAg values were observed in HBV-D (2430 IU/ml). Interestingly, HBsAg levels correlated with HBV-DNA only in non-A genotypes ($r = 0.41$, $p < 0.001$), while not in HBV-A. Subjects infected with genotype H had significantly higher HBV-DNA levels ($p = 0.01$).

Conclusions: Distribution of HBV-genotypes in Poland is more diverse then previously suggested and shows significant geographic variations. Patients infected with HBV-A show higher HBsAg levels irrespective of phase of disease, suggesting its distinct synthesis. Clinical relevance of genotype-H (common in Central and South America) and mixed genotypes needs to be established. These results suggest the importance of HBV-genotype specific validation of qHBsAg clinical application.

PLENARY SESSION 7
AUTOIMMUNE LIVER DISEASES

Autoimmune reactions in HCV infected patients

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Introduction: HCV infection may induce autoimmune processes resulting with progression of the liver disease.

Aim of the study. The prevalence and type of autoantibodies among HCV infected patients with and without immunosuppression was evaluated. The results were assessed according to HCV genotype, liver inflammation and fibrosis.

Material and methods: 125 patients with chronic HCV infection were enrolled to the study, including 25 renal transplant recipients or patients with renal diseases receiving immunosuppression. Autoantibodies: AMA-M2, SLA/LP, LKM-1, LC1, anti F-actin, anti-desmin, anti-miosin, anti-gp210 and sp-100 antigens were determined by immunoblot and ANA by ELISA. Severity of liver inflammation and fibrosis were assessed in all patients.

Results: Autoantibodies were detected in 32.5% HCV infected patients without immunosuppression and in 16% receiving immunosuppression. Single autoantibodies were identified in 26% patients. The most common were ANA (21.5%) and AMA-M2 (7.5%). Among genotype 1 HCV infected patients autoantibodies were detected more often than in genotype 3 HCV infected (36.2% vs. 22.7%; $p < 0.02$). Autoimmune hepatitis was diagnosed in none of these patients. Immunoglobulin G concentration was significantly higher in patients with detectable autoantibodies compared to patients without autoantibodies (2.49 vs. 1.21 g/dl; $p < 0.001$). There was no effect of liver inflammation or fibrosis on the prevalence of autoantibodies.

Conclusions: Autoantibodies, mostly ANA, are very common in HCV infected patients, especially those infected with genotype 1 HCV, but their presence is not associated with development of autoimmune hepatitis. Higher serum concentration of immunoglobulin G is associated with autoantibodies detection.

Overlap syndrome: AIH/PBC – diagnostic and therapeutical problems

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The presence of four distinct mostly autoimmune diseases of unknown etiology has been described as an overlap syndromes. In contrary to other overlap syndromes the overlap syndrome AIH/PBC is relatively well characterized and can occur in two distinct variants. In first variant dominate histologically AIH, but serologically and biochemically PBC (antimitochondrial antibodies – AMA strongly positive, lower titer of: IgG, antinuclear antibodies – ANA and smooth muscle antibodies – ASMA); in second variant dominate histologically PBC, but serologically and biochemically AIH (ANA, ASMA positive, AMA negative, lower than in PBC titer of IgM). Moreover second variant is similar to the another autoimmune disease: autoimmune cholangitis – AIC. Patients with dominant features AIH should be treated by immunosuppressants, e.g. prednison, azathioprine, and patients with dominant features of PBC should be treated by ursodeoxycholic acid – UDCA (15 mg/kg bw daily) on monotherapy or with combination by small dose of glucocorticosteroids – GSK, e.g. prednisone 20 mg/daily. Because of risk of osteoporosis, diabetes mellitus, glaucoma and hypertension some clinicians prefer topically acting GSK like budesonide than traditional glucocorticosteroids.

Monitoring of patient with autoimmune hepatitis

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Autoimmune hepatitis ranges from acute and/or fulminant onset to asymptomatic presentation, but once it is diagnosed and treated most patients present chronic liver disease.

Monitoring of patients with autoimmune hepatitis plays a key role in long-term management and prognosis. All patients with active autoimmune hepatitis

are candidates for treatment. Combination therapy with prednisone or prednisolone and azathioprine is preferred for both induction and a maintenance phase. The maintenance phase is continued until normalization of serum AST, ALT, bilirubin, and γ-globulin or IgG levels and resolution of the histological abnormalities. When therapy with azathioprine is ongoing blood leukocyte and platelet counts have to be monitored and suggested frequency is every 3 to 6 months. The main side effect of corticosteroids is osteopenia and regular weight-bearing exercise, vitamin D and calcium supplementation or bisphosphonates (bone densitometry) may be helpful. The average treatment duration is 22 months usually necessary to achieve normal liver tests and near normal liver tissue.

Liver biopsy and tissue examination is the preferred proof for histological resolution, but stable normal laboratory tests for 12 to 18 months are sufficient to indicate the absence of histological activity and to decide about the termination of treatment. If any signs of relapse are found prompt restart of treatment is crucial. The most valuable and simplest parameter of disease exacerbation is increase of aminotransferase level.

Monitoring differ in patients with treatment failure, incomplete response and drug intolerance. Alternative regimens must be considered and they may require monitoring of additional safety parameters.

Long term care for patients with autoimmune hepatitis

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Autoimmune hepatitis (AIH) is chronic, progressive liver disease. The epidemiological surveys from different countries show that the incidence of AIH accounts for 1,5/100 000. Severe liver fibrosis or cirrhosis is present in 10% of subjects at the moment of AIH diagnosis. Despite aggressive steroids and azathioprine therapy within 10 years of the disease 3-5% of patients will require liver transplantation and 4-6% will develop hepatocellular carcinoma. The mortality in AIH subjects is higher than that in the general population. Anti-inflammatory therapy induces AIH remission in majority of subjects however normal liver function tests do net exclude the presence of inflammatory changes in liver tissue and relapses of liver disease after treatment discontinuation are frequent. Childhood presentation of AIH, presence of SLA/LP autoantibodies, liver cirrhosis at presentation and lack of remission or frequent relapses are negative AIH outcome prognostic factors.

For these reasons subjects with AIH should remain under hepatology control. Within the last decade there were 18 hepatology pediatric centers providing the care for AIH patients in Poland and the number of children and adolescents with AIH accounted for 700-800 subjects. 250-300 of them reached the adulthood and were transferred to further hepatology care at adult sites. At the transition half of them had abnormal liver function tests and 3/4 were on anti-inflammatory treatment. These patients should be actively followed up however only 6 adult centers declared the interest in continuation of the therapy of AIH patients who completed the therapy in pediatric hepatology units.

Long term follow up of AIH children who completed at least 6 months course of budesonide and azathioprine therapy

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Introduction: Budesonide in combination with azathioprine was tested as a treatment option in patients with AIH between 2003 and 2009 (BUC-38-AIH).

Purpose: The aim of this study is to present the data of AIH patients switched from budesonide to standard of care treatment.

Material and methods: This is retrospective analysis of 15 patients (M – 3, F – 12) with AIH diagnosed at the age 7-16 (mean ± SD: 11.2 ± 2.8) years who participated in BUC-38-AIH study and received 6-12 months course of combined budesonide and azathioprine therapy. After completion of the study patients continued standard of care AIH treatment for 1.5-6 years (3.5 ± 1.7) until they reached 18-19 years of age and were transferred for further care to adult hepatology clinic. Liver function tests, IgG, gammaglobulin, liver biopsy results and treatment at the final visit at paediatric site were analysed.

Results: Laboratory results elevated at the beginning of budesonide trial were markedly reduced at the end of budesonide treatment and remained stable at the final paediatric visit (ALT 395 ± 387; 61 ± 99 and 49 ± 44 U/l; gamma-globulin 24.6 ± 6.7; 16.1 ± 2.0 and 16.9 ± 6.0 g/l and IgG: 2388 ± 715; 1606 ± 265 and

1642 ± 330 mg/dl). Grading of inflammation in liver biopsy improved from 2.5 ± 0.92 before budesonide treatment to 0.86 ± 0.7 at the end of paediatric observation and staging respectively from 2.0 ± 0.85 to 1.3 ± 1.0. At the final paediatric visit 7 patients continued steroids and azathioprine, 6 patients received azathioprine monotherapy and 2 patients were off medication.

Conclusions: Patients who completed budesonide therapy remained stable until the end of observation in paediatric site.

POSTER PRESENTATIONS

Cirrhosis

[1] Serum ADAMTS-13 as a marker of portal thrombosis in patients with liver cirrhosis

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Introduction: The liver plays a central role in synthesizing of coagulation markers. Coagulopathy in cirrhosis is parallel to reduction of both pro- and anticoagulant agents. ADAMTS13 metalloprotease cleaves von Willebrand factor (VWF), thereby inhibiting platelet aggregation and increasing risk of arterial thrombosis.

Purpose: To evaluate ADAMTS 13 plasma activity in patients with liver cirrhosis and with or without portal thrombosis.

Material and methods: ADAMTS13 plasma activity and other biochemical markers were evaluated in patients (n = 66) with liver cirrhosis with or without portal thrombosis confirmed in ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI). We compared our results to healthy controls (n = 31). All $p < 0.05$ were considered to be statistically significant.

Results: Our patients were divided into two groups with (n = 30) or without (n = 36) portal thrombosis with age 65.9 and 49.4 ($p < 0.05$) respectively. Serum ADAMTS13 was statistically different ($p < 0.05$) for this both groups (lower in patients with portal thrombosis) with no difference for INR (p = 0.92) or PLT (p = 0.72). Serum ADAMTS13 and PLT are statistically different ($p < 0.05$) in comparison to controls. We get very weak positive correlation (r = 0.24) and (r = 0.15) for serum ADAMTS13 and PLT in patients with and without portal thrombosis.

Conclusions: Lower serum ADAMTS13 can indicate the higher risk of portal thrombosis in patients with liver cirrhosis. Platelets count has very weak positive correlation with serum ADAMTS13 but can enhance diagnostic value of this marker in evaluation of risk of portal thrombosis.

[2] Prognostic value of esophageal varices in patients with compensated liver cirrhosis registered in e-HEPAR clinical database

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Introduction: The prognostic classification in compensated cirrhotic patients based on the absence or presence of esophageal varices has been suggested by some authors. The value of Child-Pugh classification for patients with liver cirrhosis is well known but still not satisfactory. Presence of esophageal varices is not included to this score.

Purpose: Evaluation the significance of presence of esophageal varices in Child-Pugh stage A cirrhotic patients.

Material and methods: We analyzed 176 compensated cirrhotic patients, HCV etiology, from our e-HEPAR Database and divided them to two groups: without (n = 68) and with (n = 108) esophageal varices, with median 208 weeks follow up. All values $p < 0.05$ were statistically significant.

Results: At admission the presence of varices was associated with higher total bilirubin ≥ 25 mmol/l, platelets count ≤ 110×10^9 and Child-Pugh A score 6 than 5 points ($p < 0.05$). During follow up the higher incidence of decompensation was observed in patients with varices 44% compare to 26.5% without, respectively ($p < 0.05$). The most common clinical causes of decompensation were ascites 74%, jaundice 72.5% and encephalopathy 27% with domination among patients with varices. Variceal hemorrhage or death due to decompensation of cirrhosis were not observed in any case.

Conclusions: The clinical decompensation occurred significantly more often in patients with compensated liver cirrhosis and varices. The presence of varices has additional prognostic value independently of the clinical and biochemical parameters contained in Child-Pugh score.

Autoimmune liver diseases

[3] Autoimmune hepatitis (AIH) in patients transferred from pediatric to adult hepatology care

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Introduction: Autoimmune hepatitis is chronic liver disease that require long term treatment and follow- up.

Purpose: This is a retrospective analysis of patients with childhood AIH onset who were transferred from pediatric to adult hepatology care. The aim of the study was to assess patient's status at the age of 18 years.

Material and methods: 110 patients (M – 34, F – 76) with AIH diagnosed between 1990 and 2005 at age 6-17 (mean ± SD: 11.7 ± 2.5) who were treated at pediatric center for 1-12 years (6.3 ± 2.5) until adulthood were analyzed.

Results: Marked reduction of mean values of laboratory parameters between disease presentation and last pediatric control were noted: ALT activity from 492 ± 421 to 57 ± 45 U/l, IgG concentration from 3241 ± 1263 to 1468 ± 478 mg/dl, gammaglobulins from 35.3 ± 12.0 to 17.1 ± 4.8 g/l and bilirubin from 3.2 ± 2.8 to 0.7 ± 4.8 mg/dl. However high rate of patients remained with abnormal laboratory results: ALAT – 50%, IgG – 38%, gammaglobulins – 56%. Liver histology (Batts-Ludwig score) improved respectively: grading from 2.7 ± 0.8 to 1.0 ± 0.9 and staging from 2.6 ± 0.9 to 1.8 ± 1.0, but 67% of patients had features of liver inflammation and 91% developed liver fibrosis. At the last control at pediatric site 51% of patients were on combined steroid-azathioprine therapy, 12% were on steroid monotherapy, 14% azathioprine monotherapy and 24% of patients did not receive any immunosuppressive treatment. Eight patients presented portal hypertension and 7 patients had marked osteoporosis.

Conclusions: AIH therapy at pediatric center improved mean values laboratory parameters and histology however the rate of patients with abnormal results remains high and most of patients require treatment.

[4] Autoimmune cholangiopathy as a variant of overlap syndrome with autoimmune hepatitis: case report

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Introduction: Autoimmune cholangiopathy or autoimmune cholangitis, introduced first by Brunner and Klinge, is a chronic inflammation of the liver, diagnosed also as a variant of autoimmune hepatitis or an overlap syndrome AIH/AIC.

Purpose: Aim of the study was to present a case of 15 years old boy with autoimmune liver disease.

Material and methods: The patient was admitted to the hospital at the age of 10 years because of increased ALT and GGTP. Patient had increased IgG and gammaglobulins and was positive for ANA (1 : 160) and SMA (1 : 160). Viral infection (HAV, HBV, HCV, CMV) were excluded as well as Wilson's disease and alfa-1-antytripisin deficiency. Liver biopsy showed marked inflammation and fibrosis (G3/S3) with minimal destruction of bile ducts. Patient received steroids + azathioprine and UDCA therapy with rapid regression of laboratory abnormalities.

Results: After two years of therapy increase of GGTP were observed and the progression of bile duct destruction in liver biopsy despite normal MRI cholangiogram was observed. Patient continued the previous therapy with satisfactory control of ALT activity for the next 2 years and subsequently steroids were discontinued due to failure to thrive. Half a year later patient presented with the flare of ALT and GGTP. Liver biopsy showed further progression of bile duct destruction while MRI cholangiogram remained normal.

Conclusions: Within six years of observation patient has a progression bile duct destruction without presence of MRI abnormalities. We think that this is a case of autoimmune sclerosing cholangitis (ASC) a variant of autoimmune liver disease.

Biliary diseases

[5] Endoscopic retrograde cholangiography in children and adolescents

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Introduction: Retrograde cholangiopancreatography (ERCP) is an advanced endoscopic technique and is rarely performed in children. This study describes the experience in ERCP performed in children with biliary tract diseases.

Material and methods: This is a retrospective analysis of 96 ERCP procedures performed in 56 children at Children's Health Memorial Institute between 2014 and 2015. We analyzed the indication for ERCP, the rate of procedure success and the rate of complication.

Results: Patient's age varied from 1 to 18 years (mean ± SD: 11.7 ± 5.4) and body weight from 8 to 85 kg (39.2 ± 21.3). 6 patients continued the therapy started at the adult endoscopy unit. ERCP was done due to: cholelithiasis (21), cholestasis (13 including 7 with PSC), biliary complication of liver transplantation (10), bile ducts distention (6), hepatic trauma (3), liver hilar tumor (2), multiple liver abscess (1). 25 (24%) of ERCP were done as emergency procedures. Successful caniulation of the bile ducts was achieved in 88 (91.7%) examinations. Sfincterotomy was performed in 48 subjects. 35 biliary stents were removed and 52 biliary stents were implanted. Biliary stones removal procedures (26) and stenosis dilatation (17) were done. Histology samples were taken in two subjects showing sarcoma in one of them. No major complications except one duodenal perforation were noted. Patients were discharged home 2-16 days after ERCP (4.4 ± 2.3).

Conclusions: The success rate (92%) and complication rate (< 5%) of ERCP in presented group of children do not differ from those observed in adult ERCP units.

[6] The significance of portal hypertension in children with biliary atresia

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Introduction: Portal hypertension (PH) is common consequence of progressive liver injury in children with biliary atresia (BA).

Purpose: The aim of the study was to evaluate the significance of PH development in children with BA.

Material and methods: We retrospectively reviewed 390 children with BA who underwent Kasai hepatoportoenterostomy (HPE) between 1984 and 2014. Significan't portal hypertension (SPH) was defined as gastrointestinal bleeding and/or varices of at least I grade and/or gastric varices.

Results: The overall 5 and 10 year actuarial survival with native liver was 38% and 29% respectively. The main indicator of good prognosis was restoration of bile flow with decrease of total bilirubin below 2 mg% within 6 months after HPE. SPH was observed in 171 (43%) patients and in 93 (24%) of them presented with variceal bleeding and mortality of 5% ($n = 20$). An average age at the moment of bleeding was 2.3 years. Development of SPH was not significant for prognosis in the whole cohort, however in patients who survived initial 2 years after HPE without liver transplantation actuarial 10-year surviaval was 70% compared to 41% in patients who developed SPH ($p < 0.001$). There was no correlation between SPH development and degree of liver fibrosis, anatomical pattern of BA, the presence of congenital anomalies or initial outcome of HPE. The only risk factor of SPH development was survival with native liver over 2 years ($p < 0.001$).

Conclusions: The development of portal hypertension is a severe condition worsening prognosis in children with BA living over 2 years after Kasai operation without liver transplantation.

HBV

[7] Combination of serum IP-10 and IL-10 levels helps to differentiate between active and inactive phases of persistent HBV-infection

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Introduction: Chronic hepatitis B (CHB) is a dynamic disease. Differentiation between inactive and active phases of CHB is fundamental for anti-HBV therapy. IP-10 has been suggested as prognostic marker for anti-HBV therapy. IL-10 is major immunomodulatory cytokine. We assessed clinical usefulness of serum IP-10 and IL-10 in CHB with regard to disease activity.

Material and methods: 205 treatment-naïve patients (119 male, median age 37 yo) with persistent HBV-infection were included. In 88 liver biopsy results and in 57 HBV-genotype were available. Patients were categorized as low replicative (LRC), high replicative carriers (HRC), HBeAg-negative hepatitis (ENH) and HBeAg-positive. Serum levels of IP-10 and IL-10 were measured by ELISA, HBsAg by CLIA (Architect, Abbot) and HBV-DNA by PCR (Amplicor, Roche). Control group consisted of 26 HBV-negative individuals.

Results: Serum levels of IP-10 were higher in CHB compared to control group (234.9 vs. 159.3 pg/ml, $p < 0.001$). Both IP-10 and IL-10 showed associations with phase of disease (ANOVA: $p = 0.02$, $p = 0.03$). Serum IP-10 levels were able to distinguish between HRC and ENH (218 vs. 275 pg/ml, $p = 0.008$), while serum IL-10 between LRC and ENH (0.45 vs. 0.93 pg/ml, $p = 0.03$), independently of HBV-genotype. Serum IP-10 correlated with IL-10 ($p = 0.01$), biochemical markers of inflammatory activity ($p < 0.001$) and fibrosis advancement ($p = 0.025$), but not with HBV-DNA nor qHBsAg. IL-10 showed trend towards correlation with HBV-DNA ($p = 0.07$).

Conclusions: Serum IP-10 reflects inflammatory activity, while IL-10 correlates with immune control in persistent HBV-infection. Combination of serum IP-10 and IL-10 helps to discriminate between active and inactive phases of persistent HBV-infection facilitating therapeutic decisions.

[8] Differences in sequences between HBV relaxed circular and covalently closed circular DNA forms

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Serum and liver biopsy samples were collected from 67 chronically infected patients at the same time point for each patient. Genotyping of RCDNA form was done directly after DNA extraction. For the cccDNA analysis samples were treated with the T5 Exonuclease which degrades ssDNA and is able to initiate nucleotide removal from the 5' termini or at gaps and nicks of linear or circular dsDNA. Additionally, the enzyme doesn't degrade supercoiled dsDNA. cccDNA was present in all liver samples and in none serum sample.

After sample preparation, the mass spectrometry analysis was performed to compare RC and cccDNA sequence. For this purpose, HBV mutations associated with drug resistance located in the HBV pol (P) region and mutations located in the HBV basal core promoter/pre-core region (BPC/PC) were included.

The BPC/PC and P sequence of RCDNA extracted from liver and blood samples were different in 38% and 11% of patients, respectively. Differences were also found in sequences between RC and cccDNA forms extracted from the same liver specimen. 60% of these samples have differed in the BPC/PC region and 40% in the pol region. The most frequently found differences were identified at codon 1764 (17%), 1899 (17%), 1762 (14%). The BCP/PC mutations were associated with increased HBeAg negativity, higher alanine aminotransferase level and lower viral load. Up to date, none of the patients from this study group have started antiviral treatment. Therefore, this is unable at this moment to analyze which sequence (cccDNA, RCDNA) is superior to determine the therapy response.

[9] Higher plasma Th17-derived interleukins are associated with immune control of HBV infection

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Introduction: Th17-lymphocytes were shown to drive inflammatory reactions in range of liver diseases. Regulatory T-cells can counteract this effect. It seems that Th17-responses may play a role in maintaining the control of chronic-HBV-infection (CHB).

Purpose: This study aims to assess plasma concentrations of Th17-associated and regulatory interleukins in chronically-HBV-infected patients with regard to the phase of infection.

Material and methods: 62 patients with HBeAg-negative-CHB and 6 with spontaneously-resolved HBV > 20-yr earlier (RES) and 3 with seroconversion during the treatment > 2 yr earlier (CONV) were enrolled. Three patterns of CHB were distinguished: low-replicative-carriers (LRC), e-negative-CHB naïve-to-treatment (ENH) and e-negative-CHB on nucleos(t)ide analogues therapy with complete HBV-DNA suppression > 24 months (SUP). Control group consisted of 16 healthy volunteers. Plasma concentrations of interleukins: 1β, 4, 6, 10, 17A, 17F, 21, 22, 23, 25, 31, INF-γ, sCD40L, TNF-α, TGF-β1, TGF-β2, TGF-β3 were assessed using xMAP-technology (multiplex system Bio-Plex200).

Results: Plasma concentrations of IL-17A, IL-17F, IL-21, IL-22 varied significantly across the studied groups (median test, $p < 0.05$) with the highest median concentration in patients with seroconversion HBsAg/anty-HBs (RES, CONV), moderate in HBsAg(+) patients with immune (LRC) or drug-induced (SUP) control of HBV infection, lower in active ENH and lowest in control group. Plasma concentrations of Th17-regulatory cytokines: IFN-γ, IL-31 and IL-33 differed across studied groups (ANOVA, median test, $p < 0.05$) with similar pattern to Th17-derived cytokines.

Conclusions: The obtained results suggest that HBV may trigger Th17-responses. Moreover, active Th17 stimulation seems to be associated with long-term immune-control of HBV infection.

[10] Longtime assessment of the health status and activity of HBV infection among patients with chronic B hepatitis infected in childhood

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Introduction: Twenty years of universal HBV vaccination of Polish infants led to an almost total elimination of acute and chronic hepatitis B in children and adolescents (1-18 years).

Purpose: To assess the current health status of the former pediatric patients with hepatitis B, treated in childhood with interferon alpha (IFN), lamivudine (3TC) and tenofovir (TDF).

Material and methods: 230 adult patients were invited to consultation (per e-mails, phone calls) and they were offered to perform clinical examination, lab tests, liver ultrasound and elastography. 53 patients (aged 19-34 years, median 22 y.) took part in this study. Infection with HBV was diagnosed at the age 1-15 years and duration of infection was 9-23 years (median: 18 years).

Results: The majority of patients have been consulted by doctors regularly and blood tests are performed properly. Almost 20% of patients does not use any medical care. Following tests were performed: HBV-DNA 22/53 (41.5%); hepatitis B surface antigen (HBsAg) – 27/53 (50.9%), white blood cells (WBCs) and alanine aminotransferase (AlAT) – 35/53(66%). Physical condition and laboratory test results (e.g. prothrombin time, AlAT activity) were good in 51 patients. Elastography of the liver revealed fibrotic changes in almost 35% of patients. One patient was diagnosed with liver cancer at the age 23 years and right lover lobe was removed.

Conclusions: General practitioners should pay more attention to the patients with chronic hepatitis B. Elastography is a good method in predicting the consequences of chronic HBV infection.

[11] Acute hepatitis B revisited

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Introduction: Acute hepatitis B is definitely less frequent in recent years in Poland owing to increasing use of vaccinations, but still occurs.

Purpose: To assess epidemiological characteristics of acute hepatitis B in last six years.

Material and methods: We analyzed epidemiological data of patients with acute hepatitis B hospitalized in our Department in Warsaw.

Results: 53 patients (38 men and 15 women), aged 20-87 years (mean 45 years) were hospitalized in the period 2010-2015 with acute hepatitis B. It represented 0.6 percent of total number of patients. Four patients were treated with lamivudine because of liver failure or immunosuppressive therapy. One patient was treated with tenofovir/emtricitabine because of HIV co-infection. In 19 cases there was anamnesis of hospitalization and/or medical procedures during last 6 months. In 5 cases patients used intravenous drugs. 10 patients (among them 5 MSM) reported risk sexual contacts, in 3 cases with confirmed HBV infection in symptomless partners. In 19 cases route of transmission was unknown – all patients were younger than 50 years, mostly male and sexually active. In younger patients (aged 20-50 years) the most common route of infection was probably sexual, whereas in older group (50-85 years) it was hospitalization, most frequently in internal medicine departments. 94% of all the patients achieved seroconversion to anti-HBs.

Conclusions: Acute hepatitis B is still present in Poland, despite of widespread use of vaccination and promotion of knowledge of disease prevention. Everybody has recommendation for vaccination against hepatitis B, regardless of age and concomitant conditions.

[12] Quality of life in patients infected with hepatitis B virus (HBV) and in healthy population – a comparative analysis

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Introduction: Subjective assessment of health status is an important factor contributing to the quality of life. Patients with hepatitis B are a large group of chronically ill patients in Poland and assessment of their quality of life is useful.

Purpose: To compare the quality of life of patients treated in childhood due to hepatitis B and healthy population.

Material and methods: 56 patients of Department of Pediatric Infectious Diseases in Wroclaw and 56 healthy people were included. We used a standardized questionnaire, the WHO Quality of Life Assessment WHOQOL-Bref. The maximum score was 20 in each area (somatic, psychological, social, environmental).

Results: The study involved 25 women and 31 men with hepatitis B (age 22.1 ± 2.9 years) and 26 women and 30 men in a control group (age 23.0 ± 1.75 years). Subjective perception of general quality of life by HBV-patients was on average 4.3 ± 0.6 vs. 4.2 ± 0.6 in a control group (scale 1-5). Self-assessment of health status was evaluated to 3.8 ± 0.7 vs. 4.0 ± 0.7 in HBV-patients and controls, respectively. There was no significant difference between the groups. Both groups assessed the somatic field as the worst (13.3 ± 1.5 in HBV-patients vs. 13.0 ± 1.8 in controls). The highest level of satisfaction, significantly higher among HBV-patients was observed in the social sphere (16.7 ± 2.5 vs. 15.7 ± 2.7, $p = 0.04$).

Conclusions: Patients chronically infected with hepatitis B virus assess their quality of life as good or even better than healthy controls at similar age. The chronic disease in young people positively affects their relationships connecting them with relatives and friends.

[13] Steatosis and fibrosis in chronic hepatitis-B patients treated with tenofovir: correlation with viral, metabolic and transient elastography with CAP option parameters

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Introduction: Chronic hepatitis B is a common disease entity leading to hepatic cirrhosis and primary liver carcinoma. In the literature on the subject there are not many data concerning liver steatosis in patients with HBV infection; they are often inconsistent and it is difficult to draw conclusions on their basis.

Purpose: The aim of our research was to evaluate the correlation between liver fibrosis and steatosis in chronic hepatitis B patients treated with tenofovir, and total cholesterol levels, LDL, HDL fraction, and levels of triglycerides, viraemia and HBs-antigen.

Material and methods: 45 patients took part in the research, whose treatment had been changed from other nucleotide or nucleoside analogues to tenofovir within the previous year. The levels of lipids in blood serum, viraemia and HBs antigens were assessed.

Results: Correlation tests were performed to evaluate simple dependencies between individual parameters. The Pearson correlation parametric test was used for continuous variables of normal distribution. In the remaining cases, non-parametric tests were performed – the Spearman rank correlation. A statistically significant positive correlation between CAP and LDL, and between CAP and BMI was noted. There was correlation between the level of HBs antigen and LDL.

Conclusions: At the steatosis affects both virologic and metabolic status of the organism.

[14] Antiviral therapy as a part of HCC treatment in HBV-positive patients

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Introduction: Hepatitis B is one of established risk factors of HCC. Antiviral therapy decreases the incidence of HCC and improves survival.

Case description: A 66-year-old male with HBV infection 28 years earlier. In 2014 he presented with cirrhosis. The CT scan July 2015 revealed focal lesions increasing in size, with severity grading. Therapy Baraclude 0.5 mg was started. In August 2015, HCC in biopsy, TACE with doxorubicine. The HBV 12 weeks 149 IU/ml. In December 2015 – AFP 200 ng. The patient was hospitalised in February 2016 due to liver decompensation, he continues treatment. Survival 23 months.

A 71-year-old male with acute hepatitis B in 2005. He was treated with Zeffix between 2005 and 2008 and Baraclude 1 mg since then until his death. Liver disease progressed towards cirrhosis. In July 2015 a 40 mm lesion typical of (HCC) within segements V and VI was observed. The patient ineligible for surgery. 2 liver biopsies – no HCC. In December 2015 liver decompensation. He died in January 2016. Survival 6 months.

A 71-year-old male with HBV-associated cirrhosis. He was treated with Zeffix 100 mg between 2005 and 2008. Zeffix was re-introduced in 2012. The USG performed in 2012 2 lesions within the liver, the CT scan revealed 3 lesions BCLC grade C. The biopsy December 2013 – G1 HCC. The patient was found ineligible for surgery and sorafenib. The Zeffix was continued. The patient died in October 2014. Survival 27 months.

Conclusion: Effective antiviral therapy prolonged the lives of HBV-positive patients with HCC.

HCV

[15] Efficacy of ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin in patients with HCV genotype 1 and 4 infection – final data from the real-world AMBER study

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Introduction: Clinical trials proved that treatment with ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV) is effective and well tolerated. AMBER is a multicentre, open-label, investigator-initiated study conducted to assess the efficacy of OBV/PTV/r ± DSV ± RBV in "real-world" setting.

Material and methods: A total of 209 patients with chronic HCV genotype 1 (mostly 1b) and 4 infection were enrolled in the study; 138 (66.0%) were non-responders to prior therapy, including 84 (40.2%) peginterferon + ribavirin null-responders and 16 patients who failed previous interferon containing triple regimens with boceprevir, telaprevir or daclatasvir. Liver cirrhosis was diagnosed in 119 (56.9%) patients and 56 (26.8%) of them were null-responders. Twenty one (10.0%) patients had a history of liver transplantation and 14 (6.7%) were classified as Child-Pugh B prior to the treatment. The dose of OBV/PTV/r (Viekirax™) was 25 mg/150 mg/100 mg daily, DSV (Exviera™) was 500 mg daily, divided in two doses and RBV was dosed 1000 or 1200 mg/day depending on the patients weight.

Results: 207 of 209 (99.0%) patients achieved SVR12 with rates ranging from 96.4 to 100.0% across subgroups. The only two non-responders were HCV genotype 1b-infected, cirrhotic, null-responders to prior PEG-IFN + RBV therapy: one relapsed after discontinuation at week 2 due to suspicion of hepatotoxicity, and one had a post-treatment relapse despite undetectable HCV RNA at the end of treatment (EOT). Among 204 patients who completed scheduled therapy 2 (1.0%) were HCV RNA positive at EOT but had viral load undetectable at FU12.

Conclusions: OBV/PTV/r ± DSV ± RBV administered in real-world setting demonstrate high efficacy, similar to clinical trials, irrespective of liver fibrosis stage and history of previous treatment.

[16] Safety of ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin in patients with HCV genotype 1 and 4 infection – final data from the real-world AMBER study

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Introduction: Clinical trials proved that treatment of chronic hepatitis C, genotype 1 and 4 infection with ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV) is safe and well tolerated. There is no published real-world data that could confirm this safety profile. AMBER is a multicentre, open-label, investigator-initiated study conducted to investigate OBV/PTV/r ± DSV ± RBV in "real-world" settings.

Material and methods: A total of 209 patients with chronic HCV genotype 1 (mostly 1b) and 4 infection were enrolled in the study. Liver cirrhosis was diagnosed in 119 (56.9%) patients, 21 (10.0%) patients had a history of OLTx and 14 (6.7%) were classified as Child-Pugh B prior to the treatment. Patients received OBV/PTV/r ± DSV and RBV was added in 156 patients (75%) according to current guidelines.

Results: Any adverse events (AEs) were more frequent in patients receiving RBV (77% vs. 58%). The most common AEs were weakness (21%), fatigue (18%), headache (14%), nausea (11%), jaundice (8%) and pruritus (8%). Hepatic decompensation was noted in 7 patients (3%). Patients treated with RBV demostrated more often grade 3/4 hyperbilirubinaemia (18% vs. 0%) and anemia (10% vs. 4%). RBV dose reduction or discontinuation due to anemia occured in 14 (9%) and 7 (4%) patients respectively. Five patients discontinued treatment due to AE (hepatotoxicity, decompensation, diarrhoea, rash, hyperbilirubinemia). Serious AEs were recognized in patients receiving RBV only, that included liver decompensation (3), anemia (2), renal insufficiency (1), hepatotoxicity (1) and diarrhea (1). No death cases were reported.

Conclusions: OBV/PTV/r ± DSV ± RBV administered in real-world settings demonstrate favourable safety profile similar to clinical trial.

[17] Predictors of decompensation during ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin treatment of genotype 1 and 4 HCV infected patients in the real-world AMBER study

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Introduction: Ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV) is not recommended in liver insufficiency.

Purpose: Aim of this analysis was to demonstrate predictors of decompensation among patients in the multicenter real-life AMBER study.

Material and methods: Hepatic decompensation (development of ascites and/or encephalopathy) on OBV/PTV/r ± DSV ± RBV treatment was analysed in 209 genotype 1b (96%) or 4 infected patients, mostly cirrhotics. Decompensation was diagnosed in 7 patients (3.3%) infected with genotype 1b, 6 with cirrhosis and 3 post-transplant.

Results: Ascites developed in 4, encephalopathy in 2 and both in 1 patient. At baseline 3 patients were Child-Pugh class B, MELD ranged from 10 to 17. Decompensation was induced by superinfection in 3 patients and by comedication in 1. All patients remained on treatment, 6 completed therapy and 1 discontinued at week 23. All patients had undetectable HCVRNA at EOT and 6 with available follow-up data achieved SVR. All except one had history of decompensation before treatment. Comparison of baseline factors in patients with and without decompensation revealed significant differences regarding bilirubin (2.4 ± 1.3 vs. 1.1 ± 0.7 mg/dl), INR (1.3 ± 0.2 vs. 1.1 ± 0.2), albumin (3.3 ± 0.4 vs. 4.2 ± 2.6 g/dl), Child-Pugh score (6.9 ± 1.1 vs. 5.3 ± 0.7) and MELD (13.0 ± 2.0 vs. 8.2 ± 2.5). No on-treatment ALT elevations > 2 × ULN were noted despite decompensation. AUROC analysis revealed

discriminating values suggesting on-therapy decompensation for albumins (AUC = 0.88), bilirubin (AUC = 0.84) and INR (AUC = 0.81) with likelihood ratio 5.7 for < 3.6 g/dl, 5.8 for > 1.65 mg/dl and 6.2 for > 1.28 respectively.

Conclusions: Hepatic decompensation on OBV/PTV/r ± DSV ± RBV therapy was related to previous decompensation history and baseline parameters showing hepatic function impairment but not to anti-HCV medications.

[18] Efficacy and safety of ombitasvir/paritaprevir/ritonavir/ dasabuvir ± ribavirin regimen for recurrent genotype 1 HCV infection after liver transplantation – multicenter, real-life, AMBER-CEE study

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Introduction: We evaluated efficacy and safety of ombitasvir/paritaprevir/ritonavir/dasabuvir ± ribavirin (OBV/PTV/r/DSV ± RBV) regimen for recurrent hepatitis C, genotype 1 (G 1), after liver transplantation in the AMBER-CEE – multicenter, real-life cohort study.

Material and methods: This study included 35 liver transplant recipients with HCV recurrence, G 1 (1 b 91%). The cohort was composed of 18 male and 17 female patients with median age of 58 years, fibrosis stage ≥ F2 (77%), non-responders (94%), tacrolims treated (82%). Two patients were experienced to telaprevir (TVR) triple regimen and 31 failed previous therapy with interferon and RBV. All patients but two were scheduled to receive 24 weeks of antiviral treatment, 34 received RBV 600-1200 mg.

Results: HCV RNA was undetectable in 97% of patients (34/35) at the end of treatment, including the patients who prematurely discontinued treatment (between 12-24 of treatment weeks, due to adverse events). Among 33 patients with available week 12 follow-up data, SVR 12 was achieved in 33 (100%), including the only patient with G 1 a and 2 TVR experienced. The most common adverse effects were anemia, fatigue, weakness, headache. Anemia was corrected with ribavirin dose reduction. No deaths, graft losses and episodes of rejection were observed.

Conclusions: This study confirms high virological efficacy of OBV/PTV/r/DSV ± RBV regimen in liver transplant recipients with reccurent G 1 HCV infection irrespective of previous treatment history and advancement of the liver disease. Drug-drug interactions were effectively controlled. Adverse events were infrequent and not life-threatening.

[19] Clearance of HCV core antigen as a predictor of virologic response in HCV genotype 1 and 4 infected patients treated with ombitasvir/ paritaprevir/ritonavir ± dasabuvir ± ribavirin

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Introduction: Interferon based treatment was demonstrated to clear HCV core antigen (HCVAg), but this effect was not stable so measurement of HCVAg was not recommended for management of chronic HCV infection.

Purpose: Aim of the study was to demonstrate effect ofdirect acting antivirals (DAA) on HCVAg levels.

Material and methods: HCVAg and HCV RNA were measured in plasma of 24 patients infected with genotype 1 (22) or 4 (2) and treated with ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV), at the baseline and after 1 day, 7 days, 4 weeks, at the end of treatment (EOT), 12 and 24 weeks after EOT. HCVAg was measured with the ARCHITECT HCVAg using microparticles coated with monoclonal anti-HCV (Abbott Diagnostics Division).

Results: Baseline HCVAg demonstrated significant correlation with HCV RNA ($r = 0.924$) and decreased significantly by 6-108 fold after one day of treatment. Negative or "grey zone" (3-10 fmol/l) HCVAg levels were found before or at the moment of HCV RNA clearancein 20 and 4 patients respectively. The lowest on-treatment HCVAg mean concentration (5.3 ± 2.5 fmol/l) was demonstrated at week 4, but at the EOT it increased to 11.0 ± 4.0 fmol/l and then significantly decreased to 2.5 ± 0.6 fmol/l at week 12 follow-up visit. All patients achieved sustained virologic response, but trace HCVAg was still detected in four patients and in one patient increased to 32 fmol/l.

Conclusions: HCVAg plasma levels declined rapidly during the OBV/PTV/r ± DSV ± RBV therapy and its clearance usually predict virologic response. Presence of low level HCVAg in some patients during the follow-up period need further monitoring for possible virologic relapse.

[20] Ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin had no significant effect on concomitant medication in HCV infected patients treated in the real-world AMBER study

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Introduction: Ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV) regimen is recognized as associated to potential drug-drug interactions (DDI) with concomitant medication. To evaluate DDI risk we analyzed effect of OBV/PTV/r ± DSV ± RBV on decisions made by physicians regarding concomitant medication among patients enrolled to AMBER multicentre, open-label, investigator-initiated "real-world" study.

Material and methods: A total of 209 patients with chronic HCV genotype 1 (mostly 1b) and 4 infection were enrolled in the study. Liver cirrhosis was diagnosed in 119 (56.9%) patients, 21 (10.0%) patients had a history of OLTx and 14 (6.7%) were classified as Child-Pugh B prior to the treatment. Accompanying diseases were present in 145 patients (69%). All patients received OBV/PTV/r ± DSV and RBV was added in 156 patients (75%) according to current guidelines.

Results: Concomitant medications were used by 140 (67.0%) patients, and 33 (15.8%) took at least 5 different drugs during the OBV/PTV/r ± DSV ± RBV treatment. The major therapeutic groups were cardiovascular and antihypertensive medications (used by 62), diuretics (used by 41), gastrointestinal agents (used by 32), immunosuppressants (used by 29), and hypoglycaemics (used by 21). Prior to the initiation of antiviral therapy concomitant medications were discontinued or replaced in 9 (4.3%) patients and modified in 24 (11.5%) in order to avoid DDI; this most frequently pertained to tacrolimus (11 patients), cyclosporine (5 patients), amlodipine (5 patients), and furosemide (3 patients).

Conclusions: In the real-world settings discontinuation or replacement of concomitant medication before the initiation of OBV/PTV/r ± DSV ± RBV therapy is necessary in about 16% patients to prevent DDI.

[21] Efficacy and safety of sofosbuvir/ledipasvir ± ribavirin in the real-world HARVEST study

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Introduction: Sofosbuvir/ledipasvir (SOF/LDV) ± ribavirin (RBV) regimen in HCV infected patients demonstrated good efficacy and safety profile in clinical trials. The aim of this multicenter, investigators initiated study was to evaluate efficacy and safety of SOF/LDV ± RBV regimen in real world.

Material and methods: Treatment was initiated in 86 patients (51 males) in age 20-80 years, 51% PegIFN/RBV experienced, 38% null-responders, 41% cirrhotics, 83% infected with genotype 1b. They were treated for 8-24 weeks (12 weeks in 73%) and 43% received RBV; 8 weeks regimen was provided to F1-F2, treatment naive, genotype 1b infected only.

Results: Sustained virologic response (SVR) was achieved in 80 among 85 patients (94%) available for evaluation after 12 weeks of follow-up (intend to treat SVR rate 93%). Non-responders were cirrhotics, two demonstrated breakthrough and three were relapsers. Nine patients treated for 8 weeks achieved SVR and retrospective analysis of baseline viral load revealed in 8 values > 1 million IU/ml (including one > 6 million IU/ml). The most frequent adverse events were fatigue (29%), headache (17%) and myalgia (7%). Laboratory abnormalities included anemia (6 patients with RBV, 1 without RBV) and hyperbilirubinemia (2 patients with RBV). SOF/LDV was discontinued in two patients, due to adverse event and treatment failure. RBV was stopped in 2 patients due to anemia.

Conclusions: In this real-world study SVR was achieved in at least 93% patients treated with SOF/LDV ± RBV. Eight weeks regimen can be sufficient for treatment naive patients infected with genotype 1b and low hepatic fibrosis. Adverse events were infrequent and mild.

[22] NKP46 and other natural killer cell receptors in HCV-infected patients

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Introduction: NKp46 (CD335) receptor is the specific antigen of NK cells that belongs to NCRs – natural cytotoxicity receptors. NK cells constitute cell subset with cytotoxic potential of innate immune response that constitutes an apparently important role in the course of chronic hepatitis C (CHC).

Purpose: The aim of this study was to search for the correlation between expression (%) and MFI (mean fluorescence intensity) of NKp46 and some other receptors on NK cells of HCV-infected patients and their viral load.

Material and methods: 98 patients, both sexes, aged 20 to 67 years, with documented HCV infection, prior to antiviral therapy entered this study. Their venous blood was evaluated for NKp46, NKG2D, TRAIL and KIR2DL2 in the reaction with anti-NK cell receptors fluorochrome-labeled monoclonal antibodies by means of flow cytometry.

Results: The difference in the limit of statistical significance has been shown for MFI NKp46 between the patients with low and high viral load. NKp46 cell expression correlated with other NK cells antigens: NKG2D (natural killer group 2 D receptor), TRAIL (TNF factor related apoptosis-inducing ligand), KIR2DL2 (killer immunoglobulin-like receptor 2DL2).

Conclusions: Expression of NK cell receptors depends on viral load. The cytotoxic potential of NK cells increases in CHC course. NKp46 receptor stimulation and its correlation with MFI TRAIL, NKG2D and KIR2DL2 may correspond to the induction of death of HCV-infected cells, thereby having an impact on reducing viral load.

[23] High efficacy and safety of ombitasvir/paritaprevir/ritonavir + dasabuvir ± ribavirin treatment in non-responders to previous interferon based triple regimens containing direct acting antivirals, in the real world settings (AMBER-PL/LT study)

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Introduction: Ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r + DSV ± RBV) is still not registered in non-responders to PegIFN based regimens containing the first generation direct acting antivirals (DAA). The aim of this multicenter, international, real-world, investigator initiated study was to confirm efficacy and safety of OBV/PTV/r + DSV ± RBV in this population.

Material and methods: 30 patients (20 males) aged 33 to 70 years, infected with genotype 1 (27 were 1b) from Polish and Lithuanian centers were included. Failure therapy contained telaprevir (15), boceprevir (12), daclatasvir (2) or danoprevir (1). Six patients were null-responders and 12 cirrhotics. Period between the last dose of previous DAA and start of current medication varied from 10 to 280 weeks. Treatment was scheduled for 12 weeks in 28, RBV was administered to 22 patients.

Results: All patients completed therapy and had undetectable HCV RNA at the end of treatment. Twenty two patients with available follow-up evaluation

achieved sustained virologic response. Early response with undetectable HCV RNA was demonstrated in 2 of 14 and in 12 of 16 patients with data available after 1 and 4 weeks of treatment respectively. Improvement of hepatic elasticity was demonstrated in 14 among 18 patients with available elastography before and after treatment. RBV dose was reduced in 4 patients due to anemia, but hemoglobin decline < 10 mg/dl was observed in one patient only. The most frequent adverse events were mild nausea and fatigue.

Conclusions: This real-world study carried-out in non-responders to PegIFN based regimen containing first generation DAA treated with OBV/PTV/r + DSV ± RBV demonstrated 100% efficacy and good safety profile.

[24] Significant improvement of FIB4 and APRI score in cirrhotic patients treated with Viekirax and Exviera

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Introduction: Chronic hepatitis C (CHC) is still a significant clinical problem in healthcare. Non-invasive serum fibrosis markers: APRI and FIB-4 were accepted for estimation of fibrosis in CHC.

Material and methods: 37 CHC patients (18 males, 19 females) were enrolled to the Viekirax plus Exviera therapy accordingly to Polish National Health Service recommendations in Outpatients Clinic, Pomeranian Centre for Infectious Diseases and Tuberculosis in November and December 2015. The change of FIB-4 and APRI score between baseline and week 12 therapy in cirrhotic (24/37) and non-cirrhotic (13/37) subjects was analyzed. Baseline aminotransferases activity, viral load and demographic data were similar in studied groups. Cirrhotic patients have significantly higher bilirubin concentration, lower hemoglobin concentration; PLT and WBC counts. Genotype 1b was detected in 36/37, genotype 4 in 1/37 case. Baseline FIB-4 and APRI scores had significant correlation with liver stiffness (R = 0.71; R = 0.75), moderate with clinical manifestation of liver cirrhosis (R = 0.47; R = 0.40), accordingly.

Results: In one case therapy was stopped after week 8 because of sepsis. A viral load was undetectable in all 20/37 finished therapy patients, in 17/37 HCVRNA is still analyzed. We observed higher reduction of mean APRI and FIB4 score in cirrhotic (3.55 ± 0.64 to 0.85 ± 0.14; and 7.91 ± 1.2 to 3.94 ± 2.06, respectively) than non-cirrhotic patients (0.33 ± 0.02 to 0.21 ± 0.05; and 1.13 ± 0.13 to 1.00 ± 0.4, respectively). Bilirubin increased in all treated patients but significantly ($p = 0.0082$) only in cirrhotic patients (week 4).

Conclusion: Successful antiviral therapy with Viekirax and Exviera associates with significant reduction of APRI and FIB-4 score in cirrhotic and non-cirrhotic CHC patients.

[25] Evaluation laboratory tests of liver function and hepatic elasticity in HCV infected patients cured with all oral directly acting antivirals

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Introduction: Treatment of chronic hepatitis C with all oral directly acting antivirals (DAA) is safe and well tolerated. The most recent real-world studies (AMBER and HARVEST) have shown excellent efficacy and safety of the treatment. We studied changes in the liver function and hepatic elasticity as a surrogate measure of liver fibrosis during and after interferon free, DAA based, regimens.

Material and methods: Thirty four patients with chronic hepatitis C mostly infected (29) with genotype 1b including 59% treatment experienced and 44% cirrhotics were enrolled in the study according to local guidelines. They received either ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OBV/PTV/r ± DSV ± RBV) or ledipasvir/sofosbuvir ± ribavirin (LDV/SOF). Laboratory parameters of value in management of liver diseases (ALT, ALP, INR, Hb, PLT, albumin, AFP, creatinine, bilirubin) and results from shear wave elastography (Aixplorer; SuperSonic Imagine) were analysed before, during the treatment and in 24 weeks of follow-up (FU24) period.

Results: All patients achieved sustained virologic response (SVR). Significant ($p \leq 0.05$) improvement

between baseline and FU24 was demonstrated in mean serum concentrations of albumin (+0,41) and AFP (–10,36), ALT activities (–74,79), Child Pugh score value (–0,38). Mean hepatic elasticity declined from 15.1 ± 2.2 kPa at baseline to 13.6 ± 1.8 kPa at the end of treatment and 11.9 ± 1.3 kPa at FU24 visit. Expression of elasticity in Metavir scoring demonstrated improvement by at least 1 point in 15 patients (44%) and by 2 or 3 points in 9 (26%).

Conclusions: Patients cured from HCV infection demonstrate improvement of liver function and hepatic elasticity during DAA based treatment and in 24 weeks of follow-up period.

[26] Prior hepatitis B virus infection has an impact on sustained virological response in HCV genotype 4 infected patients treated with pegylated interferon alpha and ribavirin

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Introduction: PegIFN/Ribavirin (PR) had been the standard of care in patients infected with HCV genotype 4 until 2014. Nowadays, the new treatment options are available including IFN-containing options. The aim of this study was to assess the efficacy (SVR24) of PR in HCV-4 infected patients. We assessed the predictors of SVR, especially the impact of prior hepatitis B virus infection.

Material and methods: 112 patients (62 males), median age 23 years were treated with PR for 48/72 weeks (107/5). Most of them were treatment-naïve (80.4%) and with fibrosis ≤ 2 (83.1%). In all patients with positive antibodies to the hepatitis B core antigen (anti-HBc), HBsAg and HBV DNA in serum were measured. Only patients with anti-HBc positive, HBsAg negative and undetectable HBV DNA were included into the analysis.

Results: Overall, SVR24 was achieved in 41.1% patients. Null response (NR) was recognized in 24.1%, partial response in 13.4%, relapse in 10.7% and breakthrough in 6.2% patients. SVR24 was associated with no treatment experience, younger age (≤ 39 years), pretreatment viral load ≤ 200 000 IU/ml and more than 10% loss of baseline body weight. The presence of anti-HBc and more advanced fibrosis reduced the probability of achieving SVR24. Anti-HBc positive were detected in 25 patients (22.5%). Four (16%) among those patients achieved SVR24 in comparison to 42 (48.8%) patients with anti-HBc negative ($p < 0.005$); in 10 (40%) of those patients NR has been observed vs. 17 (19.8%) in anti-HBc negative patients.

Conclusions: SVR24 was low. Anti-HBc positive was a negative predictive factor of SVR and correlated with NR.

[27] Alpha-fetoprotein level in patients with chronic hepatitis C (CHC) successfully treated with DAA therapy ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin: preliminary report

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Introduction: Elevated serum alpha-fetoprotein (AFP) levels are not uncommon in patients with chronic hepatitis C even without hepatocellular carcinoma (HCC). High AFP level has been identified as a risk factor for HCC in chronic hepatitis C patients.

Purpose: To evaluate the impact of DAA (ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin) therapy on the serum AFP in patients with CHC.

Material and methods: We assessed the AFP serum concentration before therapy (baseline), at the end of the treatment (EOT) and 12 weeks after treatment (SVR) in 17 patients with CHC genotype 1.

Results: We observed the decline of AFP in most (16/17) patients treated with DAA, with mean baseline – 22.4 ng/ml, EOT – 7.9 ng/ml, SVR – 6.1 ng/ml. There was statistically significant ($p < 0.05$) decline of AFP in patients with baseline AFP level > 10.0 ng/ml, with the

mean values – 37.9 ng/ml, EOT – 12.4 ng/ml, SVR – 8.84 ng/ml. Also ALT serum activity decline was statistically significant ($p < 0.05$) with baseline – 126.5 U/l, EOT – 31.0 U/l, SVR – 32.0 U/l. Decline of liver stiffness in the Fibroscan (kPa) was noticed, but not statistically significant ($p > 0.05$), with mean baseline 24.0, EOT – 18.0, SVR – 20.0. We have confirmed a positive correlation of AFP/ALP and AFP/liver stiffness Fibroscan (kPa) value – $r = 0.66$, $r = 0.53$, respectively.

Conclusions: DAA therapy with ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin reduces serum AFP levels. Significant reduction of serum AFP level after DAA-based therapy in CHC patients may be related to decrease of inflammation and liver fibrosis. The impact of the reduction of the concentration of AFP after successful DAA treatment on the development of HCC requires long-term monitoring.

[28] Predictive values of rapid virological response on sustained virological response in different stages of liver fibrosis in treatment-naïve adult patients with genotype 1 chronic hepatitis C initiated on treatment with pegylated interferon alpha-2a and ribavirin

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Introduction: Results of clinical trials for hepatitis C virus (HCV) patients suggest that both progression of fibrosis and virological response during treatment may be sustained virological response (SVR) predictors. However, the influence of rapid virological response (RVR) on SVR has never been compared in large "real life" population of patients in terms of stage of liver fibrosis.

Material and methods: A total of 172 treatment-naïve patients with chronic HCV genotype 1 infection were enrolled in our local, multi-center, observational study. During 48 weeks of treatment all patients received pegylated interferon in median dosage of 180 mcg per week given subcutaneously and ribavirin in median dosage of 1000 mg per day given orally. The follow-up period was 24 weeks. The primary end point was a predictive value of RVR on SVR by stage of liver fibrosis.

Results: Positive predictive value of RVR on SVR in all subjects was 78.9%; in subjects with liver fibrosis score 1, 2, 3 and 4 was 80.0%, 33.3%, 100% and 100%, respectively; in subjects with liver fibrosis score < 3 and ≥ 3 was 71.4% and 100%, respectively. Of 172 subjects included in the analysis 124 (77.5%) completed study in accordance to the study protocol. There were 644 adverse effects reported – of which 36 were serious.

Conclusions: Results of the study confirmed clinical significance of predictive values of RVR on SVR in patients with HCV genotype 1 and different stages of liver fibrosis with the exception of patients with liver fibrosis score 2.

[29] Chronic HCV infection: histopathology of hepatic changes revisited

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Introduction: Chronic hepatitis caused by HCV is associated with a wide range of liver injury, microscopically expressed by inflammation, fibrosis, intracellular degenerative changes and steatosis.

Purpose: Aim of the study was to examine the mutual relationship between different microscopical changes in the liver, including inflammation, fibrosis and steatosis.

Material and methods: The study group consisted of 176 patients (87 females with mean age 45.2 yrs and 89 males with mean age 45.4 yrs) with chronic hepatitis C, evaluated by liver biopsy and confirmed by HCV RNA RT-PCR.

Results: Inflammatory changes were described as mild in 88.1%, moderate in 10.8% of samples and in 1.1% biopsy did not show any inflammation in the liver. Lymphoid follicles were found in the portal tracts in 29.5% of cases independently from the grade of inflammation ($p = 0.92$). The stage of fibrosis was: none in 10.8%, mild in 74.4%, moderate in 10.2% and severe (cirrhosis) in 4.5% of patients. Steatosis (in most cas-

es mild) was found in 43.7% of patients. Usually large fat droplets were seen in zone 1 near the portal tracts or along fibrous septa. We found positive correlation between steatosis and fibrosis ($p = 0.021$). Our results also showed that inflammatory activity in HCV infection was usually mild and did not correlate neither with fibrosis nor with steatosis.

[30] GT3-HCV – demographic analysis of patients qualified for antiviral therapy

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Purpose: The aim of a study was to evaluate the incidence of the GT3-HCV in patients with chronic hepatitis type C qualified for etiotropic antiviral therapy in The Department of Infectious Diseases, Medical University of Lublin within the period of January 2014 to October 2015, taking into account demographic data.

Material and methods: The study population consisted of 340 patients: 155 males (45.59%) in age of 23-78 and 185 women (54.41%) in age of 25-82, which were divided for four age groups (18-25, 25-45, 46-65, ≥ 65). The incidence of a GT3 was evaluated in each group. The assessment of genotypes was performed with use of Linnear Array Hepatitis C Virus Genotyping Test at Department of Microbiological Diagnostic.

Results: The GT3 was detected in 38 (11.18%) patients. Genotype 3 in 2.94%, GT3a in 7.65% and GT1 and GT3 simultaneous coinfection in 0.59%. Each genotype predominantly in 46-65-years-old group, sex independently. Majority of infections (10.8% from 11.18%) occur between the ages of 26-65 and are predominant in male population with incidence of 14.84% and 8.11% among females.

Conclusion: In our study GT3-HCV infection was detected in more than one in every ten patients qualified for antiviral therapy. The infection is most common between the ages of 26-65, sex independently and concern people in productive age. Furthermore, the efficacy of a treatment based on clinical trials, which, among others, depends on a liver fibrosis stage, response to previous treatment and selection of therapeutic options, varies from 19% to 68%.

Hepatic tumors

[31] Place of transarterial chemoembolization in treatment of primary and secondary liver lesions

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Radical therapy for primary liver tumors may be applied in case of stage 0 or A patients with BCLC. The method of choice is liver resection or transplantation. In stage B or C, and in the case of secondary tumors, palliative treatment should be provided. Advanced tumor stage, general poor condition and liver dysfunction exclude the possibility of liver resection in a large number of patients. An alternative options include: ethanol injection (PEI), radiofrequency (RFA), microwave (MA), laser and cryoablation. Second-line therapy is chemoembolization with drug eluting beads (DEB TACE) or lipiodol (TACE). In BCLC-B stage of HCC, TACE is the treatment of choice. In DEB-TACE microspheres coated/filled with chemotherapeutic agents (doxorubicin or irinotecan) are used for superselctive tumor's capillary bed embolization. The ability for slow drug release, high local concentration and tumor ischemia are the keys to success. The aim of the study was to evaluate the chemeoembolization efficacy, safety and clinical outcome in primary and secondary liver tumor treatment. The study included 34 patients, 5 with HCC and 29 with metastases, mostly CRC. Total of 91 TACEs repeated every 4-6 weeks where done. Efforts to perform 3 procedures in the cycle were made. Outcomes were assessed based on MRI done after cycle. Improvement or disease stabilization was achieved in 26 patients. Progression occurred in 8 cases. TACE was complicated by liver abscess in two cases. TACE for liver primary lesions and metastatic tumors seems to be a safe and effective method to slow down the disease progression.

[32] Surgical treatment of HCC patients 2006-2015 – one center experience

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Introduction: Program of diagnostic, treatment and follow up of patients with hepatic cell carcinoma (or HCC) is conducted in our center since 2006.

Material and methods: In years 2006-2015, 446 patients were diagnosed and treated in our program. HCC was identified in 263 cases (58.9%). Remaining patients had benign tumors or metastases. Identification was based on USG, multiphase CT or NMR. Transcutaneus or laparotomy radio frequency ablation (RFA) was used in 64 cases (24%), and tumor resection was used in 102 cases (38.7%). 50 (19%) patients underwent LTx. 47 patients were primarily disqualified from surgical treatment (17.8%) and were sent to TACE or Nexavar biological treatment. All patients had postoperative radiological check in 3-6 months period, and AFP level control.

Results: Of 64 patients qualified for LTx 10 (15%) had primary HCC resection and 4 (6.25%) – RFA as a bridge therapy. In 103 cases (61.4%) recurrence was found after the operation. In 50 cases (30.1%) underwent secondary surgery. The rest of patients were disqualified from surgical treatment.

Results: The percentage of HCC recurrence maintains on high level – mean recurrence time will be estimated. Program of postoperative follow up with USG, CT or NMR scan is essential. AFP level tendency is useful but not as an independent indicator of tumor recurrence. Nevertheless the use of Milano Criteria, more adequate definition of patient qualifying for liver transplantation (LTx) or bridging HCC – RFA/resection before LTx is a benefit.

[33] Combined cancer and antiviral therapy prolongs patient's life – case report

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Introduction: Primary hepatocellular carcinoma is the 5th most common malignancy in men. Its key risk factors include liver cirrhosis. Treatment efficacy and outcomes are associated with cancer grading.

Case description: A 61-year-old male was found to be HCV-positive in 2013 during a routine check-up. Additionally, a 6 cm liver tumour (confirmed HCC in biopsy January 2015) was shown. The percutaneous alcohol injection to the tumour was administered in March 2014. In July 2014 tumour progression was shown, thermal ablation of the lesion was performed. The patient was referred to Infectious Disease Clinic and diagnosed with HCV-associated cirrhosis, Child-Pugh-A. In November 2014 further tumour progression by 15% was confirmed, 2 satellite lesions and lymph node involvement along the visceral vessels.

In February 2015 the combined treatment with Pegasys 180 mcg and Copegus 1200 mg was started, HCV-RNA 5,596,400 IU/ml. The patient reported flu-like symptoms, without significant abnormalities in follow-up results.

The CT scan June 2015 showed tumour progression (size 11 × 9 cm), with tumour infiltrated the portal vein. While continuing the anti-HCV treatment, the subsequent thermal ablation of lesion the segments V and VI were performed in July 2015, November 2015. The anti-HCV treatment was completed, HCVRNA 4825 IU/ml. The cirrhosis remained as Child-Pugh-A. 3 months later, the disease progressed to Child-Pugh-B and the patient was started on Harvony.

Conclusion: The palliative thermal ablation combined with antiviral treatment prolonged the patient's life.

Liver transplantation

[34] Coronary artery disease risk factors and 10-year risk of cardiovascular mortality in patients after liver transplantation – preliminary report

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Introduction and purpose: In patients after liver transplantation (LTx) the risk of cardiovascular diseases is increased by immunosupresive therapy.

Purpose: The aim of study was to assess the prevalence of risk factors for coronary artery disease (CAD) and to calculate 10-year risk of cardiovascular mortality based on the HeartScore in subjects after LTx.

Material and methods: We analyzed data of 29 patients after LTx (mean age 53.9 ± 10.2 years, 22 M). All individuals underwent clinical examination and lipid profile. To calculate the 10-year risk of cardiovascular death, HeartScore calculator was used, which included age, systolic blood pressure, total cholesterol level, smoking habits. The relative risk of death was compared with the risk acceptable for the age of each person. The frequency of classical risk factors were evaluated. For each subject we calculated atherogenic index.

Results: In 5 (17.2%) patients the calculated HeartScore risk value was consistent with this estimated for age, while in 7 (24.2%) it exceeded this value by 1-10% and in 17 (58.6%) it was lower. The most frequent risk factors were overweight/obesity, lipid disorders and smoking. 48.2% of patients had ≥ 2 coronary risk factor. Mean atherogenic index was low: 2.81 ± 2.5 (0.59-11.84); exceeding the norm in 4 patients.

Conclusions: In the group of examined patients after LTx, almost 25% of the population have had increased 10-year risk of death from cardiovascular causes. More than 48% of studied patients have had ≥ 2 risk factors for CAD. In some of post-LTx patients the intensive control and modification of risk factors is required.

[35] Evaluation of pulmonary function in children with cystic fibrosis (CF) after liver transplantation (LTx)

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Introduction: Pulmonary pathology remains the primary cause of mortality in patients with cystic fibrosis. Liver disease develops in approximately 25% of patients with CF, worsens lung disease and it is an independent risk factor for mortality. In patients with cirrhosis, liver transplantation may exert beneficial effect on pulmonary function.

Purpose: Thus the aim of the study was to assess respiratory capacity in children with CF after LTx.

Material and methods: We performed the retrospective chart reviewed of 15 patients with CF who underwent LTx in our hospital from March 1990 to December 2015. LTX was performed at median age 13.3 years. All children presented with portal hypertension complicated with variceal bleeding in 8 patients. The median PELD and MELD before transplantation was 8 and 12 respectively.

Results: In almost all patients we observed positive influence on nutritional status and overall increase in quality of life. Seven patients before LTx did not have significant pulmonary dysfunction. Before LTx, median FEV_1 was 84.6 FVC was 86 the median FEV_1/FVC ratio 84.51%. In the early post-transplant follow-up median FEV_1 was 87.1, median FVC 88, median FEV_1/FVC 84.12. Two patients were deceased after LTx due to septic complications (2.5 and 16 months after LTx). Currently, median post-transplant follow-up of the remaining patients is 3.3 years and median FEV_1 is 84, median FVC median 102, median FEV_1/FVC median 72.91.

Conclusions: Liver transplantation for CF patients with advanced cirrhosis and mild to moderate pulmo-

nary dysfunction offers encouraging results with possible beneficial effect on lung disease in long-term follow-up.

[36] Evaluation of body composition in terms of cardiovascular risk in patients after liver transplantation

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Introduction: Cardiovascular disease (CVD) are the leading cause of premature death. The diagnosis of CVD risk factors have a significant impact on reducing morbidity and improving the quality of life of patients after liver transplantation (LTx).

Purpose: The aim of the study was to identify metabolic disorders and to determine the prevalence of hypertension among patients after LTx.

Material and methods: The study included 72 patients after LTx treated at the Infant Jesus Teaching Hospital in Warsaw. We use the following research tools: (1) measurement of body composition – the amount of fat in the whole body (FAT%) and abdominal (VISC. FAT%), total body water (TBW), basal metabolic rate (BMR); (2) measurement of the waist circumference (WC); (3) measurement of blood pressure; (4) analysis of the past medical history.

Results: Overweight (BMI 25-29.9) was demonstrated in 40% of patients, obesity (BMI > 30) in 20% of patients. Hypertension was present in 41% of patients. FAT% for women was 29.6 ± 7.9%, for men 22.1 ± 7.7%. Total cholesterol > 190 mg/dl was found in 37% of patients. Statistically significant positive correlation was found between the WC and SBP ($R = 0.454$; $p < 0.001$) and for Hb and BMR ($R = 0.500$; $p < 0.001$) and TBW ($R = 0.500$; $p < 0.001$). The negative correlation was found between FAT% and alkaline phosphatase (ALP) ($R = –0.241$; $p = 0.047$), gamma-glutamylotransferaza (GGTP) ($R = –0.244$; $p = 0.043$) and red blood cell distribution width (RDW) ($R = –0.284$; $p = 0.019$). The negative correlation was found between visc.FAT% and ALP ($R = –0.248$; $p = 0.042$) and RDW ($R = –0.300$; $p = 0.013$).

Conclusions: Evaluation of body composition in patients after LTx is a helpful tool in the diagnosis of CVD risk.

[37] Evaluation of physical activity and energy expenditure in patients after liver transplantation

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Introduction: The healthy life style is crucial for patients after solid organs transplantation, including the adequate physical activity (PA).

Purpose: To evaluate the PA in the group of patients after liver transplantation (LTx).

Material and methods: We evaluated the PA of 27 patients (mean age 53.2 ± 9.2, 19 M) after LTx, using 3-axis accelerometer measuring skin temperature, galvanic skin response, heat flux from the body and movement. These data were processed automatically to calculate total energy expenditure and PA.

Results: The mean measurement time in studied patients was 120:14 (hours:minutes), mean lying duration 47:04, mean sleep duration 36:36. The PA duration was very low, especially at the higher levels. The dominated level of PA was sedentary (0-3 metabolic equivalents, for example sitting, houskeeping; 1 MET = equivalent to 3.5 ml/kg/min of oxygen uptake) – mean time 109:03, moderate PA (3-6 METs, for example walking) took only 10:57 hours, mean time of vigorous PA (6-9 METs, like running, jogging) was only 14 minutes at the time of registration and only in 12 patients. The average metabolic PA was extremely low (1.42 ± 0.24 METs/min). The energy expenditure due to PA at the full-time of registration was low, too.

Conclusions: The PA in the studied group of the patients after LTx was extremely limited. There is the challenge for the medical staff to motivate these patient to increase PA in the prevention of coronary artery disease as it is the drug-free method to modify selected risk factors.

[38] Evaluation of the effectiveness of vitamin D_3 supplementation in children with biliary atresia before liver transplantation

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Introduction: Biliary atresia is the most common cause of the liver transplantation in children (41.95% of transplanted pts in years 1990-2015) and is directly related with fat-soluble vitamin deficiency, including vitamin D_3.

Material and methods: 30 patients diagnosed with biliary atresia were tested for 25OH-D_3 levels in the serum before liver transplantation. All of them were treated with vitamin D (calcifediolum) supplementation before the transplantation with doses suitable to their age and weight.

Results: Only five of patients had optimum level of 25OH-D_3 (over 30 ng/ml), 9 of them had suboptimal levels (20-30 ng/ml), and 11 had levels below recommended (< 20 ng/ml) including 2 patients with extreme low level of the vitamin D_3 – below 10 ng/ml. One patients' result was potentially toxic (110.6 ng/ml).

Results: Presented data indicate how important constant monitoring of 25OH-D_3 levels in the serum and its proper supplementation is in this group of patients and how crucial is to individually adjust dose for every patient. We can also draw a conclusion that gathering and analyzing this data may have a significant impact on creating new recommendations for medical care of patients with biliary atresia waiting for liver transplantation.

[39] Assessment of risk factors for liver fibrosis in the early stages after liver transplantation

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Introduction: The presence of significant fibrosis (METAVIR F ≥ 2) in the transplanted liver after one year poses a substantial risk for transplant failure.

Material and methods: The study included 56 patients one year after liver transplantation (Ltx) who had liver fibrosis (METAVIR F ≥ 2). The control group consisted of 74 patients that had a METAVIR score of F0 and F1 one year after Ltx. Both the biopsy at the time of transplantation and a year after were examined. The endpoint was set as F ≥ 2. The analysis included donor age, gender (donor and recipient), gender mismatch, cold ischemia time (CIT), time to HCV re-infection, acute rejection episodes (AR), biliary and vascular complications.

Results: The multivariate analysis revealed a relationship between fibrosis progression (F ≥ 2) in an AR episode when the recipient received a liver from a donor > 45 years ($p = 0.007$) and when the CIT was > 8 hours in female donor/female recipient combination ($p = 0.005$). The AR episodes with biliary and vascular complications when the donor was > 45 years also demonstrated a correlation to fibrosis progression ($p = 0.02$). Statistically significant differences between the control group and the test group depended on the time to HCV re-infection: up to 6 months, up to a year, and more than a year after Ltx ($p = 0.0001$). No significant statistical differences for the remaining variables were demonstrated.

Conclusions: It is necessary to identify the key donor, recipient and transplantation-related risk factors that influence liver fibrosis progression in order to develop a strategy to prevent transplant failure.

[40] The prevalence of insulin resistance and metabolic syndrome in the liver transplant recipients

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Introduction: Poor diet and lack of exercise are the main environmental factors leading to overweight and obesity. These factors induce insulin resistance (IR) and can be a cause of metabolic syndrome (MS). This increases the risk of atherosclerosis and coronary artery disease. The aim of study was to evaluate the prevalence of IR and MS in patients after liver transplantation.

Material and methods: IR has been calculated using HOMA2 computer model, based on fasting glycaemia and insulin. IR was recognized for cut-off value > 1. MS has been identified based on presence of abdominal obesity (waist circumference > 94 cm for man (M), > 80 cm for woman (F), elevated blood pressure (systolic ≥ 130 mmHg, diastolic ≥ 85 mmHg or treatment), elevated fasting plasma glucose (> 100 mg/dl or treatment), high serum triglycerides (≥ 150 mg/dl or treatment) and low high-density lipoprotein (< 40 mg/dl in M, < 50 mg/dl in F or treatment).

Results: We present data of 30 patients (25 M, mean age 54.8 ± 7.95 years) after LTx. The average waist circumference and glucose concentration exceeded these recommended as normal: 104.79 ± 11.48 cm and 111.4 ± 27.05 mg/dl respectively. The mean values of triglycerides (138.4 ± 64.69 mg/dl), HDL-cholesterol (54.73 ± 17.32 mg/dl) and blood pressure (systolic 127.36 ± 12.2 mmHg, diastolic 78.57 ± 8.26 mmHg) were in normal range. 65% of patients presented insulin resistance (the average IR was 1.2 ± 0.62) and in 76.66% MS was recognized.

Conclusions: We observed the high prevalence of IR and MS. The diagnosis of MS was associated mainly with obesity and lipid disturbances. These patients require comprehensive prevention activities, especially the changes in nutritional habits and the reduction in body weight.

[41] Nutritional status of patients after liver transplantation. Preliminary data

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Introduction: Nutritional status and metabolic parameters are important measurements in the noncommunicable diseases' prevention.

Purpose: To assess nutritional status in patients after liver transplantation (LTx-patients).

Material and methods: Selected anthropometric parameters (bioelectrical impedance using Maltron BioScan 920-II) have been analyzed for 36 LTx-patients (mean age 53.7 ± 9.3 yrs, 27 men) recruited since September 2015. The analysis of correlation between fat percentage vs age and time after LTX has been performed with Spearman's rank correlation coefficient.

Results: No significant gender differences were observed in body mass index (BMI) (x 29.6 ± 4.4 kg/m^2, free fat mass hydration (75.9 ± 2.5%) TSH (x 2.0 ± 1.7 mU/l) and glycemia (x 108.6 ± 26.2 mg/dl). Men and women differed significantly in weight (91.0 ± 13.2 kg vs. 76.1 ± 11.4 kg respectively), waist circumference (106.5 ± 10.4 cm vs. 97.6 ± 8.8 cm respectively), fat mass percentage (FM%) (26.4 ± 8.0% vs. 36.7 ± 7.6% respectively), total body water percentage (TBW) (56.3 ± 6.2% vs. 47.3 ± 5.2% respectively), estimated resting energy expenditure (1883.4 ± 219.4 kcal vs. 1467.0 ± 129.4 kcal respectively) ($p < 0.05$). There was the significant positive correlation between the time after LTx and FM% regardless of patient's age ($r = 0.37$; $p < 0.05$).

Conclusions: The mean BMI of LTx-patients was for overweight. Although the observed anthropometric differences are typical for genders, both men and women had abdominal obesity and were overfat. The longer period after LTx was, the higher FM% was observed.

[42] Kaposi sarcoma in a liver retransplant recipient

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Case history: 65-year old male with alcoholic cirrhosis presented with hepatic focal lesion (size 4.5 cm) which was diagnosed as adenoma and termoablated in 2012. Shortly after two new nodules suspicious for hepatocellular carcinoma were discovered and the patient was listed for liver transplantation (LT). LT was performed in Nov 2013. Four nodules with a cumulative size of 9.5 cm were found in the explanted organ and HCC grade 3 confirmed. Four months later the patient was retransplanted (reLT) due to cholangiopathy in the course of hepatic artery thrombosis. Early post-retransplant period was complicated by a wound infection (*P. mirabilis*), but liver function was normal. A few weeks later the patient developed three papular hyperpigmentous skin lesions – two on the left ankle and one on the left wrist. The smallest papule was cut for the histological examination. Immunohistochemistry was consistent with Kaposi sarcoma (KS): keratin(–), SMA(+), CD31(+), MIB(+), CD30(–), HHV8(+); some of the cells showed spotty nuclear reaction. Meanwhile the patient was treated with doxycyclin due to suspicion of inflammatory angiomatosis, but after Bartonella infection exclusion remaining lesions were removed and immunosuppression modified (steroids tapered, mycophenolate mofetil reduced and tacrolimus through level kept at the lower range). Liver function remains normal. In the follow up of 22 months no new skin lesions appeared.

Conclusions: Skin neoplasms are frequent complications of anti-rejection treatment. Two liver transplants four months apart required intensive immunosuppression and that may explain KS development. Surgical excision together with immusuppression reduction are effective so far.

NAFLD

[43] Th17 cytokines imbalance influences progression of non-alcoholic fatty liver disease

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a chronic progressive disease. It is often coupled with metabolic syndrome affecting over 30% of Polish population. Additionally to metabolic abnormalities, deregulation of immune responses and cytokines is influencing progression to non-alcoholic steatohepatitis (NASH).

Purpose: We aimed to study plasma concentrations of regulatory and Th17-related cytokines in patients with NAFLD and to assess their association with progression to NASH.

Material and methods: 53 patients (22 men, median age 44 yo, median BMI 30) with NAFLD diagnosed by ultrasonography were included. Control group consisted of 13-healthy volunteers (5 men, median age 36 (31-52) yo, median BMI 23.1). Plasma concentrations of 18 cytokines belonging to Th-17, regulatory and proinflammatory families were measured by Bio-Plex™ Cytokine Assay (Bio-Rad).

Results: Plasma levels of several cytokines, TGF-B1 ($p = 0.04$), TGF-B2 ($p = 0.008$), TGF-B3 ($p = 0.04$), IL-10 ($p = 0.04$), IL-21 ($p = 0.03$), IL-31 ($p < 0.001$), IL-33 ($p = 0.015$), sCD40L ($p = 0.009$) and TNF-α ($p < 0.001$) were elevated in NAFLD compared to control group. Thirty subjects (56%) with increased ALT-activity suggesting the diagnosis of NASH had higher total cholesterol, LDL, triglycerides comparing to NAFLD. Interestingly, only Th17 cytokines (IL-22 and IL-25) were higher in NASH-group and correlated with ALT-activity. Furthermore, only IL-21 was associated with fibrosis advancement in NAFLD/NASH by BARD-score (ANOVA $p = 0.02$).

Conclusions: Plasma levels of multiple regulatory, proinflammatory and Th-17 cytokines are elevated in NAFLD underlining cytokine deregulation in pathophysiology of disease. Importantly, TH17-related cytokines IL-22 and IL-25 correlated with ALT-activity and IL-21 with fibrosis advancement suggesting the influence of Th-17 on progression of NAFLD.

[44] Taste and appetite disorders in patients with nonalcoholic fatty liver disease

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Introduction: Non-alcoholic fatty disease (NAFLD) is the most frequent cause of liver injury showing increasing incidence worldwide. While an excessive nutritional supply in NAFLD leading to overweight, obesity and type 2 diabetes is known problem, a potential taste alterations are poorly explored.

Purpose: The aim of this study was to evaluate in NAFLD taste perceptions, including all five savours (sweet, salty, bitter, sour and umami) by analysing taste sensitivity, hedonic perception of taste and food preference.

Material and methods: 46 consecutive NAFLD patients (20 M/26 F, mean age 55.3 ± 8.3 years) with compensated liver disease and age- and sex-matched 101 healthy volunteers were enrolled. The study included gustatory tests (taste recognition threshold, taste intensity with hedonic perception) and analysis of the eating-derived pleasure.

Results: Numerous taste alterations were noted in NAFLD, but the most important were associated with sweet savour. The recognition threshold of sweet taste was increased causing lower intensity of sweet savour perception. Hedonic response to the highest glucose concentration was decreased accompanied by significant decrease of the eating derived pleasure (sweet desserts). Moreover, the pleasure related to the consumption of dumplings and milk disheswas increased. Observed alterations were independent of the severity of liver fibrosis, coexisting diabetes and BMI.

Conclusions: Taste alterations, especially impaired sweet savour recognition and sequential food preference profiles may change dietary habits leading to overweight in NAFLD.

[45] Mean platelet volume in children with nonalcoholic fatty liver disease

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Introduction: There are growing evidences showing that nonalcoholic fatty liver disease (NAFLD) is related to low-grade systemic inflammation, which may plays a role in disease progression. Association between mean platelet volume (MPV)-marker of inflammation and NAFLD has recently been demonstrated in adults. The aim of the study was to evaluate MPV values in children with NAFLD.

Material and methods: The study comprised 110 obese children with suspected liver disease (hepatomegaly and/or increased ALT activity and/or liver steatosis in ultrasound). Viral hepatitis, autoimmune and metabolic liver diseases (Wilson's disease, alfa-1-antitrypsin deficiency, cystic fibrosis) were excluded. Twenty-one healthy children constituted the control group. Liver steatosis was graded in ultrasound (USG) according to Saverymuttu scale. Total intrahepatic lipid content was assessed by magnetic resonance proton spectroscopy (^{1}HMRS). AST to Platelet Ratio Index (APRI) was calculated and used as a noninvasive test for predicting liver fibrosis.

Results: NAFLD was confirmed in 39 children. Patients with NAFLD showed significantly higher values of ALT and GGT activities, ferritin, APRI, insulin resistance (HOMA-IR), BMI, waist circumferences and total amount of lipids in ^{1}HMRS compared to children without NAFLD. MPV median values were not different in NAFLD patients than in other obese children. Moreover, there were no statistical significance between NAFLD patients and healthy controls. However, we found significant correlation between MPV and APRI.

Conclusions: Our study demonstrated that MPV can not differentiate NAFLD among obese children. However, positive correlation between MPV and APRI may reflect the relationship of MPV values and liver fibrosis in children with NAFLD.

[46] Impaired body composition and its relationship to severity of liver fibrosis in patients with non-alcoholic fatty liver disease

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a multiorgan disease associated with overweight/obesity with hypertrophy of mesenteric fat. A potential relationship between body composition and progress of liver fibrosis (LF) was not sufficiently explored.

Purpose: The aim of the study was to evaluate body composition in NAFLD patients at different stages of LF.

Material and methods: 51 consecutive NAFLD patients (mean age 55.6 ± 8.9 years; 30 F; mean BMI 31.7 ± 3.7 kg/m^2) participated in the study. LF was evaluated by transient elastography (TE, cut-off for advanced fibrosis was 10.6 kPa). Anthropometric data were collected and bioimpedance was performed to determine body composition.

Results: The median values of waist circumference, body weight, whole body fat and visceral fat area (VFA) exceeded the upper limit of normal range by 28%, 26%, 112% and 90%, resp., in more than 50% of patients. NAFLD patients presented impaired ratio of the body water in the trunk and edema of the lower limbs. Twenty-eight patients with advanced fibrosis (F3/4) were older ($p < 0.01$) and had greater values of BMI ($p < 0.05$), waist circumference ($p < 0.05$), body fat content ($p < 0.01$) and VFA ($p < 0.05$) in comparison to patients with none-to-moderate fibrosis (F0/F2).

Conclusions: Advanced fibrosis in NAFLD is associated with large abnormalities of body composition, especially regarding total body and visceral fat contents. The evaluation of body components could be useful to predict severity of the liver disease.

Non B-non C hepatotropic viruses

[47] Anti-HAV positivity among blood donors from Wielkopolska region, 2009 and 2015

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Introduction: HAV infection is currently a rare cause of hepatitis in Poland. For susceptible individuals at high risk of severe disease, post-exposure prophylaxis (PEP) with immunoglobulin is recommended in some countries.

Purpose: To investigate anti-HAV prevalence among blood donors (BDs) in two random groups in 2009 and 2015.

Material and methods: We tested 200 healthy BDs aged 19-58 (M – 152, F – 48) who donated blood in 2009 (n = 100) and 2015 (n = 100) for anti-HAV using ABBOTT's (AxSYM and ARCHITECT) diagnostic systems. None of the BDs reported icteric disease in the past. Sera were bought or received from the Regional Blood Center in Poznań and used first as controls in other studies performed in our unit during the same time. Tests were funded by Poznań University of Medical Sciences.

Results: In total, 23 out of 200 BDs (11.5%) were anti-HAV-positive, 12% in 2009 and 11% in 2015. In BDs aged 19-34, HAV seroprevalence was 1.5% (2009) and 0% (2015) ($p > 0.05$) whereas in older participants it was 33.3% and 20.4%, respectively ($p > 0.05$). There was no difference in anti-HAV-positivity between men and women (in overall analysis and separate analyses for 2009 and 2015; $p > 0.05$ for all 3 comparisons). The age of BDs immune to HAV was similar when the 2009 group (43.9 ± 11.5) and the 2015 group (45.4 ± 5.9) were compared ($p > 0.05$).

Conclusions: Wielkopolska Region is clearly an area of very low endemicity for hepatitis A. In case of need for passive PEP of hepatitis A, the use of non-specific immunoglobulin manufactured in Poland could not be effective.

[48] Anti-HEV antibodies among patients from Wielkopolska region in reassessment with the use of another diagnostic test

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Introduction: The first HEV seroprevalence study in Poland was performed in a center in Poznań [Bura *et al*. Postepy Hig Med Dosw 2015]. Anti-HEV IgG antibodies (anti-HEV) were found in 16% out of 182 patients with EIAgen HEV IgG Kit (ADALTIS, Milano, Italy).

Purpose: To investigate HEV seroprevalence with the use of a different commercial assay.

Material and methods: Stored sera from 68 participants of the – above study (M – 40, F – 28) aged 21-81 years (46.4 ± 13.8) were retested for the presence of anti-HEV with Anti-Hepatitis E Virus (HEV) ELISA (IgG) (EUROIMMUN, Medizinische Labordiagnostika AG, Luebeck, Germany); this group included also HIV patients (n = 24, 35.3%).

Results: Anti-HEV were found in 7 patients (10.3%) with EUROIMMUN assay versus 24 patients (35.3%) with ADALTIS kit (p = 0.0005). Both tests were concordant in 49 cases (72.1%), that is in 6 anti-HEV-positive (8.8%) and 43 HEV-seronegative patients. None of the patients with anti-HEV participating in both assays was infected with HIV; all of them have travelled abroad during their lifetimes. Among 19 discordant results, 1 person was only EUROIMMUN-positive and 18 individuals were only ADALTIS-positive.

Conclusions: The choice of a specific anti-HEV test used for hepatitis E seroprevalence study can significantly influence the result. It should be taken into account when planning HEV serosurveys in Poland.

[49] Lack of evidence of HEV infection in a group of kidney-transplant (KTx) recipients from one center in Poland

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Introduction: Hepatitis E is an emerging infection in developed countries. It has some potential for chronicity among immunocompromised patients, including KTx recipients. Despite the fact that no locally acquired acute hepatitis E was diagnosed in Poland, some data suggest that HEV is present also in our country [Bura *et al*., Sadkowska-Todys *et al*., Ślusarczyk *et al*.].

Purpose: To assess KTx recipients from one center in Poznań for ongoing HEV infection.

Material and methods: A group of 45 KTx recipients (M – 33, F – 12) aged 22-67 (44.7 ± 13.1) was assessed for the presence of HEV RNA. The majority of patients were transplanted between October 2012 and February 2015 (in 3 cases KTx was performed in 1997, 2004 and in 2007). They were monitored at Heliodor Swiecicki Clinical Hospital of Poznan University of Medical Sciences (outpatient clinic and Department of Transplantology, General, Vascular and Plastic Surgery) between July 2014 and June 2015. For HEV RNA detection a real-time qPCR analysis in LightCycler 480 Instrument II using TaqMan approach was performed.

Results: The median time from transplantation to HEV RNA testing was 11.4 months. Six patients (all men) were positive for HBV and/or HCV serologic markers: 5 were anti-HBc total/IgG-positive (two of them were also HBsAg-positive) and 2 patients were anti-HCV-positive. The mean ALT level (n = 40) was 28.0 ± 22.2 UI/l (3-104). Only 6 out of 40 KTx recipients (15%) had an elevated ALT. All patients tested negative for HEV RNA.

Conclusions: HEV infection does not seem to be an important problem in KTx recipients in Wielkopolska Region, Poland.

[50] HDV/HBV/HCV coinfection as a diagnostic problem and therapeutic challenge

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Introduction: Coinfection with hepatitis D virus (HDV) in chronic hepatitis B associates with more rapid progression to liver cirrhosis. We present two cases of infection with hepatitis D, B and C viruses. Both male patients were primarily diagnosed as infected with HBV and HCV, HBsAg-positive and anti-HCV-positive.

Case reports: The first patient with HCV replication received 48 weeks of treatment with interferon and ribavirin. Despite of sustained viral response (HCV RNA negative) he developed severe exacerbation of hepatitis with evidence of active HBV replication and rapid progression of necroinflammatory activity and fibrosis in liver biopsy. Treated with lamivudine he achieved undetectable HBV DNA without improvement in aminotransferases activity. The detection of anti-HDV and HDV RNA confirmed infection with HDV. The patient was treated twice with pegylated interferon and a transient, significant reduction of aminotranferases activity was observed. No viral response was achieved. In the USG elastography progression of liver fibrosis to F4 was described.

The second patient, HCV RNA-negative, presented severe chronic hepatitis with low HBV viral load, hemosiderosis. During interferon treatment liver function tests transiently improved. The next therapy with lamivudine was uneffective. Rapid progression of liver fibrosis was observed. After the detection of anti-HDV and HDV RNA the patient received pegylated interferon. A full virological and biochemical response was achieved.

HDV infection should be considered in patients with HBV minireplication, the high activity of aminotransferases and progression of liver disease despite of a good virological response to anti-HBV treatment. Efficacy of interferon in HDV infection is severely limited.

[51] Infectious mononucleosis hepatitis in children – our own observations

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Purpose: Epidemiology and clinical course of hepatitis during infectious mononucleosis in children.

Material and methods: Retrospective analysis of medical records of 145 children hospitalized in 2015 year in Provincial Hospital for Infectious Diseases in Bydgoszcz, diagnosed with infectious mononucleosis was taken. Patient's age and sex, ALT, GGTP and bilirubin levels, prothrombin time, CMV co-infection and abdominal ultrasound were analyzed.

Results: In 2015 145/2055 (7%) children with infectious mononucleosis were hospitalized. EBV hepatitis was identify in 51/145 (35%) cases (34 girls and 17 boys), at the age of 1-18 years (mean 11 years). CMV co-infection was diagnosed in 13/42 (30%) children. The mean ALT level was 176 U/l (range 38-874 U/l). ALT level > 2N was reported in 18/51 (35%) children, > 5N in 12/51 (24%) and > 10N in 6/51 (12%). Increased GGTP level (N: > 60 U/l) was reported in 22/45 (49%) patients, mean 147 U/l (range 8-332 U/l). GGTP level > 2N was observed in 12/22 (55%) patients and > 5N in one. Higher ALT and GGTP levels were observed in females than in males (mean 190 U/l and 91 U/l vs. 146 U/l and 81 U/l, respectively). Increased bilirubin level > 1.0 mg/dl was reported only in one child. No haemostasis dysfunction was observed. Splenomegaly was found in 41/48 (85%) cases and hepatomegaly in 18/48 (37.5%). There were no relationship between coexisting CMV infection and hepatitis severity or splenomegaly and hepatomegaly frequency.

Conclusions: Hepatitis occurs in over 1/3 children with infectious mononucleosis and usually it has mild, self-limiting course.

[52] Acute liver failure non-HAV, non-HBV, non-HCV – should we think about hepatitis E?

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Introduction: Approximately 3 million cases of acute HEV infections are estimated worldwide annually. Clinical course is self-limiting, indistinguishable from acute viral hepatitis of another etiology. Occasionally it may cause acute liver failure (ALF) with significant fatality.

Case report: We present 32-year old male with fulminant hepatitis. He was referred to the Hepatology Department with jaundice and hepatitis. Physical examination showed no abnormality except jaundice. Laboratory findings revealed acute hepatic inflammation (ALT 3300 IU; AST 1500 IU; bilirubin 8 mg/dl) initially without features of liver insufficiency. Viral hepatitis A, B and C were excluded. Imaging examinations excluded hepatosplenomegaly, ascites, portal/hepatic veins thrombosis, neoplasms. In the diagnostic work-up another primary and secondary liver diseases were eliminated. During hospitalization patient's condition deteriorated and he developed ALF. Steroids and albumin dialysis were implemented with clinical and laboratory improvement. Serological markers of acute HEV infection were found. He was dismissed home after 43 days. During further 1.5 months the patient gradually improved. Steroids dosage reduction was continued, but unexpectedly he developed another episode of ALF with very fast progresion to severe encefalopathy and coagulopathy. He was listed to the emergency liver transplantation (OLTx) which was performed on 11th day of hospitalization. After transplantation neurological deficiencies were escalated and suspicion of brain oedema was figured out and confirmed by CT scan. The patient underwent prolonged rehabilitation with intensive treatment. He was discharged home after two months with good liver function and neuropsychiatric abnormalities.

Conclusion: Despite epidemiology HEV must be considered as the etiology of ALF in Poland.

Non-invasive fibrosis evaluation

[53] Advanced steatosis detected by transient elastography may serve as indicator of profound metabolic disorders and atherosclerosis in non-alcoholic fatty liver disease

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide strongly associated with metabolic syndrome and obesity. Controlled attenuation parameter (CAP) evaluated with transient elastography (TE)is an acknowledged method for non-invasive assessment of liver steatosis severity.

Purpose: The aim of the study was to investigate relationships between advanced steatosis and incidence of risk factors for cardiovascular disease.

Material and methods: In 50 consecutive NAFLD patients (age 55.8 ± 11.8 years; 29 F) with fatty liver index (FLI) > 60 and hyperechogenic liver at ultrasound the CAP was measured. The cut-off for advanced steatosis (S2/S3 according to Brunt histological classification) was 301dB/m. CAP, anthropometric and metabolic data, and wide spectrum of laboratory variables including liver function tests were collected. In addition, intima-media thickness was measured in carotid duplex sonography.

Results: CAP data divided NAFLD patients into subpopulations with mild (S1; n = 14, mean 254 ± 74.6 dB/m) and advanced steatosis (S2/S3; n = 36, mean 335 ± 27.7 dB/m). Patients with advanced steatosis showed lower level of HDL-cholesterol (51.6 ± 9.5 vs. 63.8 ± 10.6 mg/dl, $p < 0.001$) and higher HOMA-IR (7 ± 3.6 vs. 4.1 ± 1.8, $p < 0.05$). HOMA-IR ≥ 4.1 predicted advanced steatosis with high accuracy (AUCROC = 0.791; 95% CI: 0.619-0.964). In advanced steatosis the risk of carotid plaque incidence (intima-media thickness > 2 mm) was four-times higher (OR = 4.28; 95% CI: 0.84-22.0).

Conclusions: Advanced steatosis is associated with lower HDL-cholesterol, increased insulin resistance and higher incidence of carotid plaque. In NAFLD patients CAP measurement may identify individuals with increased risk for cardiovascular complications.

[54] Shear wave elastography for evaluation of hepatic stiffness in chronic viral hepatitis B and C

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Introduction: Shear wave elastography (SWE) is a non-invasive, quantitative assessment of liver tissue stiffness corresponding to hepatic fibrosis combined with two dimensional, real time, ultrasound imaging.

Purpose: Aim of the study was analysis of consistence between SWE stiffness and fibrosis in liver biopsy from patients witch chronic B and C hepatitis.

Material and methods: In 99 patients with chronic hepatitis B (n = 33) or C (n = 66) with available recent liver biopsy reports, hepatic stiffness assessment with SWE (Aixplorer, Supersonic Imagine) was carried out. Results were expressed in kPa and transferred to 0-4 score corresponding to stage of liver fibrosis according to manufacturer calibration. If difference between biopsy and SWE score did not exceed ±1, results were recognized as consistent.

Results: Liver stiffness varied from 3.4 to 34.6 (8.9 ± 0.6) kPa and was similar in patients infected with HBV (7.1 ± 0.7 kPa) and HCV (9.8 ± 0.8 kPa). Consistence

between SWE and liver biopsy scores was demonstrated in 27 (82%) and 55 (83%) patients respectively. Stiffness values demonstrated significant positive correlation with a stage of liver fibrosis in biopsy, particularly in HCV infected (r = 0.641). Consistence was 94% (31/33) if SWE was carried out within 24 months of liver biopsy and the only two inconsisten patients were HBV infected, so consistence for HCV reached 100%. Consistence of 77% (51/66) was demonstrated if period between procedures exceeded 24 months.

Conclusions: Liver stiffness measured with SWE showed good consistence with stage of liver fibrosis particularly in HCV infected patients, if the period between procedures did not exceed 24 months.

[55] Prevalence of advanced fibrosis in NAFLD patients – preliminary report from a single center based on transient elastography measurements

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Introduction: Non-alcoholic fatty liver disease (NAFLD) represents a broad spectrum of underlying pathology ranging from steatosis to steatohepatitis with varying degrees of fibrosis. The simple, non-invasive method providing reproducible results is needed to evaluate the basal severity of steatosis and fibrosis and monitor the disease progress.

Purpose: The aim of the study was to estimate the prevalence of advanced fibrosis and steatosis in NAFLD patients using transient elastography (TE).

Material and methods: 50 NAFLD patients (age 55.8 ± 11.8 years; 29 F) diagnosed by fatty liver index (FLI) > 60 and ultrasound hyperechogenic liver. TE using M-probe and XL-probe was performed to measure liver stiffness (LS) and controlled attenuation parameter (CAP) to determine liver steatosis degree. The cut-off for advanced fibrosis (F3/F4) was 10.6 kPa. NAFLD fibrosis score (NFS) was calculated for each patient.

Results: The LS results allowed to split the patients into groups: group 1 (n = 41) with none-to-moderate fibrosis (F0/F2, mean LS: 6.25 ± 1.47 kPa), group 2 (n = 6, 12% of all) with advanced fibrosis (mean LS: 18.9 ± 6.36 kPa).The CAP data divided NAFLD patients into group with mild steatosis (S1 according to Brunt histological classification, n = 14, mean 254 ± 74.6 dB/m) and group with moderate to advanced steatosis (S2/S3, n = 36, mean 335 ± 27.7 dB/m). In 27 patients the XL probe was also used to measure LS and CAP, but obtained results did not change the primary classification. NFS was very useful to predict advanced fibrosis (PPV was 92.9%).

Conclusions: Most of patients with NAFLD have advanced steatosis but only 12% of patients present advanced fibrosis and NFS could be used to select patients to further diagnostics.

[56] Non-invasive assessment of hepatic fibrosis in a series of patients with alpha-1-antitrypsin deficiency

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Introduction: Transient elastography (FibroScan®, FS) has been recently shown to be a valuable method in detection of liver fibrosis in adults with HBV, HCV, non-alcoholic fatty liver disease. The aim of the study was to analyze the evaluation of FibroScan in relation to other non invasive tests of hepatic fibrosis and parameters of liver function in children with portal hypertension due to alpha-1-antitrypsin deficiency (ATD PiZZ) compared to ATD patients without portal hypertension, heterozygotes of ATD and healthy controls.

Material and methods: We investigated 6 children with ATD PiZZ and portal hypertension aged 3.3 (0.8-10.3) y [med (min-max)], 31 asymptomatic PiZZ ATD aged 5.8 (1.5-17.9), 8 heterozygotes in ATD (7 PiMZ and 1 PiSZ) aged 5.3 (0.8-12.3) and 16 healthy controls aged 6.8 (0.4-12.8). Liver function parameters, abdominal ultrasound exam with Doppler and transient elastography were performed in ATD patients. AST/platelet ratio index (APRI), GGTP/platelet ratio

index (GAPRI) and FIB-4 index were calculated in ATD groups.

Results: Increased liver stiffness in elastography was found in the ATD PiZZ group with splenomegaly compared to ATD without splenomegaly ($p = 0.0001$) and in ATD PiZZ with splenomegaly compared to heterozygotes ($p = 0.002$). Both APRI and GAPRI, but not FIB-4 were significantly higher in the ATD group with splenomegaly compared to ATD group without splenomegaly and ATD heterozygotes.

Conclusions: For the first time FibroScan values were assessed in children with liver disease due to alpha-1-antitrypsin deficiency and seem to be clinically useful for predicting liver fibrosis.

Other liver problems

[57] The sensitivity and specificity of diagnostic tests in the diagnosis of Wilson's disease

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Introduction: Commonly used diagnostic tests for Wilson's disease is to determine the concentration of serum ceruloplasmin or copper and copper excretion in the urine collection. The usefulness of these tests in children require evaluation on large groups of patients.

Purpose: The aim of this work was to evaluate the specificity and sensitivity of tests and determination of the optimal cut-off points for a group of children with Wilson's disease.

Material and methods: Retrospective analysis included 162 patients which have been diagnosed with Wilson's disease. 121 patients with high levels of transaminases and/or cholestasis, in which in the course of diagnosis of Wilson's disease has been excluded, were enrolled for the control group. The sensitivity and specificity of diagnostic tests were evaluated in the study population. Then, the optimal cut-off for each of these tests were delineated using ROC analysis.

Results: ROC analysis helped to determine the optimal cut off point of serum ceruloplasmin levels: 0.18 g/l with a sensitivity of 87% and specificity of 80%. ROC analysis indicated the optimal cut-off point of copper excretion in the urine collection with a value of 52 g/24 hours with a sensitivity of 88% and a specificity of 85%. After determining the optimal cut off point of the copper concentration in the serum using ROC analysis (807 μg/l) sensitivity is 90% and specificity 72%.

Conclusions: A verification of the cut-off points for the concentration of serum ceruloplasmin and copper urine collection in the pediatric population seems to be indicated. Evaluation of copper in the serum assay is not very useful because of its low specificity.

[58] Hepatopathy of unknown etiology – is liver biopsy a good tool in differential diagnosis?

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Purpose: To assess the usefulness of liver biopsy in differential diagnosis in patients with liver disease of unknown etiology.

Material and methods: Liver biopsies, stained with H&E, by chromotrope and Gomori method, were analyzed retrospectively. Examination of the inflammatory activity, stage of hepatic fibrosis and steatosis were performed according to Batts-Ludwig and Brunt classifications. In all biopsies the material was representative and both mentioned above scoring systems had been used. In years 2014-2015 259 liver biopsies were performed in our Department. In 28 cases an initial diagnosis was "hepatopathy of unknown origin". 22 patients were female and 6 male, aged 18-65 years (mean 45 years).

Results: Histopathological features revealed: in 5 cases – toxic etiology, in 7 cases – steatohepatitis, in 2 biopsies – only steatosis without inflammation, in 10 patients – autoimmune disease in the form of AIH (4 cases), overlap syndrome (4 cases) and PSC (2 cases). In 3 patients histopathological changes were inconclusive. In 1 case the result was normal liver.

Conclusions: Despite the increasing access to the new, non-invasive methods of the assessment of liver fibrosis, liver biopsy remains an indispensable method in the differential diagnosis of liver diseases.

[59] Hyperandrogenemia in a girl with congenital hepatic fibrosis, portosystemic shunt, splenectomy and partial resection of pancreas

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Introduction: In portosystemic shunts substances absorbed through the intestine flow directly into the systemic circulation, causing delayed clearance of metabolites. Hyperinsulinemia stimulate ovarian and adrenal androgen production.

Case report: We present 14-year-old girl with hyperandrogenemia in a course of congenital hepatic fibrosis and portosystemic shunt. A female born after uneventful gestation was admitted to our Institute at the age of 17 month. She presented hepatosplenomegaly and focal lesion in left hepatic lobe with normal liver function and AFP. Liver biopsy at the age of 2 years revealed micoscopical features of periportal fibrosis with the presence of ductal changes typical for congenital fibrosis. Gastroscopy did not show esophageal varices. In a course of further observation the signs of portal hypertension increased. She undergone several variceral ligations. At the age of 5 the lesion in hepatic lobe showed typical signs of focal nodular hyperplasia. Six year later a tumor of pancreas was diagnosed. She was qualified to splenectomy, partial resection of pancreas (Gruber Frantz tumor) and resection of hepatic lesion. After surgery increasing virilization was noted. The patient presented deep voice, clitoromegaly, severe acne and hirsutism. Few month later menarche appeared. Laboratory data revealed: high concentration of testosterone (2405 pg/ml; N < 950 pg/ml). Adrenal tumors, congenital adrenal hyperplasia late onset and hormonally active ovarian tumors were excluded. Glucose intolerance with hiperinsulinism and insulin resistance were diagnosed.

Conclusions: In portosystemic shunts hyperinsulinemia may cause hyperandrogenemia in a mechanism similar to polycystic ovary syndrome.

[60] Focal nodular hyperplasia in children

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Focal nodular hyperplasia (FNH) is a benign lesion of the liver. Until recently, it was thought to be an adult problem, exclusively. About 200 cases of FNH in pediatric population have been reported in the literature. Although, the pathogenesis of FNH still remains unclear, there is more frequent occurrence of FNH in children with a history of malignancy treated with chemo- or radiotherapy and in children who underwent hematopoietic stem cell transplantation. The clinical features of pediatric FNH are variable and can be non-specific. FNH might be difficult to diagnose and differentiate from malignant hepatic lesions on the basis of imaging procedures. Liver biopsy is an adequate diagnostic procedure in these cases.

Authors presented two different cases of diagnostic difficulties in diagnosis of FNH in children. The first child underwent chemotherapy and bone marrow allotransplantation due to non-Hodgkin lymphoma and FNH was diagnosed incidentally a few years later. In the second child a diagnosis of FNH was established in the course of differential diagnosis of abdominal pain.

[61] 15-year-old boy with osteogenesis imperfecta and Wilson's disease – a case report

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Wilson's disease is a rare autosomal recessive inherited disorder of copper metabolism. Although the disease's main involvement is liver and brain, some studies revealed manifestation of various skeletal problems

such as demineralization, rickets, osteomalacia, osteoporosis and spontaneous fractures. Osteogenesis imperfecta is a group of genetic disorders characterized by bone fragility and connective tissue manifestations.

We present a case report of 15-year-old boy with osteogenesis imperfecta (OI) diagnosed at the age of 3 months. During the course of the disease he presented many fractures of the lower limbs and one of the upper. Molecular tests have never been performed, however based on clinical data and family history OI type III was suspected. The routine laboratory tests revealed elevation of aminotransferases (AspAT 70 U/l, AlAT 42 U/l), GGTP (226 U/l), coagulation disorders (INR 1.56) and low albumin level (29 g/l). Ultrasound showed hepatosplenomegaly. He was referred to our institution with liver cirrhosis for further investigation. Infectious and autoimmunological causes were excluded. Based on decreased ceruloplasmin serum level (0.1 g/l) and increased urine copper excretion (206 μg/24 h) Wilson disease was diagnosed, which was finally confirmed by molecular tests (two H1069Q mutations). Gastroscopy showed esophageal varices. Liver biopsy was not performed because of coagulation disorders and varices banding. Penicillamine therapy was started with improvement of liver tests.

Conclusions: This case report is an example of comorbidities of two rare genetic entities. Various skeletal manifestations were described in Wilson disease and sometimes may be the first clinical symptom of the disease.

[62] Congenital hepatic fibrosis in a 9-year-old girl – a case report

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Introduction: Congenital hepatic fibrosis (CHF) is a rare autosomal recessive fibropolycystic disease associated with proliferation of interlobular bile ducts and periportal fibrosis leading to a portal hypertension. CHF usually presents itself in adolescent or young adulthood. Main clinical manifestations of CHF includes hepatosplenomegaly, portal hypertension, recurrent cholangitis and renal lesions.

Case report: We report a case of a 9-year-old girl hospitalized of asymptomatic splenomegaly, leucopenia and low plates with preserved liver function. Computed tomography imaging excluded prehepatic flow block and revealed presence of portosystemic collateral vessels. There were no lesions in kidneys confirmed in imaging tests. Endoscopic examination detected a features of portal hypertension: initial esophageal varices and portal hypertensive gastropathy. Histopathological examination of the liver biopsy showed features of early phase of hepatoportal sclerosis without cirrhosis and biliary changes. Currently, the patient requires systematic endoscopic monitoring of the portal hypertension progress and prevention of varices bleeding.

Conclusions: CHF is a liver disease which may occur in children and cause diagnostic difficulties especially in asymptomatic patients. There is no specific therapy of CHF. Treatment included: prevention of the variceal hemorrhage with pharmacotherapy or endoscopic variceal ligation, surgical methods with partial splenic artery embolization, splenectomy or transjugular intrahepatic portosystemic shunts and also prophylaxis and therapy of cholangitis.

[63] Congestive hepatopathy in 67-year old female patient – a case report

Elżbieta Zając

NZOZ „Telmed" w Rytrze

Introduction: Cardiac failure affects the liver – chronic and acute heart failure can lead to congestive hepatopathy and cardiogenic ischemic hepatitis. These conditions may impair liver function and treatment should be directed towards the primary heart disease.

Case report: I present a case of congestive hepatopathy in 67-year old female patient with untreated hypertension, after cholecystectomy, who was reffered from General Practitioner, due to moderate elevations of the biochemical parameters of liver function (AST, ALT, GGT, bilirubin), hepatomegaly, moderate peripheral oedema and mild right upper quadrant pain. Liver ultrasound showed hepatomegaly with a homogeneous increase in echogenicity throughout the liver and dilation of the suprahepatic veins and inferior vena cava. There was no clinically visible jaundice, splenomegaly and ascites. Echocardiography showed impaired diastolic function and reduced ejection fraction. Treatment with torasemide (10 mg/day), ramipril (5 mg/day), metoprolol (43.7 mg/day) showed improvement of biochemical, clinical and ultrasound findings.

Conclusions: Understanding the mutual relationship between the liver and the heart is important for both hepatologists and cardiologists. Collaboration between theese two specialities is crutial in these categories of patients for better diagnosis, treatment and prognosis.

[64] The symptoms reported by patients with end stage liver disease

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Introduction: Palliative care, focusing on symptomatic treatment, is widely available for patients with cancer or HIV/AIDS. Symptoms with which patients in the End-Stage Liver Disease (ESLD) struggle, significantly affects the quality of life and require monitoring. In spite of aggravation, they differ in terms of quality from those suffered by oncological patients. The fact that caring for such patients is not included in medical personnel training stems i.a. from lack of a described profile of the most common symptoms of ESLD.

Purpose: Prepare a list of the most common conditions reported by ESLD patients in relation to cirrhosis in the course of viral hepatitis.

Material and methods: The studied population were a group of patients with viral hepatitis and at least one incident of cirrhosis decompensation. Patients were asked a series of open- and close-ended questions. The aim of open-ended questions was to prepare a list of symptoms that were later codified by the authors. Close-ended questions specified the presence of typical symptoms. For the purposes of assessment of aggravation of the conditions, the authors have adopted the Likert scale.

Results: The symptoms the authors have collected were related to physical, mental and spiritual conditions. Physical symptoms included pruritus, discomfort, pain, dyspnoea. Among mental symptoms the authors noted apathy, passiveness, annoyance, fatigue. The spiritual sphere included fear, sense of isolation, insecurity.

Conclusions: The symptoms described above, suffered by ELSD patients, require a global plan of actions including physical, mental, and spiritual domain.