XIX Conference of the Polish Association for the Study of the Liver

1-3 June 2017
Mikołajki

Programme and abstracts

Programme of events

1 June, Thursday	
15.00–15.10	**INAUGURATION OF THE CONFERENCE** Piotr Małkowski, Wojciech Lisik
15.10–15.20	**Report on past year's activities** Piotr Małkowski, Wojciech Lisik
15.20–15.30	**Presentation of awards for the best abstracts submitted for the conference** Piotr Małkowski
15.30–16.20	**INAUGURATION SESSION** **Chairs of the session:** Jacek Juszczyk, Piotr Małkowski, Robert Flisiak
	DAA treatment before or after liver transplantation in HCV recipients with and without HCC Patrizia Burra
	Liver fibrosis and steatosis measurement in the management of liver disease Jose Luis Calleja
16.20–17.45	**1st PLENARY SESSION** **Current problems associated with HCV infection therapy** **Chairs of the session:** Robert Flisiak, Waldemar Halota, Iwona Mozer-Lisewska
16.20–16.35	Management of DAA failures Robert Flisiak
16.35–16.50	HBV reactivation during direct acting antivirals treatment for hepatitis C Krzysztof Tomasiewicz
16.50–17.05	When should interferon-free therapy be stopped? Waldemar Halota
17.05–17.20	HCC in the context of HCV therapy Anna Piekarska
17.20–17.30	*Delivery of paper sent in for presentation:* Treatment of HCV infection in Poland in 2016, an interim analysis of EpiTer-2 study Robert Flisiak, Ewa Janczewska, Dorota Zarębska-Michaluk, Agnieszka Staniaszek, Włodzimierz Mazur, Dorota Dybowska, Agnieszka Czauż-Andrzejuk, Hanna Berak, Jerzy Jaroszewicz, Łukasz Socha, Iwona Orłowska, Magdalena Tudrujek, Łukasz Laurans, Jolanta Białko
17.30–17.40	*Delivery of paper sent in for presentation:* Two years follow-up after treatment with Ombitasvir/Paritaprevir/Ritonavir ± Dasabuvir ± Ribavirin, an interim analysis of CE-long study following the AMBER study Robert Flisiak, Mariusz Łucejko, Dorota Zarębska-Michaluk, Anna Piekarska
17.40–17.45	**Discussion**
17.45–18.10	**Coffee break**
18.10–19.25	**2nd PLENARY SESSION** **Hepatic lesions** **Chairs of the session:** Piotr Małkowski, Wojciech Lisik, Wiesław Kryczka
18.10–18.25	30 years of hepatic transplantation in Geneva Marek Bednarkiewicz
18.25–18.40	Adenomas and other benign lesions: to operate or not to operate? Waldemar Patkowski
18.40–18.55	Laparoscopic resection of liver tumours Andrzej Budzyński
18.55–19.10	Cancer after liver transplantation Marek Pacholczyk
19.10–19.20	*Delivery of paper sent in for presentation:* Evolution of indications for liver transplantation at the Infant Jesus Hospital in Warsaw in 2000-2017 Beata Łągiewska, Marek Pacholczyk, Olga Tronina, Krzysztof Jankowski, Dariusz Wasiak, Wojciech Lisik, Agnieszka Jóźwik, Maciej Kosieradzki
19.20–19.25	**Discussion**
20.00	**Dinner and concert of the FEEL music group**

2 June, Friday	
8.00–9.40	**3rd PLENARY SESSION** **Liver diseases associated with cholestasis** **Chairs of the session:** Marek Woynarowski, Ewa Janczewska, Piotr Kaliciński
8.00–8.20	Congenital dilatation of the bile duct Naomi Iwai
8.20–8.40	New cholestatic disorders in childhood Irena Jankowska
8.40–9.00	PSC-associated diseases – role of the surgeon Wiesław Tarnowski
9.00–9.20	PSC in children Małgorzata Woźniak
9.20–9.30	*Delivery of paper sent in for presentation:* Common variant p.D19H of the hepatobiliary sterol transporter ABCG5/8 affects cholesterol homeostasis in children with gallstones Marcin Krawczyk, Olga Niewiadomska, Irena Jankowska, Krzysztof Jankowski, Zbigiew Kułaga, Jolanta Gozdowska, Dariusz Lebensztejn, Sabina Wiecek, Dieter Lütjohann, Frank Lammert, Piotr Socha
9.30–9.40	**Discussion**
9.40–10.40	**1st SPONSORED SESSION – ABBVIE** **Viekirax & Exviera – optimum therapy for the Polish patient** **Chairs of the session:** Robert Flisiak, Waldemar Halota
9.40–10.10	Therapy of HCV infections in Polish patients with severe concomitant diseases Robert Flisiak
10.10–10.40	HCV Real Life study – The Spanish Model Jose Luis Calleja
10.40–11.00	**Break**
11.00–12.30	**4th PLENARY SESSION** **Fatty liver disease. Role of microbiota in liver diseases** **Chairs of the session:** Michał Kukla, Krzysztof Tomasiewicz, Marek Woynarowski
11.00–11.15	Role of gut microbiota in pathogenesis of nonalcoholic fatty liver disease and insulin resistance Michał Kukla
11.15–11.30	Microbiome in liver cirrhosis Anatol Panasiuk
11.30–11.45	Novel therapeutic options in non-alcoholic steatohepatitis (NASH) Krzysztof Tomasiewicz
11.45–12.00	Noninvasive assessment of fibrosis and steatosis Piotr Socha
12.00–12.15	Endocrine disorders in fatty liver disease Agnieszka Zwolak
12.15–12.22	*Delivery of paper sent in for presentation:* Hepatic fibroblast growth factor-21 and omentin-1 levels in morbidly obese patients with non-alcoholic fatty liver disease Michał Kukla, Marek Waluga, Michał Żorniak, Maciej Kajor, Łukasz Liszka, Michał Dyaczyński, Grzegorz Kowalski, Dominika Żądło, Rafał J. Bułdak, Marek Hartleb
12.22–12.30	**Discussion**
12.30–13.30	**2nd SPONSORED SESSION – BMS** **Hepatocellular carcinoma from an interdisciplinary perspective**
	Surgeon – Piotr Małkowski
	Infectious disease specialist – Jerzy Jaroszewicz
	Oncologist – Lucjan Wyrwicz
13.30–14.30	**Lunch**

2 June, Friday	
14.30–16.00	**3rd SPONSORED SESSION – GILEAD** **Clinician's toolbox** **Chairs of the session:** Anna Piekarska, Krzysztof Tomasiewicz
14.30–14.50	What we know about sofosbuvir-based therapies after treating over a million patients Tarik Asselah
14.50–15.05	Strategies for managing therapy in patients co-infected with hepatotropic viruses Jerzy Jaroszewicz
15.05–15.15	Treatment of hepatitis C after liver transplantation – presentation of own study results Michał Ciszek
15.15–15.30	HCC in the era of DAA Piotr Małkowski
15.30–15.45	Drug interactions – or how to fit the drug to the patient profile Łukasz Łapiński
15.45–16.00	**Discussion** Anna Piekarska, Krzysztof Tomasiewicz, Tarik Asselah, Jerzy Jaroszewicz, Michał Ciszek, Piotr Małkowski
16.00–17.10	**5th PLENARY SESSION** **Practical aspects in the diagnostics and treatment of HBV infections** **Chairs of the session:** Jerzy Jaroszewicz, Małgorzata Pawłowska, Andrzej Horban
16.00–16.15	Detection of hepatitis B virus infections in blood donors in Poland in 2005–2015 Aneta Kopacz, Piotr Grabarczyk; Polska Grupa ds. Badań Czynników Zakaźnych u Dawców Krwi w Centrach Krwiodawstwa i Krwiolecznictwa
16.15–16.30	Prevention of HBV reactivation in patients receiving immunosuppressive treatment – National Health Fund programme vs. real-life needs Małgorzata Pawłowska
16.30–16.45	Hepatitis B vaccinations – are boosting doses necessary? Jerzy Jaroszewicz
16.45–17.00	Current trends in the prevention of HBV infection in the transplanted liver Wojciech Lisik
17.00–17.10	*Delivery of paper sent in for presentation*: Activity of chronic HBV infection related to Th17/Treg imbalance Anna Parfieniuk-Kowerda, Andrzej Eljaszewicz, Kamil Grubczak, Magdalena Świderska, Magdalena Maciaszek, Agnieszka Czauż-Andrzejuk, Jerzy Jaroszewicz, Marcin Moniuszko, Robert Flisiak
17.10–17.25	**Coffee break**
17.25–19.05	**6th PLENARY SESSION** **Clinical problems in patients with hepatic failure** **Chairs of the session:** Anna Boroń-Kaczmarska, Joanna Jabłońska, Jacek Rózga
17.25–17.40	Hepatorenal syndrome Magdalena Durlik
17.40–17.55	Hepatic encephalopathy Anatol Panasiuk
17.55–18.10	Albumin dialysis – a therapeutic option or bridge to liver transplantation? Jacek Rózga
18.10–18.25	Pregnancy in patients after LTx Bronisława Pietrzak
18.25–18.40	Drug-induced hepatic injury Joanna Jabłońska
18.40–18.55	Hemostatic abnormalities during surgery in patients with liver disease Janusz Trzebicki

2 June, Friday	
18.55–19.05	*Delivery of paper sent in for presentation:* Serum brain-derived neurotrophic factor is decreased in patients with liver cirrhosis and minimal hepatic encephalopaty Jerzy Jaroszewicz, Agnieszka Stawicka, Magdalena Świderska, Justyna Zbrzezniak, Natalia Kilisinska, Aleksandra Swiderska, Anna Parfieniuk-Kowerda, Robert Flisiak
20.00	**Dinner and artistic show**

3 June, Saturday	
8.30–10.00	**PRESENTATION OF THE MOST INTERESTING AND CHALLENGING CASES – INTERACTIVE SESSION** **Chairs of the session:** Ewa Janczewska, Marta Wawrzynowicz-Syczewska, Piotr Socha
	Presentation of six case studies: Marta Wawrzynowicz-Syczewska, Michał Kukla, Dariusz Wasiak, Magdalena Naorniakowska, Anna Piekarska, Piotr Stalke
10.00–10.30	**4th SPONSORED SESSION – MSD**
10.30–11.30	**7th PLENARY SESSION** **VARIA I** **Chairs of the session:** Krzysztof Tomasiewicz, Wojciech Lisik, Piotr Małkowski
10.30–10.50	Abdominal vein thrombosis from the haematologist's perspective Jerzy Windyga
10.50–11.10	Lecture – VALEANT
11.10–11.30	Lecture – ROCHE Therapy of HCV genotype 3 infections in Polish clinical practice Robert Flisiak
11.30–12.40	**8th PLENARY SESSION** **VARIA II** **Chairs of the session:** Bożena Walewska-Zielecka, Marta Wawrzynowicz-Syczewska, Irena Jankowska
11.30–11.45	Liver diseases according to registers available at Polish Ministry of Health Barbara Więckowska, Marek Woynarowski
11.45–12.00	Standard therapy resistant autoimmune hepatitis – alternative treatments Marta Wawrzynowicz-Syczewska
12.00–12.15	The role of endoscopy in liver diseases Marek Woynarowski
12.15–12.30	Treatment outcomes in children with biliary atresia Piotr Kaliciński
12.30–12.40	*Delivery of paper sent in for presentation*: Molecular characterization of novel variants for improved diagnosis in children having Wilson disease Friedrich Bernick, Magdalena Naorniakowska, Sarah Guttmann, Sara Reinartz Groba, Andree Zibert, Hartmut Schmidt, Wojciech Jańczyk
12.40	**CLOSURE OF THE CONFERENCE**

ORAL PRESENTATIONS

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

PLENARY SESSION 1
Current problems associated with HCV infection therapy

Management of DAA failures

Robert Flisiak

Klinika Chorób Zakaźnych i Hepatologii, Uniwersytet Medyczny w Białymstoku

Despite of high efficacy of HCV therapy, there are still 3% patients in Poland (among 1070 registered in the EpiTer-2 database by 15-04-2017), who failed treatment containing direct acting antivirals (DAA). According to the most recent EASL and PGE HCV recommendations HCV resistance testing is not adviced before retreatment of such a patients. At the moment of abstract submission there were 25 GT1b and 6 GT3 infected patients who failed DAA containing regimens identified in EpiTer-2 database. All GT1b infected except 2 cases were treated with regimens containing NS5A inhibitors (OBV/PTV/r + DSV, SOF/LDV or ASV + DCV). According to EASL such a patients should be retreated with OBV/PTV/r + DSV, GZR/EBR or DCV + SMV with addition of SOF and RBV for 12 (F0-F2) or 24 (F3-F4) weeks. For cirrhotics PGE HCV recommend the same regimens, which are not reimbursed in Poland, but for F0-F3 we suggest waiting for more potent new therapeutic options. GT3 infected failures from the EpiTer-2 database were treated with SOF + PegIFN + RBV (n = 4) or SOF + RBV (n = 2) and according to EASL and PGE HCV they should receive SOF/VEL which unfortunately is not reimbursed right now, so the only option could be pre-registration access for SOF/VEL or GLE/PIB. Another option recommended by EASL could be SOF + DCV + RBV, which is also not available for Polish patients.

Concluding, due to 3% failure rate there is a need to broaden NFZ therapeutic program with addition of SOF to OBV/PTV/r + DSV + RBV or GZR/EBR for GT1 infected and to provide reimbursement of SOF/VEL (already registered in EU) for at least GT3 infected.

HBV reactivation during direct acting antivirals treatment for hepatitis C

Krzysztof Tomasiewicz

Katedra i Klinika Chorób Zakaźnych, Uniwersytet Medyczny w Lublinie

Patients infected with hepatitis C virus (HCV) who are co-infected with hepatitis B virus (HBV) may be at risk for reactivation of HBV infection. It may occur both during and following HCV treatment. Main risk is thought to be of importance for those who are hepatitis B surface antigen (HBsAg) positive but there are suggestions for possible reactivation in patients who are hepatitis B surface antibody (anti-HBsAb) negative, but hepatitis B core antibody (anti-HBc) positive. Recent analyses have shown that risk for the second scenario is minimal.

So far there are few reports about fatal HBV reactivation following DDAs use in HCV patients, but virologic reactivations were seen in considerable percentage of patients with no or little clinical and biochemical consequences. When compared to PEG-IFN plus RBV treatment HBV reactivation occurred earlier (mostly during therapy) and led to clinical consequences in higher percentage of patients (12% vs. 0%).

It is highly recommended that all patients have to be screened for HBsAg (obligatory) and anti-HBc (suggested) prior to HCV therapy. If HBsAg positive the level of HBV-DNA is essential for therapeutic decisions. Providers must also monitor patients on DAAs for signs of HBV reactivation with liver enzyme and, if necessary, with HBV-DNA level. HBV reactivation may be successfully treated with nucleos(t)ide analogues, that should be started immediately.

HCC in the context of HCV therapy

Anna Piekarska

Klinika Chorób Zakaźnych i Hepatologii, Uniwersytet Medyczny w Łodzi

Introduction: The long-term clinical outcomes of antiviral therapy for patients with chronic hepatitis C seems to be uncertain in context of hepatitis C virus (HCV)-related hepatocellular carcinoma occurrence or recurrence after the antiviral DAA-therapy.

Aim of the study: This study aimed to assess the impact of antiviral treatment on the development of HCC and mortality in patients with chronic HCV infection.

Material and methods: A systematic review was conducted for studies that evaluated the antiviral efficacy for patients with chronic hepatitis C or assessed the development of HCC or mortality between SVR (sustained virologic response) and non-SVR patients.

Results: In the majority of the studies antiviral treatment was associated with reduced development of HCC and this effect was intensified when SVR was achieved. Antiviral treatment was associated with lower all-cause mortality and liver-specific mortality. This rate was also intensified when SVR was achieved. Sensitivity analyses revealed robust results, and a small study effect was minimal.

Conclusions: In patients with chronic hepatitis C, antiviral therapy can reduce the development of HCC and mortality, especially when SVR is achieved.

Delivery of paper sent in for presentation:

Treatment of HCV infection in Poland in 2016, an interim analysis of EpiTer-2 study

Robert Flisiak[1], Ewa Janczewska[2], Dorota Zarębska-Michaluk[3], Agnieszka Staniaszek[4], Włodzimierz Mazur[5], Dorota Dybowska[6], Agnieszka Czauż-Andrzejuk[1], Hanna Berak[7], Jerzy Jaroszewicz[8], Łukasz Socha[9], Iwona Orłowska[10], Magdalena Tudrujek[11], Łukasz Laurans[9], Jolanta Białkowska[12], Jolanta Citko[13], Olga Tronina[14], Anna Piekarska[15], Teresa Belica-Wdowiak[16], Zbigniew Deroń[17]

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EpiTer-2 study was initiated to follow patients treated for HCV infection within interferon free therapeutic program implemented in Poland from the mid 2015. The study included patients, which completed therapy by the end of 2016. Data were accumulated with online database collecting numerous treatment related informations. Untill the abstract submission records of 1243 patients aged between 21 and 91 (mean 55 ± 13) years from 18 centers were collected. They were mostly infected with genotype 1b (80%) or 3 (15%) and 58% failed previous therapy including 152 non-responders to triple regimens. History of liver transplantation was reported in 89 patients. Hepatic fibrosis evaluated mostly (69%) with elastography, demonstrated cirrhosis in 48%. Previous hepatic decompensation was reported in 80 patients and on-treatment ascites or encephalopathy developed in 22 patients. History of hepatocellular carcinoma was reported in 51 patients. Recurrence is suspected in one case and newly diagnosed lesion was noticed in another patient during the post treatment follow-up. Coinfection with HIV or HBV were reported in 18 or 80 patients respectively. The most frequent accompanying diseases were hypertension (40%) and diabetes (18%). Kidney disease was reported in 63 patients and 25 of them demonstrated end-stage disease with eGFR < 30 ml/min. There were 14 deaths reported. At the abstract submission efficacy data were available for 837 patients and SVR24 was 97% (genotype 1a – 100%, 1b – 97%, 3 – 90%, 4 – 100%). More details will be presented at the Meeting, but this interim analysis demonstrate huge opportunities for further analysis of EpiTer-2 database in numerous subpopulations treated with different therapeutic options.

Delivery of paper sent in for presentation:

Two years follow-up after treatment with Ombitasvir/Paritaprevir/ Ritonavir ± Dasabuvir ± Ribavirin, an interim analysis of CE-long study following the AMBER study

Robert Flisiak[1], Mariusz Łucejko[1], Dorota Zarębska-Michaluk[2], Anna Piekarska[3]

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[3]Department of Infectious Diseases and Hepatology, Medical University of Łódz, Poland

CE-long study was initiated for a long term follow-up of patients treated due to HCV infection with interferon free regimens. The first stage of the study include patients treated with Ombitasvir/Paritaprevir/ Ritonavir ± Dasabuvir ± Ribavirin in 2014-2015 and within the AMBER study, the first real world experience with this regimen in Europe. Among 209 participants of the AMBER study, at the moment of abstract submission 2-years follow-up (2yFU) data were available from 30 patients, mostly cirrhotics (20), infected with genotype 1b (24). No death cases or need of liver transplantation were reported during 2yFU up to now. Hepatocellular carcinoma was diagnosed in one patient and hepatic decompensation (ascites) in another one. Statistically significant reduction of bilirubin concentration was observed during 2yFU, but no changes were noticed regarding: albumin, INR, creatinin, BMI, Child-Pugh and MELD score. Mean hepatic tissue stiffness decreased from 18.1 ± 2.7 kPa at the start of treatment, to 15.5 ± 2.3 kPa at the end of treatment and finally to 12.0 ± 1.5 kPa after 2yFU, but statistically significant difference was demonstrated between start and 2yFU values only. Concluding, available data demonstrated no worsening of measures related to hepatic and renal function during 2 years follow-up in patients with advanced hepatic disease cured from HCV infection. Tendency of hepatic stiffness reduction need further evaluation in larger number of patients and longer follow-up period.

PLENARY SESSION 2
Hepatic lesions

30 years of hepatic transplantation in Geneva

Marek Bednarkiewicz

We started hepatic transplantation in Geneva, Switzerland, in 1987. We have done over 800 transplantations.

I have been a vascular surgeon in the team of transplantation from the very beginning and I will share my experience with you.

Cancer after liver transplantation

Marek Pacholczyk, Beata Łągiewska

Katedra i Klinika Chirurgii Ogólnej i Transplantacyjnej, Warszawski Uniwersytet Medyczny

Cancers in liver transplant recipients may occur at different times after liver transplantation. The development of the tumor in the recipient may occur as a result of the transfer with the organ from the donor (donor transmitted disease), *de novo* tumor development, or recurrence of a recipient disease present before transplantation. The risk of donor transmitted cancer is very low since careful screening of the donor is a common practice in Europe and United states of America, and is currently less than 0.03%. The policy to accept organs from donors with a known history of cancer must be balanced against the risks of death awaiting liver transplantation and strict adherence to current guidelines is mandatory in each case to avoid increased recipients death. Organs from selected patients i.e. high grade central nervous system malignancy can in some circumstances be utilized. Development of *de novo* malignancies emerges as a serious complication following liver transplantation and the relative risk depends of the time from transplantation, type of immunosuppression, as well as recipients age. Among the malignancies observed in liver recipients skin and lip cancer are most frequent but renal cell cancer, upper airway, colon cancer and post transplant lymphoma (PTLD) are also more common in liver recipients than in general population. The overall cancer risk increase 2.6 fold to that seen in the general population. Recurrent cancer disease in liver recipients transplanted for primary liver tumor (HCC, CCC) or liver metastases (i.e. Franz tumor, neuroendocrine tumor) depends of histological type of malignancy, acceptance criteria used and adjuvant therapy. For primary liver cancer (HCC) the recurrence rate vary between 16 and 35%.

Delivery of paper sent in for presentation:

Evolution of indications for liver transplantation at the Infant Jesus Hospital in Warsaw in 2000-2017

Beata Łągiewska[1], Marek Pacholczyk[1], Olga Tronina[2], Krzysztof Jankowski[3], Dariusz Wasiak[4], Wojciech Lisik[1], Agnieszka Jóźwik[1], Maciej Kosieradzki[1]

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In the period between June 2000 and April 2017, 592 cadaveric liver transplantations were performed in our center. The growing experience of the clinic team, the introduction to clinical practice effective anti-hepatitis C drugs (DAA), and the publication of the Zurich Consensus Criteria (December 2010) could potentially influence the spectrum of indications for this treatment.

All patients undergoing liver transplantation were divided into 3 groups depending on the period of operation. In the years 2000-2005 (period A) a total of 140 transplants were performed, in the years 2006-2010 (B) 177 operations. After 2010 (C), 275 liver livers have been transplanted to date. At all times, the most common indication for transplantation was post-inflammatory HCV cirrhosis (A – 28.5%, B – 40.6%, C – 40.3%, respectively). The second most common indication was autoimmune diseases (PSC, PBC and AIH), which incidence in all three periods was 25.8% (A – 22.1%, B – 29.4%, C – 25.4%). The greatest change in the number of indications for liver transplantation was an increase in the frequency of oncological indications. The percentage of patients diagnosed with HCC in the liver is 13.5% in the whole group, and in the individual periods it was A – 4.3%, B – 8.4%, and C – 21.5% respectively. Indications for retransplantation due to hepatic artery thrombosis remain at a constant 3.3%.

PLENARY SESSION 3
Liver diseases associated with cholestasis

New cholestatic disorders in childhood

Irena Jankowska

Klinika Gastroenterologii, Hepatologii, Zaburzeń Odżywiania i Pediatrii, Instytut ,,Pomnik – Centrum Zdrowia Dziecka'' w Warszawie

Differential diagnosis of cholestasis is difficult, due to a multitude of causes, often present diagnostic and therapeutic challenge. The rate of patients designated by the term "idiopathic neonatal cholestasis" decreased in last 10 years with advancements in diagnostic evaluation and discovery of next generation DNA sequencing technologies.

In the last (2017) published recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) any formula-fed infant noted to be jaundiced after 2 weeks of age should be evaluated for cholestasis with measurement of total and conjugated (direct) serum bilirubin (1A). Conjugated (direct) hyperbilirubinemia (> 1.0 mg/dl, 17 mmol/l) is considered pathological and warrants diagnostic evaluation (1A). The most common causes of cholestatic jaundice in the first months of life are still biliary atresia but also infections, autoimmune, genetic, metabolic, endocrine and congenital disorders. Basic laboratory tests in examination of cholestatic child are alanine and aspartate aminotransferase, (ALT and AST), gamma glutamyltranspeptidase (GGTP), international normalized ratio (INR), and glucose concentration in serum.

Until recently in children with normal or low GGTP progressive familial intrahepatic cholestasis (PFIC) type 1, (ATP8B1 deficiency) or 2 (ABCB11 deficiency) were suspected.

In recent years, new diseases causing cholestasis have been described, such as bile acid synthesis disorders, citrin deficiency, arthrogryposis-renal dysfunction-cholestasis (ARC), and mutations in TJP2, MYO5B or in the nuclear bile acid receptor FXR deficiency. Other conditions including Alagille'a syndrome, alpha-1-antitrypsin, CF, PFIC3 (due to ABCB4 deficiency), in which a high GGTP concentration is frequently present, can mimic biliary atresia and have to be excluded in early steps of diagnosis.

Quick diagnosis is crucial in detecting infants with cholestasis, referring them to paediatric gastroenterologist who can provide the essential diagnostic and proper treatment to optimize outcome.

PSC in children

Marek Woynarowski, Małgorzata Woźniak

Klinika Gastroenterologii, Hepatologii, Zaburzeń Odżywiania i Pediatrii, Instytut „Pomnik – Centrum Zdrowia Dziecka" w Warszawie

PSC is rare cholestatic, progressive liver disease of unknown etiology. Almost 700 papers on pediatric PSC have been published until today but the most complete publication are recent papers coming from international consortium including 36 hepatology units from Europe, Asia and America. The current lecture provides the summary of the results published by consortium.

The consortium analyzed the group of 781 children with PSC (M – 61%, F – 39%) and median age at diagnosis 12 (QIR: 8-15) years. Thirty three % of patients had PSC-AIH overlap syndrome, 76% had coexisting IBD and 7% had other autoimmune mediated diseases.

The international consortium data show that:

1. The biliary complication (a cholangitis clinical picture with a biliary stricture requiring an intervention in the form of endoscopic or percutaneous stenting, balloon dilation, or drainage) or hypertensive complication (ascites, hepatic encephalopathy, or esophageal varices with or without bleeding) are frequently present within 10 years form PSC onset.
2. Majority of patients with biliary or hypertensive complications will require liver transplantation within 3 years.
3. Increased bilirubin (> 0.86 mg/dl), GGTP (> 309 U/l) and APRI (> 1.33) at presentation of PSC are risk factors for unfavorable outcome.
4. AIH-PSC overlap syndrome does not worsen the course of PSC.
5. UDCA treatment does not influence the complication or survival rate.
6. Recurrent PSC may develop in almost 25% of grafts at 5 years after liver transplantation.

Delivery of paper sent in for presentation:

Common variant p.D19H of the hepatobiliary sterol transporter ABCG5/8 affects cholesterol homeostasis in children with gallstones

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We demonstrated that presence of the p.D19H variant in the hepatobiliary cholesterol transporter ABCG5/8 increases the risk of developing gallstones in children (Krawczyk/Socha, ESPGHAN 2016). Serum levels of CH precursors and plant sterols represent valid surrogate markers for CH biosynthesis and intestinal absorption, respectively. The comparison of serum surrogate markers informs about the sources of CH and its transport in a given individual.

The aim of the current study was to assess the effects of the p.D19H polymorphism on CH homeostasis in children with gallstones.

In total, we measured serum concentrations of CH precursors and plant sterols using GC/MS in 52 children with gallstone disease. Fasting serum specimens for sterol measurements were collected and stored at –70°C. The ABCG5/8 p.D19H variant was genotyped using TaqMan assays.

15 children carried at least one copy of the prolithogenic ABCG5/8 [p.19H] allele and 37 carried the common ABCG5/8 [p.19GG] genotype. Patients carrying the prolithogenic allele had significantly lower concentrations of the natural phytosterol sitosterol (p = 0.045) and decreased serum phytostanols, i.e. campestanol (p = 0.028) and sitostanol (0.029). In line with these results, the ABCG5/8 p.D19H variant was associated with decreased ratios of phytosterols to CH precursors (sitosterol : desmosterol, p = 0.008; campesterol : desmosterol, p = 0.013).

The ABCG5/8 prolithogenic variant p.D19H is associated with increased output of cholesterol in the setting of relatively low intestinal cholesterol absorption in children. This trait is present already at young age and might substantially contribute to the increased gallstone risk among carriers of the ABCG5/8 p.D19H risk allele.

PLENARY SESSION 4
Fatty liver disease. Role of microbiota in liver diseases

Role of gut microbiota in pathogenesis of nonalcoholic fatty liver disease and insulin resistance

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Nonalcoholic fatty liver disease (NAFLD) is a consequence of obesity and metabolic syndrome (MS). Some studies suggested altered gut microbiota to be a pivotal contributor of obesity by affecting energy harvest from the diet and energy storage in the host. Recent evidence has linked gut microbiota to the development of NAFLD through the gut-liver axis. A couple of mechanisms have been proposed for the microbiome role in NAFLD development, progression and its complications. These encompass microbiome-induced regulation of gut barrier and inflammatory responses and some metabolites produced or modified by the microbiota such as short chain fatty acids (SCFAs), bile acids and ethanol. With bacterial overgrowth and increased intestinal permeability due to impaired gut barrier observed in NAFLD patients, gut-derived bacterial products such as endotoxin (lipopolysaccharide, LPS) and bacterial DNA are being delivered to the liver through the portal vein. They activate Toll-like receptors (TLRs) and their downstream cytokines and chemokines, contributing to the onset of NAFLD and potentiate progression to nonalcoholic steatohepatitis (NASH) by activation of macrophages and hepatic stellate cells (HSCs). Because gut microbiota are a source of TLR ligands, their compositional change is eventual trigger in the activation of hepatic TLR signaling. Actinobacteria, Bacteroidetes, Cyanobacteria, Deferribacteres, Firmicutes, Proteobacteria, Tenericutes, TM7, and Verrucomicrobia are components of human gut microbiota at the phylum level. Firmicutes are increased whereas Bacteroidetes are decreased in obesity and NAFLD/NASH in humans. Up-regulated Firmicutes/Bacteroidetes ratio seems to be a potential phenotype of obesity. Additionally, pathogen and damage-associated molecules induce the formation and activation of a cytoplasmic multi-protein complex termed the inflammasome leading to interleukin(IL)-1b production, induction of liver inflammation, fibrosis and hepatocyte apoptosis. Bacterial LPS is a ligand for the LPS-binding protein, which interacts with CD14 located on macrophages in the lining sinusoids. In response to pathogens macrophages contribute to development of hepatic inflammation. They activate HSCs and sinusoidal endothelial cells to produce transforming growth factor(TGF)-β and α-smooth muscle actin, which promote fibrosis.

Short chain fatty acids (SCFA), including acetate, propionate and butyrate, are produced by bacterial fermentation of polysaccharides. SCFA involvement in NAFLD development and progression may result from their potential contribution to the maintenance of body weight, intestinal homeostasis, and improved glucose and lipids metabolism. Another mechanism related to NAFLD development could include microbial production of ethanol within intestines as a potential liver toxin. Increased number of alcohol-producing bacteria with higher serum ethanol levels were found in NASH patients. LPS-induced metabolic endotoxemia plays an essential role the development of insulin resistance (IR). Circulating LPS stimulates the TLR-2 mediated inflammatory response, activates adipose tissue macrophages and increases the secretion of pro-inflammatory cytokines and adipokines by the adipose tissue. LPS levels are significantly increased in diabetic subjects, compared to controls. IR is strictly associated with oxidative stress, steatosis and fibrosis progression. Moreover, it is a risk factor of hepatocellular carcinoma development, independently of advanced liver fibrosis.

In conclusion, gut microbiota affects the susceptibility to develop fatty liver and NASH. Bacterial ethanol production, alterations of bile acids and SCFAs metabolism and the development of an increased intestinal permeability leading to metabolic endotoxemia are the main mechanisms involved. The complex interaction between microbial antigens and TLRs, macrophages and cytosolic inflammasomes engaging wide spectrum of signalling pathways, affects the activation of inflammatory cascade, hepatocyte apoptosis and the development of hepatic fibrosis. Additionally dysbiosis and metabolic endotoxemia contribute to IR which potentiates inflammatory process and fibrosis progression. The general display of microbiota detrimental effects seems to be influenced by tricky interactions involving diet, lifestyle, environmental and metabolic factors, genetic predisposition, as well as a complex relationship between intestinal microbes and the host's immune system.

Microbiome in liver cirrhosis

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Liver cirrhosis (LC) is complicated by disturbances of microbiome profile. Specific intestine conditions in LC lead to microbiome reconstructon with increase pathogenic flora. Dysbiosis is asscociated with endotoxemia and liver function impairment. Pathogenic microflora is mainly the source of ammonia which has toxic efect on brain function and may lead to hepatic encephalopathy. Generally liver transplant (LT) significantly improves intestinal microbiota with decrease in potentially pathogenic bacteria. But in about 30% patients after LT have dysbiosis (high amounts of Proteobacteria and lower Firmicutes) and persistent abnormal psychological test with low quality of life. The composition of the microbiome in liver cirrhosis depends on stage of liver decompensation, portal hypertension and nutrition. Modification of microbiome is the effective menagement of LC complications. Chronic administration of pre-/probiotics or rifaximine is advisable in those patients.

Novel therapeutic options in non-alcoholic steatohepatitis (NASH)

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Non-alcoholic steatohepatitis (NASH) is form of NAFLD is characterized by steatosis as well as presence of inflammation and hepatocellular ballooning or other evidence of hepatocyte injury. It may lead to liver cirrhosis and is associated with increased mortality. For many tears many therapeutic options for NASH have been studied, however, there is very little evidence supporting the efficacy of most regimens. Recent research has improved our understanding of the pathogenesis of NASH and resulted in new and promising concepts for the treatment of NASH. A number of drugs is in phase 2 and 3 and it is expected to enter clinical practice in the near future.

The possible targets and compounds for therapeutic intervention include: bile acid receptors (e.g. obeticholic acid), fatty acid-bile acid conjugates, peroxisome proliferator-activated receptors (PPAR), Glucagon-like peptide-1, Chemokine receptors, Regulatory T cells, hepatocyte apoptosis (e.g. pan-caspase inhibitors), hepatic iron metabolism (iron chelators), vitamin D deficiency and mitochondrial protectant. As resolution of NASH does not mean reversal of fibrosis combination therapy with antifibrotic drugs would be the logical next step. Physician and particularly patients are awaiting these agents and hopefully they become available soon.

Additional problem is development of reliable biomarkers of NASH activity, as liver biopsy is not desirable or practical for treatment response monitoring.

Endocrine disorders in fatty liver disease

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Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the Western world. It is often seen in patients with different endocrinopathies and it is supposed that the hormonal abnormalities could play the role in the pathogenesis of NAFLD.

NAFLD can be considered as a hepatic manifestation of the metabolic syndrome and it is particularly associated with insulin resistance, obesity and abnormalities of glucose and lipid metabolism. Over 90% of NAFLD patients accomplish one or two MS criteria and 30-40% of patients meet the criteria of MS recognition. Increased prevalence of NAFLD has been reported in female patients with polycystic ovary syndrome (PCOS), which is both reproductive and metabolic disorder. Obesity, central adiposity and insulin resistance are proven to be the main factors related to NAFLD in PCOS. Moreover, existing data support that androgen excess, which is the main feature of PCOS and which is related to insulin resistance, may be an additional contributing factor to the development of NAFLD. Among other endocrine disorders coexisting with NAFLD hypothyroidism, hypogonadism, hypopituitarism may occur. Life style interventions is the standard treatment for NAFLD, PCOS, metabolic syndrome and diabetes type 2 patients.

Patients with NAFLD should be screened and treated for associated to NAFLD endocrinopathies. The aim of this review was not only to examine the association and possible causal relationship between endocrinopathies and the development of NAFLD but also to raise awareness within the endocrine and hepatology community.

Delivery of paper sent in for presentation:

Hepatic fibroblast growth factor-21 and omentin-1 levels in morbidly obese patients with non-alcoholic fatty liver disease

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Fibroblast growth factor-21 (FGF21) and omentin-1 have been recognized as potent antidiabetic agents, with potential hepatoprotective activity.

The aim of this study was to evaluate hepatic FGF21 and omentin-1 mRNA levels and their serum concentration as predictive markers of liver injury and insulin resistance in morbidly obese women with NAFLD.

The study included 56 severely obese women who underwent intraoperative wedge liver biopsy during the bariatric surgery. Hepatic FGF21 and omentin-1 mRNA were assessed by quantitative real-time PCR, while their serum concentrations with commercially available enzyme-linked immunosorbent assays.

FGF21 serum level was significantly higher in patients with more extent steatosis (grade 2 and 3) compared to those without or with mild steatosis (grade 0/1) ($p = 0.049$). However, ROC analysis showed poor discriminant power for FGF21 serum level in differentiation between more and less extensive steatosis with AUC = 0.666. There was evident tendency to higher hepatic FGF21 mRNA levels in patients with lobular inflammation and fibrosis, and to lower levels in the case of hepatocyte ballooning and steatosis. There was positive mutual correlation between hepatic FGF21 and omentin-1 mRNA levels ($r = 0.73$; $p < 0.001$). Fibrosis stage was associated with serum glucose and HOMA-IR ($p = 0.03$ and $p = 0.02$, respectively). Serum omentin was not associated with histopathological features. Hepatic omentin-1 mRNA levels exerted the tendency to be lower in patients with advanced steatosis and hepatocyte ballooning.

In conclusion our study, which focused on hepatic FGF21 and omentin-1 mRNA levels, confirmed a marked expression of both molecules in the liver of morbidly obese patients with NAFLD. mRNA levels were affected by histopathological abnormalities. More extent steatosis was associated with evident change in serum FGF21 concentration in morbidly obese women with NAFLD. The vast amount of fat, both visceral and subcutaneous in severely obese patients may affect FGF21 and omentin-1 serum levels.

PLENARY SESSION 5
Practical aspects in the diagnostics and treatment of HBV infections

Detection of hepatitis B virus infections in blood donors in Poland in 2005-2015

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Introduction: The infection rate of asymptomatic HBV is poorly recognized in the Polish population.

Aim of the study: Analysis of epidemiological data from hepatitis B virus (HBV) screening of Polish blood donors.

Material and methods: In 2005-2015 period HBsAg and DNA HBV screening was performed for 12.513.283 donations collected from 6.408.819 donors. Only confirmed repeat reactive results (in NAT or neutralization) were considered positive.

Results: In the analyzed period 10.714 infections were detected: 10.519 HBsAg(+) and 195 DNA HBV yield [HBsAg(–)/DNA HBV(+)]: 44 window period (WP) and 151 occult HBV infections (OBI). The cumulative prevalence (95% confidence interval – CI) per 100.000 donors amounted to 164.11 (160.99-167.30) for HBsA (+) and 3.04 (2.62-3.47) for DNA HBV yield. The rates were higher for men than women (OR = 1.38; 95% CI: 1.32-1.45; $p < 0.05$). Steady decrease in HBsAg(+) infection rate (from 264.5 to 53.1/100.000 donors) and fluctuation in frequency of DNA HBV yield (in range 0.83-6.62/100.000 donors) were reported. At first the highest HBsAg(+) infection frequency (449/100.000 donors) was observed in the ≤ 20 age group, in the following years it decreased to 21/100.000 donors in 2015 ($p < 0.05$). OBI detection frequency increases with donor age. Infection frequency (per 100.000 donors) shows geographical variation: the highest for Blood Transfusion Center (BTC) Lodz (351), Kalisz (231) and the lowest for BTC Lublin (88) and Rzeszow (52).

Conclusions: HBV infections (seropositive and seronegative) were detected in 0.17% blood donors. Infected donors – 1372 - 337 – were annually directed to general practitioners and then to infectious disease specialists for in-depth testing and treatment.

Hepatitis B vaccinations – are boosting doses necessary?

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Vaccinations against hepatitis B virus yield very high efficacy but also induce long-term protection in general population. Nevertheless, it is still debatable to which extent anamnestic response is protective in vaccinated subjects with anti-HBs levels below 10 mIU/ml. Hence it is without any doubt that patients with deficits of immunity require anti-HBs monitoring and vaccine boosting, it is not clear if general population should receive booster doses when anti-HBs decreases or becomes undetectable. Some recent data suggest a need of booster doses in adolescents young adults. The complexity of the subject is partially a consequence of lack of clinical trials assessing long-term efficacy of anti-HBV vaccines. Furthermore, it is important to underline variety of factors associated with no response to primary vaccination which include errors during vaccination, coexisting disorders but also variety of host factors (ex. IL-17, IL-22 CXCR5 polymorphism). The procedures in non-responders as well as efficacy of new anti-HBV vaccines including PreS/S will be also discussed.

Current trends in prophylaxis of HBV infection in transplanted liver

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According to the WHO, about 260 million people worldwide are infected with hepatitis B virus (HBV), almost one million people a year die in the course of this infection complications: cirrhosis and hepatocellular carcinoma.

In developed countries, mandatory vaccination against hepatitis B and access to the latest antiviral therapy has significantly reduced the rate of hepatic transplantation in the course of HBV infection alone, but the

number of patients with hepatocellular carcinoma is increasing.

Risks of reinfection are increasing in high-risk recipients, most in patients actively replicating on the transplant day, therefore the aim is to strive for elimination of the virus before transplantation.

Using the anti-HBs globulin and nucleos(t)ide analogs with high resistance barriers – entecavir and tenofovir, significantly improves the survival of the graft and the patient. It is advisable to personalize the therapeutic algorithms depending on the risk factors associated with both the recipient and the virus itself, before and after transplantation.

A specific complement of management in this group of patients is the optimization of the immunosuppressive regimen, with its minimization and rapid reduction of glucocorticoids that stimulate the glucocorticosteroid receptor in the HBV genome.

The increased demand for vascularized organs, with relatively constant supply of them, leads to accept donors with serologic evidence of HBV infection. In such cases, the skilful selection of the recipient, the attempt active immunization, or adequate post-transplant prophylaxis guarantee the safety of such proceedings.

Huge hopes are emerging for research into new antyHBV drugs and cccDNA inhibitors, which have the potential to revolutionize chronic hepatitis B therapy by permanently eradicating the virus and preventing reinfection in the transplanted organ.

Delivery of paper sent in for presentation:

Activity of chronic HBV infection related to Th17/Treg imbalance

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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). This study aims to assess phenotypes of blood Th17 and Treg cells populations and plasma concentrations of Th17-associated and regulatory interleukins in chronically-HBV-infected patients with regard to the phase of infection.

Material and methods: 25 patients with HBeAg-negative-CHB, 3 with spontaneously-resolved HBV-infection (RES) and 3 with seroconversion during the treatment (CONV) were enrolled. Three patterns of CHB were distinguished: low-replicative-carriers (LRC), e-negative-CHB naive-to-treatment (ENH) and e-negative-CHB on nucleos(t)ide analogues therapy with complete drug-induced HBV-DNA suppression > 24 months (SUP). Control group consisted of 10 healthy volunteers. Phenotypes of peripheral blood Th17 and Treg-cells were distinguished by flow cytometry (BD FACS Calibur). Plasma concentrations of Th17-associated interleukins were assessed using xMAP-technology.

Results: The ratio of IL17A+ or IL-17F+RORγt +CD4+ cells was different across the groups (ANOVA, $p < 0.01$), with the highest frequency in control group, and lower in CHB groups (ENH > LRC > SUP). Plasma IL-17A, IL-17F, IL-21, IL-22 varied significantly across the groups (median test, $p < 0.05$) with the highest median concentration in RES and CONV groups, moderate in LRC and SUP patients, lower in ENH and lowest in control group.

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.

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PLENARY SESSION 6
Clinical problems in patients with hepatic failure

Hepatic encephalopathy

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Liver cirrhosis (LC) leads to many serious complications, among hepatic encephalopathy (HE). HE can be divided into minimal/covert and overt HE depending on the stage of liver decompensation. Most of patients with LC have symptoms of minimal HE detected only by critical flecker frequency. The diagnosis of HE remains mainly clinical with elimination of other causes for the altered mental status. There are some factors precepitating of HE: infections, dehydratation, constipation, bleeding from the upper gastrointestinal tract. Patients with HE must be treated by hepatologists or gastroenterologists experienced with liver decompensation. Elimination of HCV infection in patients with LC decreases the risk of HE and prolongs life without liver decompensation. Long term prophilaxis with the use of rifaxymin proctects against recurrence episodes of HE, hospitalization and improved quality of life.

Albumin dialysis – a therapeutic option or bridge to liver transplantation?

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Currently, there is no direct therapy for liver failure. Extracorporeal liver support devices commonly employed include MARS®, Prometheus® and SPAD technique (single-pass albumin dialysis). Improvements in clinical variables and blood chemistry were demonstrated in clinical trials, however, no agreement has been reached on indications and qualification criteria to these therapies. Furthermore, failure to demonstrate survival benefit in large-scale controlled trials RELIEF (MARS®) i HELIOS (Prometheus®) indicate the need to search for novel, effective liver support (replacement) therapies. The RELIEF and HELIOS trials together with other evidence-based data demonstrated both advantages and disadvantages of albumin dialysis. Among the disadvantages is inability of this technique to effectively lower blood levels of proinflammatory mediators and toxins covalently bound to albumin. Among the advantages – beneficial effects of early treatment (lowering 30-day and 90-day predicted mortality), in alcoholic liver disease, and in liver transplant candidates (bridge to transplant). Both MARS® and Prometheus® appear to be gradually eliminated from the market. Among new liver dialysis devices available in Poland is the OPAL System. It is the equivalent of the MARS® system boasting user-friendly loading and priming, lesser need for 20% albumin, and a novel adsorber with a greatly enhanced detoxification capacity. The SPAD technique has as yet not been tested in properly designed controlled clinical trials. Preclinical data on albumin apheresis using a hemodiafilter with increased permeability to albumin (ALEX – albumin apheresis and exchange) is presented as a novel approach to extracorporeal support of the failing liver. Preclinical data on this technique provide rationale for clinical evaluation of the ALEX hemodiafilter for blood detoxification and albumin apheresis in liver failure.

Clinical problems in women after liver transplantation

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Liver transplantation represents an effective method of improving the survival and quality of life and reducing the mortality in people with end-stage liver failure. Women represent 1/3 of all liver recipients and most of them are in the child-bearing years. A factor determining whether a reproductive-aged women who has undergone liver transplant has made a full recovery is the return of a healthy hormonal cycle and the possibility of pregnancy and childbirth. This poses new challenges for obstetricians who are increasingly encountering, and managing, pregnancy and childbirth among women who have undergone liver transplantation. Despite advances in medicine, pregnancy among these patients is still considered high risk. The patient is vulnerable to transplant organ failure, acute rejection, and obstetric complication such as a preeclampsia, intrauterine growth restriction, preterm delivery, diabetes, cholestasis, and anemia. Most of them de-

pend largely on the function of the transplanted liver, not the time elapsed since transplantation or the age of the patients. Women after liver transplantation receive immunosuppressive therapy to protect the transplanted liver against rejection, which therapy also unfortunately predisposes them to chronic infection and malignancies. Liver transplant recipients have a high risk of developing anogenital tract malignancies: carcinoma of uterine cervix, vulva and uterus. All women should have regular gynecological care including Papanicolau tests and mammography.

Drug-induced hepatic injury

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Many different substances can evoke liver injury, among others alcohol, drugs, food-borne toxins including mushrooms. Toxic reactions can be caused by direct damage of hepatocytes or idiosyncratic reactions. Direct hepatotoxicity caused by a toxin or toxic metabolite are usually predictable and are directly related to the dose of the agent ingested. Idiosyncratic hepatotoxicities comprise a complex group of rare, unpredictable, non-dose-related adverse events that are not expected based on an inciting agent's pharmacology. About 10% of patients demonstrate features of hypersensitivity or drug reaction with eosinophilia and systemic symptoms (DRESS). Both mechanisms of liver injury can coexist. Drug-induced hepatotoxicity is still underreported. It is an important cause of acute liver failure. Drugs causing drug-induced hepatotoxicity include antibiotics, lipid lowering agents, oral hypoglycemics, psychotropics, antiretrovirals, food suplements, alternative and herbal medications. The most common cause of toxic hepatitis (and the most common cause of acute liver failure) is acetaminophen. 7-15% cases of acute liver failure are caused by toxic drug reactions (excluding acetaminophen poisoning). Liver toxicity is the most common form of adverse drug reaction resulting in aborted drug development or withdrawal after licensing.

Hemostatic abnormalities during surgery in patients with liver disease

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Hemostasis in patients with liver disease differs significantly from that of healthy individuals. These patients are thought to be at higher risk of bleeding due to abnormal routine laboratory tests of coagulation. Over the past decade new aspects of hemostasis were revealed in liver cirrhosis. Hemostatic abnormalities among this group are more complex than previously believed, with unpredictable clinical consequences. Liver disease causes abnormal synthesis and function of many clotting factors, resulting in both procoagulant and anticoagulant effects – a state called "rebalanced hemostasis". The functional balance is typically maintained, but with a tendency to shift easily either towards bleeding or thrombosis.

There is no evidence that prophylactic transfusion of plasma prevents perioperative bleeding. Correction of hemostatic abnormalities before surgery based on routine laboratory tests is not currently recommended. In our hospital, thromboelastometry is used as a tool for global hemostasis assessment. Based on our observations, excessive fluid therapy and liberal use of colloids and fresh frozen plasma result in increased bleeding during surgery. Also, fibrinogen has been observed to be the most important factor for stable clot formation.

The new paradigm of rebalanced hemostasis has a very strong implications for the clinic.

Delivery of paper sent in for presentation:

Serum brain-derived neurotrophic factor is decreased in patients with liver cirrhosis and minimal hepatic encephalopaty

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Minimal hepatic encephalopathy (MHE) is a common complication of liver cirrhosis not only leading to decrease in quality of life but also predicting a development of overt encephalopathy. The diagnosis of MHE relays usually on combination of neuropsychological tests, while robust biomarkers are lacking. Brain-derived neurotrophic factor (BDNF) has an important role in protection and recovery of CNS after damage. It's serum lower levels were described after ischemic brain injury, depression, Alzheimer's disease, schizophrenia and associated with poor prognosis. We aimed to assess serum concentrations of BDNF in liver cirrhosis with special emphasis on minimal hepatic encephalopathy.

Serum free BDNF was assessed by Quantikine ELISA (R&D Systems) in 78 patients with liver cirrhosis (53 male, median age 55 yo) of various etiologies and 10 healthy individuals. Forty-one subjects underwent extensive evaluation for MHE by PHES and ICT (inhibitory control test) or CFF (critical flicker frequency) tests.

Serum BDNF was twofold lower in liver cirrhosis compared to healthy subjects (15.9 ± 1.1 vs. 33.7 ± 2.9 ng/ml, $p < 0.001$) and its decrease reflected a degree of liver insufficiency assessed by MELD. BDNF shown an inverse correlation with bilirubin ($r = –0.35$, $p = 0.005$) and INR ($r = –0.37$, $p = 0.003$) and positive with platelets ($r = 0.35$, $p = 0.004$), while no associations with age, sex, BMI, WHR, creatinine and ammonia were noted. Importantly subjects with diagnosis of minimal hepatic encephalopathy by PHES-test (≤ –5 points) showed lowest levels of BDNF (10.1 ± 2.0 vs. 19.7 ± 2.1 ng/ml, $p < 0.01$). Also patients with self-reported sleep disturbances showed significantly lower serum BDNF (13.1 ± 2.3 vs. 19.9 ± 2.2 ng/ml, $p = 0.04$).

Serum BDNF shows an association with liver function impairment. Importantly, the lowest serum BDNF is noted in patients with MHE and sleep disturbances, which suggest its role in pathophysiology of hepatic encephalopathy but also potential use as a biomarker.

INTERACTIVE SESSION
Presentation of the most interesting and challenging cases

Autoimmune hepatitis or Wilson disease or both?

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Wilson disease (WD) is an autosomal-recessive human copper storage disorder caused by mutations within the gene ATP7B located on chromosome 13 with a prevalence in most populations of one in 30000. It may present with variable features (hepatic and neuropsychiatric). Establishing the diagnosis of Wilson disease is straightforward if the major clinical and laboratory features are present.

Autoimmune hepatitis (AIH) is a progressive inflammatory liver disorder characterized serologically by high levels of transaminases and immunoglobulin G, presence of autoantibodies and histologically by interface hepatitis, in the absence of a known etiology. Both autoimmune hepatitis (AIH) and Wilson disease (WD) may present as acute fulminant or chronic hepatitis. Sometimes there is a significant risk of misdiagnosis even if standard diagnostic approach is applied. We present a challenging case where ultimate diagnosis could not be established at primary diagnostic approach and we point out the importance of the correct diagnosis and selecting the appropriate therapy.

Cholestatic hepatitis – unusual clinical presentation of primary sclerosing cholangitis

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K.W., female, aged 34, was admitted to the Hepatology Outpatient Clinic PCChZiG because of cholestatic hepatitis. Disease symptoms in the form of pruritus and cholestatic liver damage appeared during first pregnancy in 2012 and they did not subside after delivery. Chronic hepatitis B and C infections were excluded. Patient was admitted in July 2016 to the Department of Infectious Diseases MUG because of suspicion of autoimmune disease. UDCA therapy (250 mg t.i.d.) with good response was started before hospitalization. Autoantibodies (ANA, SMA, LKM, ANCA, AMA) and exponents of metabolic diseases (hereditary haemochromatosis, Wilson diseases, NAFLD, alpha1 antitrypsin deficiency) were absent. Only mild hypergammaglobulinemia without hiperproteinemia with normal electrophoresis of gamma globulins was noted. The abdominal US examination revealed mild fatty liver and splenomegaly without portal hypertension signs. Liver biopsy was done in January 2017 and discovered chronic portal/periportal hepatitis (grade 2) with severe fibrosis praecirrhotic lesions (stage 3-4) in Scheuer score with cholestasis. Pathologist comment: chronic inflammation of bile ducts, probably autoimmune reaction to the toxic liver injury. Proteinogram, ALT, AST activity and bilirubin concentration were normal; ALP and GGTP were above normal range. Two weeks later patient reported severe pruritus and jaundice with normal activity ALT, AST and GGT with flu like symptoms. She was admitted to hospital in February 2017, metabolic diseases and HEV, HCV infections were excluded. A high bilirubin concentration (9 mg/dl) and high bile acids concentration (200.2 μmol/l) were detected. MRCP examination showed multiple stenosis in bile ducts and liver cirrhosis with early portal hypertension. Final diagnosis: primary sclerosing cholangitis was established.

PLENARY SESSION 8
VARIA II

Liver diseases according to registers available at Polish Ministry of Health

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Introduction: The health policy and health care organization are highly dependent on the knowledge on the burden of the diseases including the epidemiology and treatment complexity. The lecture presents the status of liver diseases in Poland according to data collected by National Health Found and analyzed by Ministry of Health within EU POWER program.

Material and methods: All patients hospitalized in Poland for liver disease in 2014 are included in this analysis. Patients were identified by ICD-10 classification number reported by the hospital as the primary reason for hospitalization. Liver diseases were classified into the following categories: LC – liver cirrhosis (K74), LF – liver failure (K72), LS – liver steatosis (K76.0), ALD – alcohol liver disease (K76.6, T51.0), LDC – liver disease complications (K76.6-7), CLM – congenital liver malformations (Q44-45), TLD – toxic liver diseases (K71, T39.1, T64), GBD – gallbladder diseases (K80.0-2, K81-2), BDD – bile duct diseases (K80.3-5, K80.8, K83), OLD – other liver diseases (B67.0, B67.5, B67.8, E83.0, E83.1, I81, I82.0, K73.0 K75.0-3, K75.8-9, K76.1-5, K76.8-9) and VH – viral hepatitis (B15, B16, B17, B18,0-2). The surgical and endoscopic procedures were described by ICD-9 classification and mortality data were based on PESEL registry.

Results: Total number of hospitalization in Poland in 2014 was 8.86 mln including 190.3 thousands due to nonviral liver diseases and 18.1 thousands due to viral liver diseases. The number of hospitalization for nonviral liver diseases in different country regions was 501-672/100 thousands of adult inhabitants and 40-170/100 thousands children. The number of hospitalization for viral liver diseases in different country regions varied from 23 to 122/100 thousands of adult population while in children varied between 0.2 and 8/100 thousands. The distribution of different categories of nonviral liver diseases differs according to patient's age: biliary tract diseases (GBD + BDD) accounts for 2/3 of liver problems in adult population (20% in children) while OLD and TLD dominate in children (44% vs. 10%) (Table 1).

Table 1. Category of nonviral liver disease as % of all hospitalizations in age group

Liver disease category	Age: 0-17	Age > 18
GBD	13	50
BDD	5	17
LF	1	2
LS	2	3
LC	5	5
ALD	26	13
TLD	5	2
OLD	39	8

Majority of nonviral liver diseases patients were hospitalized in surgical (55.5%) general medicine (21.6%) and gastroenterology (7.0%) departments.

The number of surgical procedures is inverse proportional (approx. 50-20%) to number of patients with liver diseases in the hospital while the number of endoscopic procedures is directly proportional (approx. 8-12%) to number of liver subjects admitted to hospital.

High 60 days mortality was noted in patients with LF (adult: 32.5%, children: 10.8%), LDC (26.7%; 0%), LC (18.3%, 0.4%) and ALD (14.0%; 0.1%).

Conclusions: According to data available in the registries available for state institutions in 2014:

1. Liver diseases accounted for approximately 2.3% of indication for hospitalization in Poland.
2. The highest proportion of liver disease patients are subjects with biliary tract diseases.
3. The highest proportion of liver disease patients are hospitalized in surgery departments.
4. The highest mortality due to liver disease both in children and adults is noted in patients with liver failure.

Standard therapy resistant autoimmune hepatitis – alternative treatments

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Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease resulting from loss of tolerance against hepatic tissue. Usually affects people older than 40, mostly women, but should be considered at any age. There is no single test for the diagnosis of AIH; diagnosis relies on a combinations of clinical, laboratory and histopathological criteria in the form of scoring system with the exclusion of other causes of chronic liver disease. The most striking laboratory features include elevated immune globulins, especially gamma globulins, and circulating autoantibodies. Clinical spectrum of AIH ranges from asymptomatic disease to a severe acute hepatitis with a fulminant presentation. The natural course of AIH can be fluctuating with periods of exacerbations and spontaneous remissions. Exacerbations are responsible for the progression of the disease. There is a frequent association of AIH with extrahepatic autoimmune disorders such as vitiligo, autoimmune thyroiditis, rheumatoid arthritis, ulcer colitis and diabetes mellitus.

Autoantibodies are one of the distinguishing features of AIH, but the absence of them does not rule out the diagnosis. According to the scoring system patients are classified to have probable of definite AIH. Autoantibodies directed against different cellular targets allow to divide AIH into three subclasses: type I AIH with the presence of antinuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA), type II AIH characterized by the presence of anti-liver/kidney microsomal antibodies (LKM-1) and sometimes antibodies directed against UDP-glucuronosyltransferases (LKM-3) and type III AIH with the presence of autoantibodies against a soluble liver antigen (SLA/LP). Type II AIH is more common in young age patients in comparison with the classical type I AIH. It is worth noting that heterogeneity of autoantibodies does not influence treatment decisions.

Histological appearance of AIH is quite characteristic, but similarly to the lab abnormalities, there is no single histological feature which can prove the diagnosis. Typically, histological features of AIH include: periportal hepatitis with lymphocytic infiltrates, plasma cells and piecemeal necrosis. Biliary involvement is not common, but does not rule out AIH.

AIH is a treatable chronic disease which responses very well to a standard therapy with predniso(lo)ne alone or in combination with azathioprine in the majority of cases. Therapeutic failure is seen in about 10% of patients. Untreated or treatment resistant AIH has a very poor prognosis. It was reported that 5- and 10-year survival does not exceed 50% and 10%, respectively. Approximately 30% of adults and 50% of children are already cirrhotic at diagnosis. Nevertheless, the frequency of remission is comparable in patients with and without cirrhosis at presentation. Termination of treatment should be done only after confirmation of histological remission in liver biopsy. Relapse following tapering of steroids is very common and happens in 50% of patients within first six months after treatment discontinuation and reaches 80% after 3 years. Juvenile AIH usually requires life-long treatment. About 15% of children and adolescents develop chronic liver failure and need transplantation before the age of 18 years.

Treatment is indicated in any patient with the diagnosed AIH, elevated liver enzymes, high gamma globulin level and histological evidence of interface hepatitis or necroinflammation. Treatment is debatable in the inactive phase of the disease in the absence of inflammatory activity. In decompensated cirrhosis of the patients on the waiting list for liver transplantation treatment seems not to be beneficial and is not recommended. Standard therapy is usually administered over the course of two years. Both strategies – predniso(lo)ne alone or in combination with azathioprine – are effective. The choice of therapeutic regimen is principally guided by the side effects. A postmenopausal woman with hypertension, osteoporosis and glucose intolerance is rather a candidate for combination therapy with a lower dose of steroids. In young women who are or wish to become pregnant, or in the individuals with haematological abnormalities predniso(lo)ne monotherapy is a treatment of choice.

In approximately 10% of treated patients remission is not achieved and progression of the disease can be observed. In these cases the diagnosis of AIH has to be carefully revised in order to exclude other etiologies. In case of treatment resistance or intolerance alternative therapies have to be considered and in the end-stage liver disease liver transplantation seems a good option. Alternative therapies include: budesonide and other synthetic steroids, cyclosporine (CsA), tacrolimus (TAC), mycophenolic acid, cyclophosphamide, rapamycin (RAPA) and ursodeoxycholic acid (UDCA). The efficacy of most of these drugs in autoimmune hepatitis has not yet been definitely confirmed and is only reported in small case studies.

Budesonide

Budesonide is a synthetic steroid which undergoes a high degree (90%) first-pass metabolism in the liver, reducing a systemic bioavailability and limiting systemic side effects of steroids. Acts as an anti-inflammatory and immunosuppressive drug, mostly used in a dose of 3 mg BID or TID, alone or in combination with azathioprine. Budesonide is a valuable treatment option in AIH patients who are either intolerant to predniso(lo)ne and azathioprine or prednisone-dependent. In comparison with standard therapy budesonide shows higher efficacy in AIH patients without cirrhosis and as a first-line treatment. In patients who were previously treated with conventional steroids and azathioprine budesonide therapy is associated with a low frequency of remission. Therefore budesonide is not recommended in cirrhotic patients and in patients who failed standard therapy with pred/aza.

Deflazacort

Similarly to budesonide, deflazacort belongs to the second generation synthetic steroids and has been studied in AIH because of its feature of lower systemic exposure and fewer side effects in comparison with conventional steroids. In a s small pilot study AIH type I patients who failed to standard treatment reached a sustained biochemical remission in a follow-up of two years. However, the role of deflazacort in a long-term second-line treatment needs to be confirmed in controlled studies.

Cyclosporine A

CsA became the first really effective immunosuppressing drug and revolutionized transplantology. It is a lipophylic cyclic peptide that acts on calcium-dependent signaling and inhibits T cell function via the interleukin 2 gene. There is a considerable experience with CsA as an alternative treatment in steroid resistant AIH, but the major difficulty is a toxicity profile, particularly in a long-term use. Typically, CsA increases risk of hypertension, malignancies and infections, causes renal insufficiency, hirsutism, hyperlipidemia and goat attacks. Treatment with CsA has to be carefully monitored due to a narrow therapeutic window of the drug and dosing of CsA has to be modified accordingly.

Tacrolimus

Tacrolimus is a macrolide lactone compound. The mechanism of action is similar to that of CsA, but TAC binds to a different immunophillin and manifests much stronger immunosuppressive effect. The application of TAC in AIH patients was shown in patients treated for one year with a good response and a minor influence on kidney function. TAC was also effective as a second-line treatment in steroid-refractory patients improving inflammation and the activity of liver enzymes. It seems to be a promising candidate drug in the alternative therapy, but larger randomized trials are necessary to assess its role in difficult-to-treat AIH patients. Similarly to CsA, TAC is toxic, particularly in a long-term use, and requires concentration monitoring due to a narrow therapeutic window. Most common side effects include: neurotoxicity ranging from slight tremor to grand mal seizures, hair loss, renal insufficiency, glucose intolerance, impairment of malignancy and infection control.

Mycophenolic acid

This compound belongs to antimetabolites and inhibits inosine monophosphate dehydrogenase which blocks purine synthesis and markedly reduces both T and B lymphocyte proliferation. Mycophenolic acid is widely used in post-transplant patients. In a small pilot study at the beginning of this century it was used in seven AIH patients who did not tolerate azathioprine or did not respond to standard therapy. ALT normalization was achieved in five patients within three months. It was suggested that mycophenolic acid might be a promising alternative therapy in case of standard treatment failure. However, in a retrospective study with 37 patients who were azathioprine intolerant or irresponsive, statistically significant beneficial effect of mycophenolate was not confirmed, particularly in patients who were azathioprine non-responders. It was decided that mycophenolate might have some role as a second-line therapy in azathioprine intolerant patients. Recently published real-world study focused on the long-term efficacy of mycophenolate mofetil as a first-line treatment of AIH patients opened discussion on mycophenolate mofetil again and results deserve further clinical trials.

Cyclophosphamide

It was shown, that concomitant use of cyclophosphamide in a dose of 1-1.5 mg/kg daily in combination with steroids induces remission in the majority of AIH cases. However, a long-term use of the drug is related to a potentially severe haematological side effects and that is why it is still considered a highly experimental therapy.

UDCA

Ursodeoxycholic acid is a hydrophilic bile acid with a presumable immunomodulatory potential. There are some evidences that UDCA influences immune globulin synthesis and alters HLA class I expression on the cell surface. In single controlled studies it was shown that in patients with autoimmune hepatitis UDCA in combination with standard therapy improves biochemical parameters and histological abnormalities as well as reduces patients' complaints. Unfortunately, there is no evidence that UDCA slows down the disease progression. Further trials are necessary to confirm the role of UDCA as an alternative treatment in steroid resistant AIH.

The role of endoscopy in liver diseases

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Endoscopy is advanced technique for diagnostic and therapeutic procedures. Although liver parenchyma is not directly accessible for endoscopy, the hepatology patients are frequently referred to endoscopy unit for evaluation or treatment of extrahepatic manifestation of liver disease. Well trained endoscopist is aware of the challenges present in patients with liver diseases.

The frequent indication for endoscopy in patients with liver cirrhosis is the evaluation of portal hypertension. Several techniques were developed for endoscopy treatment of esophageal or gastric varices. These techniques are safe and reduced the variceal bleeding risk thus markedly improved the prognosis.

The most typical hepatology use of endoscopy is endoscopic retrograde cholangiopancreatography (ERCP). The main indications for ERCP are cholelithiasis and bile ducts abnormalities. ERCP gives the access to biliary tract and allows to use the therapeutic procedures like sfincterotomy, gall stone removal, bile duct stenosis dilatation, biliary or pancreatic stent implantation or obtaining of tissue specimens.

The colonoscopy is less frequently used in hepatology patients but it is certainly indicated in those with primary sclerosing cholangitis as many subjects may have coexisting colonic involvement.

The modern hepatology require multidisciplinary approach to patients with liver disease thus hospital for patients with liver disease should have the access to endoscopy unit with the proper equipment and trained endoscopists.

Delivery of paper sent in for presentation:

Molecular characterization of novel variants for improved diagnosis in children having Wilson disease

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Introduction and aim of the study: Wilson disease (WD) is cause by a mutation in the ATP7B. There is a high clinical demand to classify novel ATP7B variants with an unknown disease-causing phenotype.

Material and methods: Children were diagnosed according to Ferenci score. DNA derived from peripheral blood was analyzed. Stable cell lines were generated by retroviral vectors expressing the variants in a human hepatoma ATP7B knockout cell line (PLoS One 2014; 9: e98809). Functional characterization was achieved by determination of the copper transport using MTT assay and by determination of intracellular copper using atomic absorption spectrometry (AAS). Intracellular trafficking was determined by confocal fluorescence microscopy.

Results: Two children were borderline positive for WD with a score of 4 and 3, respectively. Two novel variants, p.L168P and p.S1423N, were detected in one child, while p.L168P was associated with p.H1069Q in the other. Using viability assays of stable cell lines, variants p.L168P and p.S1423N had significant functional activity, but it was reduced as compared to wild type ATP7B. A comparison of p.L168P and p.S1423N expressing cells with p.H1069Q revealed a higher activity of the novel variants suggesting that both amino acid changes result in a relative mild phenotype. Intracellular copper determination as well as assessments of protein stability further corroborated the functional phenotype of the two variants.

Conclusion: Our functional analysis of novel ATP7B variants may represent a valuable methodology that adds to the established scoring system. This is the first report of a functional characterization of novel ATP7B variants in children for early start and improvement of therapy.

POSTER PRESENTATIONS

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

[1] Comparison of accuracy of the liver biopsy and transient elastography in staging of liver fibrosis among adult chronic hepatitis C virus infected patients

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Introduction: Staging of liver fibrosis is crucial not only to the estimation of the prognosis, but also to the indication and type of anti-viral agents in chronic hepatitis C (CHC) patients. By following the appropriate standards, unidimensional transient elastography (TE) seems to be a suitable alternative for liver biopsy of which the main advantage is both its safety and reproducibility.

Aim of the study: In clinical practice the non-compatibility between the results of liver biopsy and liver stiffness measurement (LSM) by FibroScan® is noticeable, which may prove that one or both of the methods are imperfect. There are still no national guidelines which determine precisely the accuracy of TE, including the cut-off values for the distribution of liver staging, according to the METAVIR scoring system, in an appropriate cohort of patients.

Material and methods: There were 238 consecutive CHC adult patients, who had never been treated anti-virally, retrospectively included in the study. All of them had undergone both liver biopsy and LSM by FibroScan® at the Hospital for Infectious Diseases in Warsaw.

Results: The fibrosis stage distribution in biopsy specimens was as follows: F0: 16.8%, F1: 55.9%, F2: 17.2%, F3: 4.6% and F4: 5.5%. The results of fibrosis assessments through TE were as follows: F0/1: 65.1%, F2: 18.1%, F3: 4.6% and F4: 12.2%. In 30.7% of cases results were discordant.

Conclusions: Transient elastography appears to be a reliable tool for detecting absent or mild fibrosis and cirrhosis in CHC patients. LSM results must be interpreted in a clinical and biochemical context by an experienced hepatologist in order to insure high quality results.

[2] Association of Budd Chiari syndrome, essential thrombocytosis and celiac disease

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We are reporting the case of a girl with association of Budd-Chiari syndrome (BCS), essential thrombocytosis (ET) and celiac disease (CD).

This is one out of eight cases in the literature of BCS complicated with CD, and the only one complicated with CD and ET. A 4-year-old girl treated with anagrelide, was admitted with suspicion of BCS. Laboratory tests revealed anemia (Hgb 8.4 g/dl; normal range 10.9-14.2), thrombocytosis (516×10^3; 140-400), hypoalbuminemia (2.7 g/dl; 3.5-5.2), coagulopathy (INR 1.77; 0.9-1.25). An ultrasound and computed tomography imaging revealed enlargement of the caudate lobe, obstructed hepatic veins with loss of the flow, splenomegaly, umbilical vein recanalization, ascites, pleural effusion. The liver biopsy showed sinusoidal dilatation and centrizonal congestion with no features of vein occlussive disease or drug-induced liver toxicity. Gastroscopy revealed small esophageal varices, hypertensive gastropathy, grooving and scalloping of the duodenum. The diagnosis of CD was confirmed by either villous atrophy IIIa according to the Marsh scale, increased intraepithelial lymphocytes 60/100 or serology (EmA IgA 1 : 800, tTG IgA > 130 U/ml). The patient received diuretics, albumin, gluten free diet, anticoagulant therapy with unfractionated heparin followed by low-molecular-weight heparin, with restoration of hepatic outflow and resolution of ascites. Two years later Duhring's disease was confirmed histologically with recovery after diet modification. Four years later she is still being treated with anagrelide, anticoagulant drugs and is on well controlled gluten-free diet. We suggest the use of serology to exclude CD in patients with BCS as a risk factor of thrombosis.

[3] Cardiovascular risk assessment in children with biliary atresia and Alagille syndrome

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Chronic cholestatic liver diseases are associated with disturbed lipid metabolism, which potentially could influence caradiovascular (CV) risk. The aim of the study was to evaluate the CV risk in children with billiary atresia (BA) and Alagille syndrome (AGS).

A prospective, single-centre study in children with BA (18 pts, 11.8 ± 6.1 years) and AGS (16 pts, 11.9 ± 5.4 years) with combined analysis of lipid metabolism, oxidative stress parameters, cIMT, PWV, obesity and hypertension in BA and AGS in relation to normal values. In AGS observed: higher levels of urea, aminotransferases, markers of cholestasis, total cholesterol (TC) (236.5 mg/dl vs. 179 mg/dl), LDL (166 mg/dl vs. 114.5 mg/dl), apo B, TC/HDL and LDL/HDL ratio. We observed increased TC in 13/16 pts with AGS and 8/18 pts with BA and triglycerides in 4/16 and 0/18 pts. However, cIMT was increased only in 2 pts with AGS and in 6 with BA. No significant difference was detected in cIMT-SDS between both groups. TC/HDL and LDL/HDL ratio correlated with cIMT in BA, no in AGS. PWV value was lower in patients with AGS compared with BA (p = 0.046). 1 patient with AGS and 3 pts with BA had PWV SDS value above normal. In AGS was a negative correlation between LDL and PWV and positive between TG and left ventricular mass index. We observed elevated blood pressure in 1/16 children with AGS and in 1/18 with BA.

Despite significant disturbances in lipid parameters only some children have increased IMT, still blood pressure in these patients is usually within the normal range. Thus, CV risk seems not to be significantly increased in children with BA or AGS.

[4] Hepatitis B virus reactivation or exacerbation during direct acting antivirals' therapy in patients with chronic hepatits C

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Introduction: Introduction of direct acting antivirals (DAAs) for general use in the treatment of chronic hepatitis C have brought reports about possibility of reactivation of HBV infection due to viral interferences in HCV/HBV.

Aim of the study was the analysis the frequency of HBV reactivation/exacerbation in patients infected with HCV treated with DAAs, who underwent liver or kidney transplantation or were prepared for such transplantations.

Material and methods: 110 patients (40 – liver and 35 – kidney recipients, 25 cirrhotic and 10 with renal insufficiency) were enrolled to the analysis. HBV infection status (HBsAg, HBV DNA in HBsAg (+) patients, HBcAb) was identified prior to DAAs initiation. During DDAs therapy, ALT activity was monitored every 2-4 weeks and HBV DNA in HBsAg positive patients was evaluated.

Results: Before DAAs treatment, 100% patients had HBsAg testing and 1 patient was positive with low HBV viremia; 74.5% had an anti-HBc test of which 32.9% were positive. During and after therapy with DDAs, no unexpected ALT peaks were detected. In HBsAg (+), peritoneal dialyzed patient, HBV viremia increased from 356 IU/ml to 7800 IU/ml in the end of treatment with DDAs and with ALT and GGT activity over 10-times upper limit and viremia 1.7 x 10^6 IU/ml six months later.

Conclusions: Patients after liver or kidney transplantation or with end-stage liver or kidney disease patients severe HBV exacerbation during DAAs therapy due to HCV infection seems to be rare, however possible, therefore routine monitoring of ALT activity in all treated patients with serologic evidence of HBV infection is mandatory.

[5] Achieving sustained virologic response (SVR) after DAA therapy for chronic hepatitis C (HCV) is associated with regression of liver stiffness, assessed by serial transient elastography (Fibroscan)

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Introduction: Presence of significant liver fibrosis determines clinical outcomes from chronic HCV infection.

Aim of the study was to assess the effect of DAA therapies on changes in liver fibrosis using transient elastography.

Material and methods: 65 patients with chronic hepatitis C who achieved SVR after DAA therapy were enrolled in this study. At 6 months after the treatment we repeated Fibroscan. In obese patients we used the XL Probe and performed subanalysis including only patients with baseline ALT levels < 100 U/l.

Results: In the studied population median TE prior to DAA therapy was 17.99 kPa, median TE 6 months post treatment was 12.79 kPa which equals a TE regression of 28.9%. In the subgroup of patients with baseline ALT < 100 U/l median TE prior to DAA therapy was 16.22 kPa, median TE 6 months post treatment was 12.03 kPa which equals 25.8% of TE regression. In the subgroup of F4 fibrosis median TE prior to DAA therapy was 26.15 kPa, median TE 6 months post treatment was 17.96 kPa which equals a TE regression of 31.3%. In the subgroup of F4 patients with baseline ALT < 100 IU/ml median TE prior to DAA therapy was 24.89 kPa, median TE 6 months post treatment was 18.14 kPa which equals a TE regression of 27.1%.

Conclusions: Treatment of chronic HCV with DAAs leads to regression of TE values over the first 6 months post-treatment, regardless of the basic ALT levels. The most spectacular changes were seen in the F4 group where 36% of patients experienced improvement fibrosis stage < 12.5 kPa.

[6] Long-term outcome of the patient with PFIC1 after successful partial external biliary diversion (PEBD) in early childhood

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7-months old patient with diarrhoea, intrahepatic cholestasis and rickets was transferred to our Clinic from the local hospital for further evaluation.

On admission severe pruritus, growth failure, jaundice, neurotic excoriations and hepatomegaly was found in clinical examination. Blood tests showed increased bilirubin and bile acids concentration in serum, slightly increased aminotransferases level and low GGTP activity. Other causes of intrahepatic cholestasis were ruled out. USG revealed hepatomegaly and gallstones. Test results indicated progressive familial intrahepatic cholestasis (PFIC) but histological examination of liver biopsy showed normal liver tissue. Genetic analysis confirmed the diagnosis of PFIC1. During hospitalization normalization of bilirubin and bile acids concentration was observed. Patient was released from hospital in a good general condition with specific medical therapy and was monitored in our outpatient clinic. At the age of 15-months clinical condition of the child deteriorated. Severe itchiness and jaundice occurred. Blood tests showed very high bile acids levels and worse hepatic cell function. Second liver biopsy showed bile plugs in bile ducts with fibrosis. Patient underwent partial external biliary diversion (PEBD). After PEBD general condition of our patient was mostly stable. He underwent all tests needed for liver transplant (LTx) for several times, but was disqualified each time because of quick improvement of liver function after antibiotic therapy, good histological results of liver biopsy and high risk of hepatic steatosis after LTx. He was last seen in our department as a 17-years old adolescent, 16 years after PEBD. Blood tests results were within normal limits.

[7] Cryptosporidiosis in a 10-year-old girl after liver transplantation – a case report

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Cryptosporidiosis (CP) is a common parasitic disease, caused by *Cryptosporidium*, which affects the small intestine and can affect the respiratory tract. Immunocompromised patients are in a risk group. Immunosuppressive treatment can lead to severe symptoms and form of CP.

We report a case of a 10-year-old girl after living donor liver transplantation (LT) performed in the first year of her life (due to hepatoblastoma), with plural hemangioma of the liver and portal hypertension. The girl received standard immunosuppressive treatment for ABO-incompatible liver transplantation (tacrolimus, mycophenolate mofetil, MMF). Eight years after LT, the histopathology examination of the liver biopsy showed ductopenia and early lesions of cirrhosis. The treatment was modified and MMF was switched to sirolimus. After that, the girl presented a chronic diarrhea and a loss of weight was observed (1.5 kg per 4 months). Three months after modification of immunosuppression, the girl was hospitalized of severe varicella. Chronic diarrhea caused high blood concentration of tacrolimus and sirolimus, due to that a reduction of drugs doses was applied. Parasite feces examination revealed oocysts of *Cryptosporidium* and identified CP as a cause of diarrhea. The girl was treated with Azithromycin for 14 days. Improvement was observed after the therapy, additionally control stool examination confirmed eradication of parasitic infection.

CP and chronic diarrhea may lead to dehydration and increased level of immunosuppression's drugs in patients after LT. Parasitic infections have to be included in differential diagnosis of diarrhea in patient after organ transplantation.

[8] Occurrence and clinical features of hepatocellular carcinoma among patients from the northeastern Poland

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Introduction: Hepatocellular carcinoma (HCC) is fifth in the incidence of malignancy and the third leading cause of death among patients with all cancers.

Aim of the study was conducted to assess the prevalence of HCC among patients in the North-East of Poland.

Results: The study included 67 HCC patients diagnosed according to the ICG for HN. 10% of patients aged 30 to 50 and in 90% over 51 years of age. In the period 2011-2015, an increase in HCC detection was observed. The most common (31%) patients with two focal lesions in the 6, 7 or 8 liver segments were observed. In 15% of patients metastatic tumors and 9% of portal vein thrombosis. In 72% of HCC patients coexisted with cirrhosis, 33% with HCV infection, 30% HBV, and 15% with NASH. In patients with cirrhosis, elevated AFP was observed in 83% and 58% in patients without cirrhosis ($p < 0.05$). The best therapeutic effects have been observed after liver transplantation. The efficacy of ablation in combination with sorafenib or partial resection was comparable.

Conclusions: In recent years, there has been an increase in the number of HCC cases in northeastern Poland. HCC is more common in men mostly after 50 years of age. AFP is a useful marker in the diagnosis and monitoring of HCV treatment in people with liver cirrhosis.

[9] *Helicobacter pylori* infection among patients with liver cirrhosis

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Introduction and aim of the study: Inflammatory changes in the stomach caused by *H. pylori* indirectly and directly affect liver function. Moreover, the bacteria may worsen course of the liver cirrhosis. The study aimed at evaluating the incidence of *H. pylori* infection among patients with liver cirrhosis, depending on the etiology and injury stage, scored according to Child-Pough classification. Stage of esophageal varices as well as endoscopic inflammatory lesions in the stomach were evaluated, depending on the presence of *H. pylori* infection.

Material and methods: The study included 147 patients with liver cirrhosis: 42 HCV infected, 31 HBV infected, 56 with alcoholic liver cirrhosis and 18 with primary biliary cirrhosis (PBC). Diagnosis of *H. pylori* infection was performed based on the presence of IgG antibodies in serum.

Results: *H. pylori* infection was found in 46.9% patients. The incidence of *H. pylori* infection among patients with post-inflammatory liver cirrhosis was significantly higher ($p = 0.001$), as compared to patients with alcoholic liver cirrhosis. Ammonia concentration was significantly higher in patients infected with *H. pylori*, compared to non-infected individuals (129 vs. 112 μmol/l; $p = 0.002$). Incidence of *H. pylori* infection in patients without esophageal varices was significantly lower, compared to patients with esophageal varices (14% vs. 60%; $p < 0.001$).

Conclusions: *H. pylori* infection is significantly more frequent among patients with post-inflammatory liver cirrhosis (infected with HCV or HBV) than in patients with alcoholic liver cirrhosis or PBC. *H. pylori* infection correlates with elevated concentration of blood ammonia and the incidence of esophageal varices.

[10] Influence of direct-acting antivirals on patients with history of hepatocellular carcinoma treatment

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Introduction: New interferon-free direct-acting antiviral (DAA) therapy caused major progress in HCV treatment. Current outcomes are promising especially in compensated cirrhosis. However, there are reports of accelerated HCC recurrence after surgery in patients treated with DAA. Influence of DAA therapy on timing and frequency of the recurrence after surgical treatment needs further documentation.

Material and methods: Thirty-nine HCV infected patients with advanced liver cirrhosis and history of surgical treatment for HCC in 2010-2016, were analysed in a case-control study. Fourteen patients received DAA therapy (DAA group) after tumour remission achieved by surgery and 25 patients were not treated with DAA (NDAA group). Follow up included multiphase CT-scan or MRI of the liver and AFP level in 3-6 month intervals.

Results: HCC recurrence was observed in 7 (50%) patients from DAA group and in 12 (48%) from NDAA group. One year relapse-free survival (RFS) was 80% in NDAA group vs. 50.7% in DAA group ($p = 0.15$). In DAA treated group the SVR was achieved in 13 patients (93%).

Conclusions: Use of DAA therapy in patients with a history of HCC may result in accelerated relapse of the disease, although the numbers in our study are too small to prove it statistically. Further observation with longer follow up and bigger patients group is needed. Contemporary HCV treatment is highly effective.

[11] Exposure to HAV infection in Polish HCV-positive patients

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Introduction: Hepatitis C virus (HCV) infection is an important public health problem in Poland. Superinfection with hepatitis A virus (HAV) can complicate the clinical course of chronic hepatitis C (CHC).

Aim of the study was to assess the HAV seroprevalence and factors related to anti-HAV positivity in Polish HCV-infected patients.

Material and methods: One thousand of HCV-positive, HBsAg and HIV-negative patients (M – 550, F – 450) aged 18-85 (42.4 ± 15.1) were evaluated for anti-HAV, then the relation of simple demographic and clinical parameters to HAV seroprevalence was investigated. Recent HAV infection was excluded in all doubtful cases.

Results: Anti-HAV prevalence in different age groups was as follows: 18-30 years – 4.5%, 31-40 years – 12.1%, 41-50 years – 34.5%, 51-60 years – 59.3%, > 60 years 83.2%. In univariate analysis, parameters related to the presence of anti-HAV in CHC patients (n = 986; anti-HAV-positive individuals who reported vaccination for hepatitis A were excluded) were: age (> 40 years), lower level of education, advanced liver disease (cirrhosis), birth place (rural area) and living place (town or city). In multivariable analysis, exposure to HAV was significantly more common in patients older than 40 (OR = 14.2; p = 0.0001), who were born in the country (OR = 2.6; $p < 0.0001$), who had lower level of education (OR =1.56; p = 0.012) and who were cirrhotic (OR = 1.55; p = 0.02).

Conclusions: Polish CHC patients should be informed about the opportunity of active prophylaxis of hepatitis A. In individuals older than 50 years it is reasonable to perform pre-vaccination anti-HAV assessment. We hypothesize that some HAV-induced factors (e.g. undefined autoimmune phenomena) could be related to progression of liver disease in CHC patients.

[12] Role of TNF-α promoter polymorphisms in chronic hepatitis B patients treated with PEG-IFNα

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Introduction and aim of the study: Despite the availability of the effective vaccine, hepatitis B virus (HBV) infection is a major health problem worldwide, with more than 240 million chronically infected individuals. Treating chronic hepatitis B (CHB) with PEG-IFNα suppresses virus replication and reduces the risk of liver damage, but is effective only in about 30% patients. Additionally, PEG-IFNα therapy is both expensive and associated with severe adverse effects. Therefore, identification of PEG-IFNα treatment response predictors is highly desirable. In this study we investigated whether common single-nucleotide polymorphisms in the TNFα promoter region might influence the susceptibility of CHB and response to PEG-IFNα.

Material and methods: Two hundred and thirty one patients diagnosed with CHB constituted the study group and one hundred healthy individuals were included in the control group. Treatment response was assessed in 86 patients by HBV DNA and ALT normalization at week 48 after treatment accomplishment. Genotyping of TNFα polymorphisms: rs1799964 (–1031), rs361525 (–238), rs1800629 (–307), rs1800630 (–863), and rs1799724 (–857), was performed using MALDI-TOF mass spectrometry.

Results: Allelic distribution of rs1799964 (p = 0.022) and rs1800630 (p = 0.03) differed significantly between the study and control groups. ALT activity normalized more frequently in response to treatment among rs1799724 CC homozygotes (p = 0.0385). Rs1800629, rs1800630 and rs1799724 genotypes predicted HBV DNA presence after treatment accomplishment (p = 0.0098, 0.04 and 0.012, respectively).

Conclusions: TNFα promoter region polymorphisms might determine response to HBV infection. Better understanding of host genetic background in the susceptibility to HBV infection and treatment response might be crucial for the proper management of CHB.

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[13] Liver abscess in a 11-year-old boy after liver transplantation

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Liver abscess is a rare pathology caused by bacteria, fungi or protozoa. Most often pyogenic liver abscess (PLA) is a consequence of the abdominal infections – cholangitis, appendicitis, and diverticulitis. One of the risk factors for PLA is immunosuppression.

The immunosuppressed (Tacrolimus) patient, 11-year-old boy after liver transplantation in his first year of life due to biliary cirrhosis, was admitted to CMHI with a several-day history of fever, vomiting, diarrhea, and jaundice. Laboratory tests showed increased inflammatory markers, cholestasis, and elevated activity of transaminases. An abdominal ultrasound examination did not reveal any abnormalities. During diagnosis PTLD, sepsis, and urinary tract infection were excluded. Empirical antibiotic therapy was applied (Tienam, Metronidazol, Amicacin), which resulted in lower inflammatory parameters and decreased transaminase activity. Due to the recurrence of subfebrile temperature and re-growth of inflammatory markers, after one week of treatment, antibiotic therapy was modified (Meronem). The abdominal ultrasound was repeated, this time with a focus on heterogeneous and hypodense area in the liver. Computed tomography confirmed the diagnosis of a liver abscess. The patient was qualified for intensive, long-term, antibiotic therapy (Sulperazon, Targocid). After two weeks of treatment a control ultrasound examination was performed and a significant reduction in the previously observed change was noticed. Another CT scan, seven months after the end of treatment, showed no abnormalities in the liver.

PLA is a focal change in the liver and unrecognized can lead to many complications. The case underlines the importance of the differential diagnosis in hepatic abscesses, especially in patients with the risk factors.

[14] Liver copper concentration in differential diagnosis between presymptomatic Wilson disease and autoimmune hepatitis

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Introduction: Liver copper concentration is regarded to be a sensitive and specific diagnostic test in Wilson disease (WD). Concentrations above 250 μg/g dry weight have high positive predictive value in adults, whereas concentrations below 50 μg/g practically exclude diagnosis of WD. Differential diagnosis of WD should include autoimmune hepatitis (AIH) with autoantibodies as one of the diagnostic criteria. However they can be positive in about 50% of WD patients. There is no data concerning liver copper in children with WD in comparison with AIH.

Material and methods: 74 patients with WD diagnosed according to Ferenci score were the study group. 41 patients with AIH were the control group. They all have liver biopsy performed with liver copper measurement. Sensivity and specifity were assessed for cutoff value of 250 μg/g and discriminant ability and optimal cutoff point were established with ROC curve analysis.

Results: Liver copper concentrations were 882; 626; 1124 (median, Q1, Q3) μg/g and 47.2; 28.37; 73 μg/g in study and control group respectively. For cutoff point of 250 μg/g, the sensivity was 0.96 (0.89; 0.99 [95% CI]) – 3 out of 74 patients had liver copper under 250 μg/g; and the specifity was 1 (0.91; 1) – all patients had liver copper below 250 μg/g. Area under ROC curve was 0.998. The optimal cutoff point for our groups was 304 μg/g with sensivity 0.96 (0.89; 0.99) and specifity 1 (0.91; 1).

Conclusions: Liver copper concentration has high discriminant ability in differential diagnosis between presymptomatic WD and autoimmune hepatitis in children.

[15] Liver copper concentration in differential diagnosis between presymptomatic Wilson disease and primary sclerosing cholangitis

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Introduction and aim of the study: Liver copper concentration is regarded to be a sensitive and specific diagnostic test in Wilson disease (WD). Concentrations above 250 μg/g dry weight have high positive predictive value in adults, whereas concentrations below 50 μg/g practically exclude diagnosis of WD. Previous studies have suggested that the majority of patients with the primary sclerosing cholangitis (PSC), had increased hepatic copper. There is no data concerning liver copper in children with WD in comparison with PSC.

Material and methods: 74 patients with WD diagnosed according to Ferenci score were the study group. 15 patients with PSC or overlap syndrome (autoimmune hepatitis/PSC) were the control group. They all have liver biopsy performed with liver copper measurement. Sensivity and specifity were assessed for cutoff value of 250 μg/g and discriminant ability and optimal cutoff point were established with ROC curve analysis.

Results: Liver copper concentrations were 882; 626; 1124 (median, Q1, Q3) μg/g and 54.5; 31.6; 117 μg/g in study and control group respectively. For cutoff point of 250 μg/g, the sensivity was 0.96 (0.89; 0.99 [95% CI]) – 3 out of 74 patients had liver copper under 250 μg/g; and the specifity was 0.88 (0.63; 0.98) – 2 out of 15 patients had liver copper over 250 μg/g. Area under ROC curve was 0.985. The optimal cutoff point for our groups was 304 μg/g with sensivity 0.96 (0.89; 0.99) and specifity 0.93 (0.68; 0.998).

Conclusions: Liver copper concentration has high discriminant ability in differential diagnosis between presymptomatic WD and PSC, however optimal cutoff point (304 μg/g) should be slightly higher.

[16] Mesenchymal hamartoma of the liver – a rare benign pediatric tumor

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Mesenchymal hamartoma of the liver (MHL) is a rare developmental lesion concerning young children under 2 years of age, however it can occasionally develop in the adults. This lesion is also recognized under synonimes as cystic hamartoma, cavernous lymphangioadenomatoid tumor or benign mesenchymoma. MHL is the second most common pediatric hepatic tumor after hemangiomas. It is usually a big solid-multicystic slowly growing lesion with a slight elevation of serum alpha-fetoprotein. MHL can be complicated with rupture and ascites, vascular shunts or exceedingly rarely malignant progression. Some tumors undergo partial regression. Diagnosis of this lesion is based on its radiological and clinical presentation. Histopathology is specific with morphological spectrum.

During last 10 years, six children with mesenchymal hamartoma were diagnosed and operated in our center. There were two girls and four boys in the age ranged 4-17 months. All tumors presented with abdominal enlargement, moreover AFP level was increased in five children from 20 to 20000 IU. Radiologically five lesions were problematic, showing some indefinite features of vascular lesion (2), hepatoblastoma (2) or inborn defect as gastro-intestinal doubling (1). One tumor was mainly solid, while the rest were multicystic. Two cases primarily underwent needle biopsy, with erroneous hepatoblastoma diagnosis in one boy causing consecutive neoadjuvant chemotherapy, and inconclusive answer in the second child. In three patients intraoperative exam was performed with two generalized diagnoses of non-malignant lesion and inconclusive decision in the third one. The final histo-

logical diagnosis of MHL was based on morphology and immunophenotyping. One case showing complex picture, diagnosed as mixed vascular-hamartomatous lesion.

[17] Challenges in genetic confirmation of clinical diagnosis in patients with autosomal recessive polycystic kidney disease

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Introduction: Autosomal recessive polycystic kidney disease (ARPKD) is caused by mutations in PKHD1, which encodes fibrocystin. Before the era of next-generation sequencing (NGS), diagnosis of ARPKD was based mainly on clinical criteria due to the large size of this gene.

Material and methods: Two female patients (A and B) with a clinically established diagnosis of ARPKD, after combined liver and kidney transplantation, were tested for PKHD1 mutations by Sanger sequencing. Patient A was screened at the age of 4 years when the same clinical diagnosis was made in her younger brother. Patient B has a negative family history of ARPKD. In both patients liver involvement included hepatosplenomegaly, increased liver echogenicity and histologically confirmed congenital hepatic fibrosis, while abnormalities of the kidney were associated with bilateral cysts and poor corticomedullary differentiation.

Results: Although both patients fulfilled the clinical criteria of ARPKD, surprisingly Sanger sequencing did not reveal any mutations in the coding sequence of PKHD1. Broader molecular analysis with NGS is intended.

Conclusions: These two cases show that Sanger sequencing of PKHD1 might be insufficient to confirm the diagnosis of ARPKD in some patients fulfilling all clinical criteria of the disease. We hope that NGS might be helpful in identifying potential changes in the non-coding region of PKHD1, or in other genes associated with polycystic kidney disease, as well as in the selection of candidate genes responsible for the ARPKD phenotype.

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[18] Iron accumulation in skeletal muscles of patients with diagnosis of hereditary hemochromatosis

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In HFE-hereditary hemochromatosis (HH) iron overload leads to progressive damage of parenchymal organs. Patients frequently complain of generalized muscle weakness which has been associated with endocrinopathy. However, potential iron accumulation in muscles may result in the reduced exercise capacity. The aim of the study was to evaluate iron content in skeletal muscles in HH.

15 patients with HH, carriers of HFE gene mutations (age range: 18-65 years) were compared to 15 healthy controls. All subjects presented exponents of excessive iron accumulation in serum. T2* mapping by MRI (MyoMaps application on Siemens Aera 1,5 T scanner, Siemens AG,, Germany) was performed to assess for myocardial and liver iron overload. T2* maps were also assessed for skeletal muscle T2* values and compared to skeletal muscle T2* of healthy controls. All T2* measurements were performed in regions of interest (ROIs) with low residual error (< 10%) as assessed by the Segment software (Medviso AB, Sweden). Statistical analysis was done using STATISTICA data analysis software, version 12. The *p*-value less than 0.05 was considered as being significant.

No unequivocal cases of cardiac iron deposits were identified in the study group. Two patients had myocardial T2* values below the reference range. While the control group was younger, T2* values showed no significant correlation with age in both groups and it confirmed the presence of iron deposits in the liver in the majority. T2* values in ROIs placed over the latissimus dorsi (LD) and pectoralis major (PM) muscles in HH patients were significantly lower compared to controls.

Results indicate higher iron content in skeletal muscles of HH patients. The assessment of skeletal muscle T2* values provides additional insight in muscle tissue involvement, may explain muscle weakness and fatigue observed in some, and potentially guide management decisions. Further investigation is warranted in larger patient cohorts.

[19] The correlation of autoantibodies positivity with the microscopical changes in the liver in HCV infected patients

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Introduction: HCV infection may lead to the incidence of autoimmune processes and production autoantibodies such as ANA, SMA, LKM, AMA, APCA. The clinical significance of these autoantibodies is still unknown. Some authors report that the autoantibody-positive chronic hepatitis due to HCV is more common in females and exhibits a more severe biochemical and histological activity.

Material and methods: A total of 363 patients infected by HCV (197 males and 166 females, median age 41 years) with consecutive liver biopsies were included in the study. All patients were diagnosed on the basis of plasma presence of anti-HCV antibodies by immunoenzymatic method (Abbot, Chicago, USA) and presence of, HCV RNA by PCR and RT-PCR, retrospectively. The sera of all patients were screened by IIF parallel to the liver biopsy examination and positive titer was considered by dilution of the examined serum > 1 : 80. Statistical analysis was performed using Statgraphics Plus v. 4.1. software.

Results: Between 363 HCV infected autoantibodies were found in 66 patients (18%). The difference between the age of patients with antibody positivity and negativity was statistically significant ($p = 0.0052$). The presence of autonatibodies was marginally significant in males ($p = 0.084$, 22% males vs. 15% females). In the group of autoantibody positive patients we have found ANA in 26%, ANA/SMA in 14%, ANA/APCA in 5%, ANA/LKM in 2%, ANA/AMA in 2%, ANA/SMA/APCA in 2%, SMA in 21%, APCA in 20%, LKM in 8%, AMA in 5%.

Conclusion: We found only marginally significant difference in the necroinflammatory activity in autoantibody positivity (LKM+) vs. negativity ($p = 0.064$). The grade of fibrosis was similar in patients with and without autoantibodies. The distribution of lymph follicles and steatosis was similar in patients with and without autoantibodies.

[20] Histopathological findings in congenital hepatic fibrosis

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Introduction: Congenital hepatic fibrosis is an autosomal recessive malformation of the small interlobular bile ducts resulting with the presence of immature bile ducts with persistent ductal plate and an abundant fibrous tissue between portal tracks. It represents a group of developmental disorders termed hepatorenal fibropolycystic diseases.

Aim of the study was to analyse microscopical changes in the liver to make possible the differentiation of congenital hepatic fibrosis from idiopathic portal hypertension and early liver cirrhosis.

Material and methods: Four patients with the heaptosplenomegaly and signs of portal hypertension undewent liver needle biopsy. The material was fixed in 4% buffered formalin, stained with H&E, PAS, PAS', Gomori, Azan and mapped using Dako CK7 i CK19.

Results: By microscopical examination of the liver, widened fibrous bands are observed in the portal and periportal areas, containing an increased number of irregularly shaped or rounded proliferating bile ducts lined by cuboidal epithelium. Severe fibrosis was observed in all four cases. Characteristic proliferation of

small bile ducts showed strong expression of CK7 and mild to moderate CK19. In the contrast to liver cirrhosis, hepatic lobules presented a normal architecture and contained normal hepatocytes. In one case, associated cholangitis was observed.

Conclusion: Liver biopsy with the exact analysis of portal fibrosis and ductular proliferation is necessary for the definite diagnosis of congenital hepatic fibrosis.

[21] Analysis of liver fibrosis and steatosis, HBsAg concentration and selected lipids values in patients with chronic hepatitis B tenofovir treated

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Introduction and aim of the study: Influence of lipid metabolism on liver steatosis and fibrosis and its association with HBsAg concentration.

Material and methods: We have studied 27 CHB patients with HBeAg negative status, treated with tenofovir in 2015-2016. Patients were between 21 and 75 years of age (mean 50 ± 18.79). The control group consisted of 11 healthy volunteers. Measurements of total cholesterol, triglycerides, LDL, HDL and LDL receptor concentration, quantitative HBsAg, as well as transient elastography using Fibroscan® with CAP option were performed on an average of three times during one year of follow-up.

Results: There were no statistically significant differences in total cholesterol, triglyceride, LDL, HDL levels. The virological response indicated a reduction HBV DNA levels to undetectable levels after one year of treatment. Significant differences in LDL receptor concentrations were seen in patients treated with antiviral (mean 3.66 ± 2.2 ng/ml) compared to control (mean 18.9 ± 5.7 ng/ml). A small decrease in the amount of HBsAg was observed ($p < 0.88$) and an increase in the LDL receptor concentration ($p = 0.44$). The liver fibrosis value was lowered (mean value 7.5 ± 2.7 kPa to mean value 5.7 ± 2.91 kPa). HBsAg levels were negative correlated with fibrotic changes ($p = 0.001$) and LDL receptors ($p = 0.00028$).

Conclusions: The CHB patients have disturbances of the lipid metabolic pathway. Normal lipid metabolic pathway is being restored in the hepatocytes during tenofovir treatment.

[22] Acute HCV after OLT with successfully 8 weeks treatment with ledipasvir (LDV)/sofosbuvir (SOF)

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Introduction: Treatment of acute HCV infection can be started if HCV RNA is maintained 12 weeks after diagnosis of HCV infection and PegIFN-alpha 2a or 2b monotherapy is used for 12 weeks. Naive patients with genotype 1 or 4 and contraindications to PegIFN-alpha can be treated with the noninterferon therapy – ledipasvir 90 mg and sofosbuvir 400 mg (LDV/SOF). There is small data about efficacy of LDV/SOF in immunosuppressed patients after orthotopic liver transplantation (OLT) in acute phase of HCV infection.

Case report: A 53-year-old Polish woman after OLT (May 2016) because of polycystic liver diseases – with coexistent arterial hypertension, renal insufficiency with polycystic disease, pancreas cysts, pulmonary embolism, 2 hemorrhagic brain strokes – 2012 right and 2014 left with paresis on the left and thyroid nodular goiter-euthyreosis had a liver biopsy (December 2016) caused by elevation of AST – 838 U/l, ALT – 800 U/l, GGTP – 99 U/l, ALP – 75 U/l.

In biopsy: Acute lobular inflammation, less severe portal inflammation, spilled swelling, fatty acidosis and degeneration. No features of acute rejection. Serum CMV-DNA and HBV-DNA negative, HCV-RNA – 107 IU/ml/Genotype 4. Anti-HCV-negative also in later studies. She began treatment with LDV/SOF (February 2017). We assessed the baseline HCV-RNA 15 x 108 IU/ml and in 4, 6, 8 week of treatment. We observed the HCV RNA < 15 IU/ml in 4 week and undetectable serum HCV-RNA in 6 and 8 week and stable serum Tacrolimus concentration and activity of aminotransferases. She completed LDV/SOF therapy without adverse effects.

Conclusion: LDV/SOF for 8 weeks is effective and well tolerated in immunosuppresed patient with acute HCV after OLT.

[23] Familial occurrence of hepatocellular carcinoma (HCC) in chronic hepatitis B – case reports

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We present a case of familial occurrence of HCC in 2 brothers (Polish) with chronic hepatitis B. The older brother was diagnosed in age of 22 with hepatitis B infection, HBeAg(+), mild hepatitis in histopathology (2002: G1, S1), HBV DNA > 10^8 IU/ml. He did not agree for the antiviral treatment and gave up regular medical controls in years 2007-2012. In 2012 after detection of thrombocytopenia liver cirrhosis and multifocal HCC with expanded criteria of liver transplantation were confirmed. Treatment with entecavir was started and liver transplantation was performed. The patient continued treatment with entecavir in combination with hepatitis B immunoglobulin and remained with undetectable HBV DNA and HBsAg for 4 years. In 2016 a reseroconversion of HBsAg was observed without relapse of HBV DNA. The younger brother (born in 1984) was diagnosed with chronic hepatitis B HBeAg(+) at the stage of cirrhosis in 2012 (liver stiffness: 28.0 kPa), thrombocytopenia, HBV DNA > 10^8 IU/ml. He started treatment with entecavir and achieved HBeAg/anti-HBe seroconversion, undetectable HBV DNA, significant reduction of liver stiffness (7.3 kPa). Despite that HCC was diagnosed based on regular screening USG and AFP examinations. The patient is qualified to liver transplantation. Patients' father died at the age of 45 due to HBV cirrhosis and HCC.

Conclusions: Patients with chronic hepatitis B require regular outpatient specialist care. Good response to antiviral treatment and liver stiffness regression should not diminish oncological vigilance, especially in patients with familial history of HCC.

[24] Predictive power of Model for End-stage Liver Disease and Child-Turcotte-Pugh score in acquiring bacterial infection in patients with liver cirrhosis

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Aim of the study was to assess the performance of CTP and MELD scores and the changes of these scores during hospitalization in predicting bacterial infection incidence in patients with liver cirrhosis.

Material and methods: There were selected 174 hospitalizations of patients with liver cirrhosis. The diagnosis of cirrhosis was made on the basis of clinical, biochemical, ultrasonic, histological and endoscopic findings. CTP, MELD at admission and ΔCTP and ΔMELD were calculated.

Results: Bacterial infection has been diagnosed in 28.7% of cirrhotic patients vs. 7.5% in control group ($p < 0.001$). The most common was urinary tract infection (UTI), followed by pneumonia and sepsis. The more severe liver failure, the greater bacterial infection prevalence and mortality. Patients with decompensated liver cirrhosis was infected more often than subjects with compensated cirrhosis (48.6% vs. 13.0%, $p = 0.003$). Calculated MELD score was also related to the bacterial infection prevalence and mortality. The most common bacteria isolated from patients with UTI were *Escherichia coli*, *Enterococcus faecalis* and *Klebsiella pneumoniae*. Gram negative bacteria were also responsible for SBP and together with Gram positive streptococci and staphylococci were the microorganism isolated from blood culture in septic patients. Significant differences were found between albumin and bilirubin concentration, prothrombin index, CTP classification, MELD score and red blood cell count in cirrhotic patient with or without bacterial infection.

Conclusions: Bacterial infection prevalence is relatively high in patients with liver cirrhosis. The combination of CTP and MELD scoring method combined with their kinetics allow to predict bacterial infection occurrence and higher short-term mortality.

[25] Complete blood count of deceased liver donors and the results of transplantation

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Introduction: Evaluating donor characteristics is mandatory for the recipients' safety and aiding predicting outcomes.

Aim of the study was to assess whether abnormalities in complete blood count (CBC) of DBD liver donor present risk factors.

Material and methods: Early and long-term results [1-year recipient (1RS+/1RS–) and graft (1GS+/1GS–) survival, 5-year recipient (5RS+/5RS–) and graft (5GS+/5GS–) survival rates] of liver transplantation were evaluated in connection with donor CBC [HGB (g/dl), HCT (%), WBC (k/mm^3), PLT (k/mm^3)] respectively for 2804 transplantations in the years 1998-2013 and 1724 in the years 1998-2009. Data originated from Poltransplant's records.

Results: 1RS and 1GS for total group: 84.3% (2364/2804) and 81.3% (2279/2804). 5RS and 5GS: 72.8% (1255/1724) and 68.8% (1186/1724). HGB for: 1RS+ = 11.4, 1RS– = 11.5, p = 0.327; 1GS+ = 11.4, 1GS– = 11.6, p = 0.093; 5RS+ = 11.1, 5RS– = 11.3, p = 0.071; 5GS+ = 11.0, 5GS– = 11.4 – was statistically (p = 0.009) lower for 5GS+. HGB < vs. ≥ 12 had no effect on: 1RS+ vs. 1RS– (84.8% vs. 84.0%, p = 0.535) and 1GS+ vs. 1GS– (82.3% vs. 80.4%, p = 0.194); 5RS+ vs. 5RS– (74.0% vs. 71.5%, p = 0.264) and 5GS+ vs. 5GS– (70.6% vs. 66.2%, p = 0.059). HCT for: 1RS+ = 34.4, 1RS– = 34.9, p = 0.171; 1GS+ = 34.4, 1GS– = 35.0, p = 0.076; 5RS+ = 33.6, 5RS– = 34.1, p = 0.174; 5GS+ = 33.5, 5GS– = 34.2 – was statistically (p = 0.048) lower for 5GS+. HCT < vs. ≥ 36 did not affect: 1RS+ vs. 1RS– (85.0% vs. 83.3%, p = 0.23) and 1GS+ vs. 1GS– (82.5% vs. 79.8%, p = 0.074); 5RS+ vs. 5RS– (73.2% vs. 71.6%, p = 0.454) and 5GS+ vs. 5GS– (69.8% vs. 66.8%, p = 0.197). WBC for: 1RS+ = 13.8, 1RS– = 14.4, p = 0.072; 1GS+ = 13.8, 1GS– = 14.4 – was statistically (p = 0.044) lower for 1GS+; 5RS+ = 13.6, 5GS– = 14.2, p = 0.079; 5GS+ = 13.6, 5GS– = 14.2 – was statistically (p = 0.026) lower for 5GS+. WBC < vs. ≥ 10 did not affect: 1RS+ vs. 1RS– (85.5% vs. 83.8%, p = 0.28), 1GS+ vs. 1GS– (82.9% vs. 80.7%, p = 0.204); 5RS+ vs. 5RS– (75.2% vs. 72.0%, p = 0.19) and 5GS+ vs. 5GS– (71.8% vs. 67.7%, p = 0.102). PLT for: 1RS+ = 184, 1RS– = 188, p = 0.414; 1GS+ = 184, 1GS– = 189, p = 0.261; 5RS+ = 176, 5RS– = 183, p = 0.154; 5GS+ = 175, 5GS– = 184, p = 0.057. PLT < vs. ≥ 150 did not affect: 1RS+ vs. 1RS– (84.4% vs. 84.0%, p = 0.831) 1GS+ vs. 1GS– (81.4% vs. 81.0%, p = 0.808); 5RS+ vs. 5RS– (74.6% vs. 71.0%, p = 0.109), 5GS+ vs. 5GS– (70.9% vs. 66.8%, p = 0.077).

Conclusions: 1. Abnormalities in donor CBC do not influence the early and long-term recipient survival. 2. PLT does not affect the early and long-term transplant outcomes. 3. WBC affects early and late graft survival; reaches lower values in donors providing recipients with at least 1 and 5-year graft function, possibly because of the corresponding risk of infection transmission. 4. Significant deviations of HGB and HCT in groups of grafts that survived and not survived five years, do not display clinical justification.

[26] Safety of regional citrate anticoagulation for continuous renal replacement therapy in patients with liver failure – case report

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Introduction: Continuous renal replacement therapy (CRRT) with regional citrate anticoagulation is currently a first-line treatment of patients with acute kidney injury (AKI) in the ICU. Impaired citrate metabolism is expected in liver failure. In severe hepatic impairment, as in end-stage liver disease, lack of citrate metabolism is observed, which leads to increased blood citrate level and metabolic acidosis, a potentially fatal complication. Many studies prove that in this group regional citrate anticoagulation is safe with close monitoring and prompt treatment when complications develop.

Case report: 40-year-old patient was admitted to the ICU with acute respiratory failure in course of pneumonia and decompensated chronic liver failure. Concomitant AKI required CRRT, citrate-based method was used. After 24 h of treatment, metabolic acidosis developed with an increase in total-to-ionized calcium ratio. Despite 50% reduction in citrate dose, acidosis progressed with total-to-ionized calcium ratio exceed-

ing 2.5. Citrate anticoagulation was stopped. CRRT without anticoagulation was temporarily used due to present coagulopathy. After two days, improved liver function allowed for reintroduction of citrate anticoagulation, which was then continued with good tolerance.

Conclusions: Citrate anticoagulation for CRRT can be effectively and safely used in patients with liver failure. Close monitoring of acid-base balance, total and ionized calcium is required. Change of anticoagulation method is advised with signs of citrate accumulation and metabolic acidosis.

[27] APRI as a fibrosis marker in children with autoimmune hepatitis (AIH)

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Introduction: Autoimmune hepatitis has aa progressive course thus it is important to find easy and reliable clinical test that could allow early detection of the disease progression. Liver biopsy is a standard for the assessment of staging of liver disease but the procedure is invasive, painful and there is risk of complication thus alternative methods of liver fibrosis assessment are under investigation. APRI-AspAT-to-Platelet Ratio Index is simple indirect fibrosis test and could be obtain during routine blood test.

Aim of the study was to correlate the APRI with staging of liver disease assessed by liver biopsy in children and adolescents with AIH.

Material and methods: Blood samples and standard liver biopsies were taken from 46 children (F – 33, M – 13) aged 5.5-18 (14.5 ± 3.8) with AIH. Routine blood samples were collected from all patients and Aspat to Platelet Ratio was calculated. All children had routine liver biopsy. Liver biopsies were scored according to Batts and Ludwig classification and patients were classified according to staging into two groups. Patients with no or minimal fibrosis (staging 0-1) and patients with well visible fibrosis (staging 2-4). APRI between two groups was compared and receiver operating characteristics (ROC) analysis was used to calculate the power of the assays to detect advanced liver fibrosis (AccuROC, Canada).

Results: Mild liver fibrosis was present in 8 and advanced fibrosis was found in 38 patients. Children with advanced fibrosis had significantly higher APRI (1.59 vs. 0.30, $p < 0.01$) than children with mild or no fibrosis. Significant ability to differentiate children with advanced fibrosis from those with mild or no fibrosis was found. Area under ROC curve was 0.736111 (AUC = 0.7361) with sensitivity (95% CI) 0.58 (0.407565 to 0.744859) and specificity (95% CI) = 1 (0.630583 to 1 [97.5% one-sided CI]).

Conclusions: APRI can differentiate children with advanced fibrosis from those with mild or no fibrosis. Aspat to Platelet Ratio Index as a non-invasive test can be useful to detect the progression of the fibrosis in AIH children.

[28] Overlap syndromes of autoimmune hepatitis in adult patients

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Introduction: Overlap syndromes represent a variant of autoimmune hepatitis (AIH) with histopathological and serological features of primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC) or autoimmune cholangitis (AICH), frequently with the coexistence of biochemical cholestasis. Clinical course and incidence of these diseases is yet not fully understood.

Material and methods: We analysed 124 consecutive liver biopsies of patients with initial diagnosis of autoimmune hepatitis. 19 patients were males and 105 females, median age 41 yrs. The serum samples of all patients were screened for the presence of ANA, AMA, ASMA, anti-LKM, cANCA and pANCA by the indirect immunofluorescence test (IIF) parallel to the liver biopsy examination.

Results: Overlap syndrome was diagnosed by histopathological criteria in 16 patients (13%). 3 patients were diagnosed as AIH/PSC, 5 patients as AIH/PBC and 8 patients as AIH/AICh. Presence and pattern of autoantibodies not always corresponded with histopathological picture. Unexpectedly all patients with overlap syndrome had positive pANCA antibodies.

Conclusion: Liver biopsy is important tool in diagnosis of overlap syndrome. In all cases of AIH liver biopsy should be performed.

[29] Efficacy, Safety and Clinical Outcomes in HCV Genotype 1-Infected Patients Receiving Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir ± Ribavirin: TOPAZ-I Interim Data from Russia, Bulgaria, Poland, and Romania

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Aim of the study: Ombitasvir/paritaprevir*/ritonavir (*identified by AbbVie and Enanta) and dasabuvir (3-DAA) ± ribavirin (RBV) treatment is effective and safe for patients infected with hepatitis C genotype 1 (HCV-GT1). The primary goal of TOPAZ-I, an ongoing global phase 3b trial, is to evaluate the impact of sustained virologic response 12 weeks post-treatment (SVR12) on liver disease progression over five years' follow-up in 3-DAA ± RBV-treated patients. We present final efficacy and safety data and interim results on liver stiffness evolution (up to post-treatment week 24 [PTW24]) and clinical outcomes in patients from Russia, Bulgaria, Poland, and Romania.

Material and methods: In TOPAZ-I, adults with chronic HCV-GT1 infection, treatment-naïve or interferon-therapy-experienced, without cirrhosis or with compensated cirrhosis, received 3-DAA ± RBV, per label. These interim results include SVR12, adverse events (AEs), clinical outcomes (hepatocellular carcinoma, liver decompensation, liver transplantation, death) and liver stiffness evolution. SVR12 data were analyzed using the intent-to-treat (ITT) population (missing data imputed as failures).

Results: Among the 290 patients enrolled (treatment-naïve, 40%; GT1b, 96%; F4, 21%), SVR12 was 99%: two patients relapsed by PTW12. The only treatment-emergent AE occurring in ≥ 10% of participants was headache (10%). There were no AE-related trial discontinuations. Two serious AEs and one death were reported, none deemed related to study drug. Preliminary data (PTW24, GT1b, $n = 41$) show liver stiffness decrease in cirrhotic patients (median change from baseline [min, max], kPa: –5.7 [–33.1, 8.3]).

Conclusions: These regional TOPAZ-I results confirm the efficacy and safety of 3-DAA ± RBV in HCV-GT1-infected patients. Liver stiffness decrease was observed in cirrhotic patients.

[30] Family outbreak of hepatitis A

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This thesis presents a family history of the hepatitis A outbreak. The 6-year-old girl was admitted to the hospital due to several days of gastrointestinal symptoms (abdominal pain, vomiting) and jaundice. At the same time the patient's mother reported the symptoms of a flu-like infection complicated by jaundice and vomiting. According to an epidemiological anamnesis, the father of the child had been hospitalized a month before due to jaundice. Then he was suspected of hepatitis C because of the presence of anti-HCV antibodies in serum. At the admission, the girl's laboratory results: ALT – 834 U/l, AST – 374 U/l, with cholestasis (direct bilirubin – 5.62 mg/dl, GGTP – 99 U/l, ALP – 356 U/l, bile acids – 77 μmol/l) were found. Mother's tests results also reported elevated aminotransferases (ALT – 2560 U/l, AST – 876 U/l), hyperbilirubinemia (5.65 mg/dl) and elevated GGTP – 201 U/l, ALP – 216 U/I. HCV and HBV infection were excluded in both patients. The presence of anti-HAV IgM antibody in serum in ELISA test was revealed. Acute hepatitis A was diagnosed. The course of the disease in the patient was mild. During the first week of hospitalisation an im-

provement of laboratory results was observed. Father and two siblings were also admitted to the ward from a home contact for diagnostic purposes. HAV infection in the child's father was serologically-confirmed as well. Both the 17-year-old girl and the 15-year-old boy did not have any anti-HAV antibodies. As a post-exposure prophylaxis HAVRIX JUNIOR vaccine was administered.

[31] Liver tumors. Diagnostic puzzles – unexpected diagnoses

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The authors have been dealing with the diagnosis and treatment of liver tumors for years. Between 2011 and 2013 they were co-organizing a training program, financed by the Human Capital Operational Program, designed for radiologists, radiology technicians and physicians referring patients with diagnosed or suspected liver tumors.

Technological advances and the good preparation of diagnostic physicians allow to diagnose liver tumors with nearly 96% certainty, based on radiological tests. However, we are still encountering surprises in the inconsistency between diagnostic tests and surgical reality. In this study we would like to present interesting cases of such inconsistencies.

[32] Liver transplant acquired food allergy (LTAFA) in a child who received a split liver graft in the neonatal period – case report

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Introduction: Allergic disease is increasingly reported after pediatric liver transplantation. It occurs in about 14% of pediatric liver transplant recipients, with manifestations including food allergy, eczema, allergic rhinitis, and asthma. The pathomechanism of this abnormality is still unclear, but has been ascribed by some to tacrolimus treatment. Tacrolimus induces an imbalance in T-helper type 1 (Th1) and T-helper type 2 (Th2) cells in the food allergy process. We report a case of the child who developed LTAFA 4 months after liver transplantation.

Methods and results: We present 20-months old boy who received a split liver graft at 3 weeks of age due to acute liver failure of undetermined cause. Immunosuppression therapy after transplantation was typical and included: tacrolimus, corticosteroids and mycophenolate mofetil. The first manifestation of allergy occurred 4 months after liver transplantation (LT) as atopic dermatitis. He needed to use elimination diet based on an ultrafiltrated whey hydrolysate (Bebilon pepti), combined with avoidance of solid foods during the first 6 months of life. As the therapy was unsuccessful, we prescribed diet based on casein hydrolysate formula (Nutramigen). Treatment consists of elimination of the allergenic foods, administration of hypoallergenic formula, antihistamine medication, emulsifying ointment to the skin twice daily, corticosteroid ointment to his skin twice daily, protopic 0.1% twice daily to face. In spite of all, he did not respond to the therapy. Moreover, he manifested severe and recurrent respiratory tract infections during the first year of his life. Total eosinophil count and serum immunoglobulin (Ig) E were increased, and specific IgE was positive for some food allergens (alpha-lactalbumin, beta-lactoglobulin, casein, egg white, egg yolk and rice). Therefore 15 months post transplantation immunosuppression therapy was changed from tacrolimus to cyclosporine A, after which total eosinophil count decreased and atopic dermatitis improved.

Conclusions: Allergic diseases developed after liver transplantation have great impact on children. Modification of immunosuppression from tacrolimus to cyclosporine A is an effective method of treatment in patients with allergic diseases, which cannot be controlled in typical manner.

[33] Primary adrenal insufficiency and hemochromatosis

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The accumulation of iron in organs leads to liver injury, diabetes, cardiomyopathy, hypopituitarism. A 25-years old male patient complaining of muscle weakness, weight loss and darkening of the skin was admitted to the Department of Internal Diseases. Laboratory tests revealed hyperkalemia and increased activity of aminotransferases. Cortisol levels in serum and urine were measured and the primary adrenal insufficiency was diagnosed. The autoimmunological character of the disease was not confirmed because of the low titre of adrenal antibodies. Viral and autoimmune hepatitis were ruled out. Elevated serum iron levels, accompanied by hepatomegaly, corresponded with the diagnosis of iron overload.

Histopathological assessment of liver biopsy specimen confirmed moderate iron deposition within hepatocytes with no evidence of inflammation or fibrosis. Hemochromatosis was diagnosed and phlebotomy treatment was initiated. Genetic testing revealed H63D homozygosity of the HFE gene.

MRI of the abdomen and adrenal glands was performed. The left adrenal was visualized as hypointense to the liver on T2-weighted images. The T2* and R2* values of the adrenal ROIs were consistently out of the reference range. This was suggestive of the presence of iron deposits in the adrenals. T2* relaxation times of the liver were inhomogeneous, which suggested mild heterogeneous iron deposition in the liver or, possibly, the reduction of iron deposits in response to treatment.

In this case, adrenal injury secondary to hereditary hemochromatosis cannot be ruled out. The genetic cause of hemochromatosis is unclear – probably, the H63D mutation, is accompanied by a mutation in another gene, and their interaction leads to an aggravation of iron overload symptoms.

[34] Do we miss liver steatosis in obese children? Application of FibroScan® in obese/overweight children increases detection of steatosis

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Introduction: At present NAFLD (non-alcoholic fatty liver disease) detection is based on ultrasound (US) and elevated levels of ALT. Still, US has limited sensitivity. Fatty liver seems to be common in children with overweight/obesity, but is detected in a small percentage of children based on US and assessment of ALT.

Aim of the study was to find out whether overweight/obese children in whom primarily liver steatosis excluded have features of fatty liver measured by FibroScan®. Recent studies in pediatric population assessing hepatic steatosis compared liver biopsy and FibroScan® with option Controlled Attenuation Parameter (CAP) found that optimal threshold to detect steatosis CAP > 225 dB/m. Quantification of Liver stiffness by ultrasound based transient elastography using FibroScan® haven't been established yet in this population.

Material and methods: We used FibroScan® with CAP for more precise assessment of hepatic steatosis and stiffness of the liver in 3 groups of patients matched for age (age 8-20 years). We analyzed 42 patients with obesity and NAFLD (steatosis detected by US and elevated ALT value l), 40 patients with simple obesity (qualitative exclusion of steatosis by US using Saverymuttu criteria and with normal ALT value) and 30 healthy controls with BMI value. Exclusion criteria in all groups were: diabetes (type 1 and 2) and arterial hypertension for group with simple obesity. For group comparison we used Mann-Whitney *U* test and for associations-Spearman *R* test.

Results: There were no differences in age among groups: median age in children with simple obesity was 14.3 (range 8.8-18.5), in NAFLD – 13.8 (range 9.8-19) and in control group – 13.8 (range 8.5-20.5). Liver fibrosis measured by FibroScan® was statistically higher ($p < 0.05$) in NAFLD group (median E = 5.4 kPa) compared to controls (median E = 4.3 kPa) and compared to the group with simple obesity (median E = 4.0 kPa). The median steatosis measured by CAP in NAFLD group was significantly higher – 300 dB/m

(range 186-393) than in patients with simple obesity – 247.5 dB/m (range 100-349) and controls – 195 dB/m (range 100-273) ($p < 0.05$). Still, CAP was also significantly higher in simple obesity compared to controls. CAP values correlated with age only in the NAFLD group ($R = 0.5$), whereas CAP was significantly related to liver stiffness (E) in children with simple obesity ($R = 0.33$). 35/42 (83.3%) patients with NAFLD and 29/40 (72.5%) patients with simple obesity received CAP > 225 dB/m using FibroScan® which are regarded to be diagnostic for NAFLD.

Conclusions: FibroScan® can detect and quantify liver steatosis in obese children in whom fatty liver was primarily excluded based on normal ultrasound and ALT measures. Liver steatosis seems to be commonly associated with obesity in children. Liver steatosis is significantly higher in patients primarily diagnosed to have NAFLD compared to those with simple obesity and lean controls.

[35] Focal nodular hyperplasia in a child with cystic fibrosis

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Introduction: Liver is commonly affected in cystic fibrosis with manifestations including hepatic steatosis, biliary fibrosis and cirrhosis. Hence, hepatologic screening consisting of liver biochemistry and ultrasonography is recommended. Herein, we present a girl diagnosed by neonatal screening with cystic fibrosis, in whom focal nodular hyperplasia (FNH) of the liver was incidentally observed at the age of 12 yo.

Case report: A routinely performed abdominal ultrasound showed a homogeneous liver parenchyma with hypoechoic mass in the IVb segment (20 x 17 x 10 mm in size) with internal vascularity. Normal flow in the portal area and normal spleen size were noted additionally. The child was asymptomatic. Serum α-fetoprotein level, aspartate and alanine aminotransferase activities as well as γ-glutamyl transferase activity and bilirubin concentrations were normal. A suspicion of FNH was conducted. On MR imaging, the lesion appeared to be hyperintense on T2 weighted sequence with homogeneous contrast uptake on the arterial phase. During 1-year follow-up the size of hepatic lesion slightly increased up to 22 x 17 x 18 mm. Liver biochemistry and serum α-fetoprotein level remained normal.

Conclusions: FNH is a benign lesion of the liver which diagnosis is rare in children. We would like to emphasize that is the first report in the literature of FNH in children with cystic fibrosis. In asymptomatic children with FNH which do not progress in a size, an observation management is recommended.

[36] Esophageal varices bleeding as a primary manifestation of Caroli's syndrome in a 11-year-old boy

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Caroli's syndrome is a rare hereditary hepatic disease. The disorder consists of two components, i.e. Caroli's disease and congenital hepatic fibrosis. In the clinical picture typical for Caroli's disease are recurrent episodes of acute cholangitis. On the other hand, the main complication of progressive liver fibrosis is portal hypertension. Overloading the venous system of the gastrointestinal tract may result in esophageal varices, which are potential source of bleeding.

We present a case report of an 11 year-old previously healthy boy, without an any family history of liver disease, who was transferred to our hospital after a massive esophageal variceal hemorrhage, treated with banding ligation during endoscopy. Physical examination revealed no significant abnormalities, except splenomegaly and pallor. In laboratory tests, features of hypersplenism and anemia were present. Liver function parameters were normal. Infectious causes of the liver injury, Wilson's disease, AIH, α1-antitrypsin deficiency and cystic fibrosis were excluded. MRCP performed during the subsequent hospitalization, revealed fragmentary stenosis of the bile ducts. Percutaneous liver biopsy revealed bile duct proliferation, with their partial cystic enlargement, surrounded by fibrous connective tissue. Clinical features, MRCP and histology indicated a recognition of Caroli's syndrome.

Laboratory tests performed 9 months later showed a slight elevation of aminotransferases (AspAT 63 U/l, AlAT 66 U/l), cholestasis parameters (direct bilirubin 0.44 mg/dl, GGTP 83 U/l, bile acids 29.9 μmol/l), coagulation disorders (INR 1.21).

This case report shows that Caroli's syndrome may initially manifest itself in the form of gastrointestinal tract bleeding. It is especially important, because this state is a direct threat to the patient's life.

[37] Markers of iron overload and polarization of immune response in patients with chronic hepatitis C

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An imbalance in helper T-cell type 1 (Th1), type 17 (Th17) and type 2 (Th2) cytokines plays an important role in the pathogenesis of chronic hepatitis C (CHC). Immune dyregulation as well as iron overload, diagnosed in almost 40% of CHC patients, both link tightly with the risk of development of hepatocellular carcinoma (HCC). Although directly acting antivirals significantly improved CHC treatment efficiency, the risk of HCC still persists even after 10 years of viral cure. Therefore monitoring strategies of CHC patients and developing risk markers of HCC is urgently needed.

We have previously shown that iron indices associate with aberrant interferon (IFN) signaling in CHC. In this work our aim was to evaluate if markers of iron load link with specific cellular immune pathways. Hepatic expression of 11 selected genes involved in immune response was measured in liver biopsy samples from 130 CHC treatment naive patients. Standard biochemical tests as well as histopathological analyses were performed for each individual.

Serum ferritin specifically correlated with expression of genes involved in Th2 type of response (IL4R, TH2-LCR lncRNA) and IFN signaling (lncCMPK2, RSAD2), while serum iron level associated with Th1 and Th17-specific gene expression (AC096579.7, IFNg, lnc-DC). Additionally, expression of type Th1-specific, but not Th2-specific genes, associated with ALT, AST, GGTP levels in serum as well as with fibrosis, necroinflammatory activity and steatosis in liver biopsy samples.

These results show that ferritin and iron levels link with distinct immunological polarization pathways and they could possibly serve as indicators of immune status in CHC patients.

[38] HEV – not fully recognized problem in Poland – preliminary data

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Aim of the study: Evaluation of the probability of acquiring HEV infection in Polish patients.

Material and methods: 73 patients were tested for HEV IgG antibodies with ELISA test. One group, 23 persons, consisted of patients diagnosed with liver disease of unknown etiology. The second group, 50 persons, were HIV positive patients.

Results: In 42% of the whole group HEV IgG antibodies were detected. In the patients with hepatitis of unknown etiology we found HEV IgG in 10 of 23 patients (43%). In HIV+ patients we found HEV IgG in 20 of 50 patients (40%). We did not find any statistically significant difference in the level of liver enzymes between the patients with anti-HEV and those without anti-HEV in the group of HIV+ patients.

Conclusion: HEV infection might be important, still unrecognized problem in Polish patients.

[39] FibroScan liver assessment in patients with protein loosing enteropathy – preliminary study

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Introduction: Protein loosing enteropathy (PLE) is characterized by the severe loss of serum proteins into intestinal tract. Primary PLE is rare disease with unclear etiology related to intestinal lymphangiectasia. Secondary PLE may occur in patients with high

central venous pressure usually following Fontan operation made in children with functionally single ventricle. PLE patients may present abnormalities in liver function. FibroScan is a rapid, noninvasive, and reproducible measurement of liver stiffness (LS) widely applied for assessment of liver fibrosis.

Aim of the study was to assess liver stiffness in children with primary or secondary PLE.

Material and methods: Nine children with PLE were enrolled into the study. Five patients (M – 1, F – 4, aged 2-11 years) had primary PLE and 4 subjects (M – 3, F – 1, aged 7-13 years) had diagnosis of post-Fontan secondary PLE. FibroScan (FibroScan 502; S+, M+, XL+ probes) measurements of liver stiffness (LS) was performed in standard location 2 h after meal.

Results: LS in pts with primary PLE was normal and ranged from 2.8 to 4 kPa (2.8/2.8/3.6/3.7/4.0). Children with secondary PLE had increased LS ranging between 10.3 and 13.5 kP (10.3/12.7/13.1/13.5).

Conclusions: FibroScan show differences of liver stiffness in patients with primary and secondary PLE. Increased liver stiffness following Fontan operation can be related to liver fibrosis or hemodynamic disorders in Fontan circulation. Protein-losing enteropathy remains one of the greatest challenges in the management of post-Fontan single-ventricle patients.

[40] Prevalence of anti-HEV antibodies among patients with immunosuppression and hepatic disorders

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Introduction and aim of the study: Hepatitis E virus (HEV) is the most frequent cause of acute hepatitis in Europe. Among patients with immunodeficiencies of diverse aetiology or patients with chronic liver diseases, HEV may cause chronic hepatitis or lead to aggravation of pre-existing liver disease.

Material and methods: 450 patients (mean age: 50.35 years) were enrolled: 180 – renal or liver transplant recipients, 90 – HIV(+) and 180 – with liver cirrhosis (alcoholic – 123, HCV – 20, mixed ALD/HCV – 5, HBV – 5, autoimmune – 2, other/unknown – 18). Serum anti-HEV IgG, IgM and HEV-antigen were detected by ELISA.

Results: Serum anti-HEV IgG in transplant recipients were detected in 40.6%, IgM in 4.4% and HEV-Ag in 5%. There were no associations between presence of anti-HEV-antibodies or HEV-Ag with the type of post-transplant immunsupression. In HIV population 37.7% had anti-HEV-IgG, 1.1% had anti-HEV-IgM and none HEV-Ag. In group with alcoholic liver cirrhosis anti-HEV-IgG seroprevalence was 52%, anti-HEV IgM – 5.7% and HEV-Ag – 2.4%. In patient with liver cirrhosis other than alcoholic (n = 57) the anti-HEV-IgG prevalence was 35.1%. The mean age of patients anti-HEV-IgG (+) was significantly higher (54 years, 25-80) than group HEV-seronegative (46 years, 21-71). There were no differences related with the frequency of anti-HEV antibodies or HEV-Ag detection to the gender or place of residence in studied groups.

Conclusions: In this large cohort a high prevalence of anti-HEV was confirmed. Among specific risk groups highest prevalence was noted in alcoholic liver disease and in transplant recipients.

[41] Occurrence of HBV and HCV infection in adult population who were subjected to medico-legal autopsy

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Material and methods: 186 blood samples, taken during medico-legal autopsies (performed in 2015, in Forensic Medicine Department, Wroclaw Medical University), were analysed with immunoenzymatic assay in VIDAS system, for presence of HBsAg, anti-HBc total IgG and anti-HCV. The cases were randomly selected. All liver samples were precisely analysed. Autopsy protocols were checked for diseases and death circumstances. 42 cases in the research group were women; the cadavers' age ranged from 19 to 94 years, average 52.9.

Results: Anti-HCV antibody presence was discovered in 11 (5.9%), HBsAg in 44 (23.7%), anti-HBc alone in 25 (13.4%) and HBV/HCV coinfection in 4 cadavers (2.2%). Their age (HBsAg and anti-HCV positive) ranged from 24 to 81 years (70.5% of HBV infected ≥ 50 years), 8/55 were women. The main causes of death: circulatory diseases – 53 cases, trauma – 41, alcohol intoxication – 25, pneumonia – 17. Histopathological changes in liver: inflamation – 83/186 cases (44.6%); fibrosis (HAI) 68/186 (36.6%), 3-4 – 24/186 (12.9%); steatosis (Dixon scale) – 128/186 (68.8%), 4 – 63/186 (33.9%). Liver cirrhosis was diagnosed in 18 cases – viral in 4. 66 (35.5%) of the deceased abused alcohol; 70 had postoperative scares, 46 tatoos. 10 cadavers were undernourished, 85 overweigh (31 obesity).

Conclusions: There is a possibility of postmortem hepatotropic viruses serological examination both for epidemiological and medico-legal purposes. The incidence of HBV infection in people over 50 years is substantially higher than overall, thus there is a need of routine screening diagnostics in this age group.

[42] Selective screening for lysosomal acid lipase deficiency in patients with fatty liver disease

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Introduction: Lysosomal acid lipase deficiency (LAL-D) is a rare disorder of cholesterol metabolism with an autosomal recessive mode of inheritance. Nonspecific clinical manifestations can lead to a delay in the diagnosis of both children and adults.

Aim of the study was to identify children with a LAL-D in risk groups. Diagnosis was based on assessment of the enzymatic activity of acid lipase from dried blood spot.

Material and methods: The study included 207 children with increased ALT activity, and/or fatty liver on ultrasound at the age of 0-18 years old with suspected liver disease. We investigated the following parameters: ALT, AST, liver ultrasound, total cholesterol and acid lipase activity. The dry blood spot (DBS) test was performed according to the method described previously by Hamilton *et al.* DBS values of 0.37-2.30 nmol/punch/h were interpreted as normal, 0.15-0.40 nmol/punch/h as suspicious for LAL-D and < 0.03 nmol/punch/h as LAL-D patients.

Results: The increase of ALT activity above 100 U/l was found in 17 patients. LAL activity in DBS samples obtained from children with liver disease (n = 207) varied from 0.17 to 82.2 nmol/punch/h. Deficient concentrations were found in 2 children (0.17 and 0.23 nmol/punch/h). One of them finally was diagnosed to have early onset LAL-D.

Conclusion: DBS test appears to be easy to perform for screening of high risk groups. Results show the method differentiates clearly between normal controls, carriers and affected cases. Widely applicated DBS method will allow screening for LAL-D in high risk populations, even if prevelance of the disease is low.

[43] Macroenzyme investigation in children of isolated elevation of aspartate aminotransferase

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Introduction: Elevated aspartate aminotransferase (AST) can be related to the presence of macroAST in serum. MacroAST is an unusual combination of molecules of AST with serum macroglobulins. MacroAST should be suspected in asymptomatic patients with persistent hypertransaminasemia.

Aim of the study was to evaluate the prevalence of macroenzymes in children with increased aspartate aminotransferase activity in whom clinical diagnosis was not established.

Material and methods: Among 800 children mean age 5.57 ± 5.66 years (from 0.03 to 18.1 years) with isolated hypertransaminasemia we performed laboratory tests to detect macro-AST: at the first stage we precipitated serum componets with polyethylene glycol (PEG) by Levitt and Ellis. The activity of PEG precipitation (% PPA – polyethylene glycol precipitable

activity) greater than 54% is typical for the presence of macro-AST in blood serum. At the next step we used immunobloting method to confirm immunologically macroAST.

Results: We identified in total 70 patients with macroAST by precipation method and confirmed macroAST in 37 by immunobloting.

Conclusions: MacroAST has to be considered in the diagnostics of isolated high AST levels and can be confirmed in a significant number of selected patients.

Praca wykonana w ramach zadania statutowego Instytutu „Pomnik – Centrum Zdrowia Dziecka" w Warszawie nr 151/06 pt. „Makroenzymy – przydatność diagnostyczna, obserwacje kliniczne u dzieci".

[44] Reduction of aminotransferase activity is more likely in obese patients after lifestyle modification in children with nonalcoholic fatty liver disease

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Nonalcoholic fatty liver disease (NAFLD) is the most common liver problem due to sedentary life style and improper eating habits. Children develop fatty liver along with insulin resistance and metabolic syndrome.

Thirty seven children were enrolled in the study, age range 3-17 years (mean 10.20 ± 3.41), 25 boys and 12 girls. NAFLD was diagnosed on the basis of abdominal ultrasound examination. Differential diagnosis of the liver steatosis was performed to exclude underlying liver diseases. All patients underwent weight and height measurements, physical examination and blood collection for hematologic and biochemical parameters. Patients received lifestyle modification advices regarding diet and physical exercises. All children were followed during control visits. End-point parameters were reduction of aminotransferase activity and body weight. In 5/39 cases weight reduction was observed. 17/37 children had increased BMI. Elevated liver enzymes 2 x UNL were present in 18/37 patients; in 12 patients a decline in aminotransferase activity was detected. No decline in aminotransferase activity as observed more often in the group with low BMI (0.50 ± 0.84 vs. –0.19 ± 0.33; $p = 0.012$). In children with reduction of aminotrasferase activity higher initial values of AST (52.72 ± 30.79 vs. 30.09 ± 12.43 IU/l, $p = 0.013$) and APRI (0.56 ± 0.40 vs. 0.26 ± 0.12; $p = 0.006$) were observed.

Weight reduction is not a common effect in children with NAFLD. Children with NAFLD and normal body weight are less likely to achieve a reduction in aminotransferase activity due to lifestyle modification. Liver injury expressed as AST activity does not exclude significant reduction of aminotransferase after lifestyle modification.

[45] LiverMultiScan® – new non-invasive method of assessment liver inflammation, steatosis and fibrosis – preliminary report

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Introduction: Liver biopsy (LB) is an invasive procedure used for diagnose and treatment monitoring of liver diseases. We present preliminary experience with a new non-invasive method LiverMultiScan® (LMS) assessing hepatic fibrosis, steatosis and inflammation.

Material and methods: Two children with autoimmune hepatitis (AIH) and one with Wilson disease have been performed a diagnostic or control liver biopsy (LB) and LMS. We compared grade of liver fibrosis, inflammation and steatosis (based on LB) to LIF-score (based on multiparametric NMR, measurements of fat and iron liver content). LMS analysis was performed also in one healthy child (as a control).

Results: In a 12-year-old male (recently diagnosed as AIH, not receiving therapy) LB revealed 3rd grade of fibrosis and 3rd grade of portal and lobular inflammation. LMS analysis reports corresponds closely with this findings: fat 0.7%, iron 0.9 mg/g, LIF-score 3.08%. In a 16 year-old female with AIH (on Azathioprine)

the biopsy showed: fibrosis 1c, portal (2nd grade) and lobular (1st grade) inflammation. In LMS: fat 3.2%, iron 0.8 mg/g, LIF-score 1.97%. In a 7.5-year-old female with Wilson disease (on Zincteral) in LB: steatosis 3rd grade, ballooning 2nd grade, fibrosis 2nd grade, portal and lobular inflammation 1st grade. In LMS: fat 32.6%, iron 1.4 mg/g, LIF-score 3.08%. LMS analysis in a 17 year-old healthy girl without liver disease revealed: fat 1.2%, iron 1.2 mg/g, LIF-score 1.73%. According to the experience in adults LIF-score < 2% seems to be normal, and higher levels correlate with fibrosis and inflammation.

Conclusions: LIF-score corresponds closely to the grade of fibrosis and inflammation on liver biopsy, and liver steatosis described by NMR is confirmed also by liver histopathology. LiverMultiScan® is a new promising non-invasive method that may be used for monitoring of liver diseases in children. Larger cohorts are needed to confirm and further delineate these findings.

[46] Hepatocellular carcinoma in a 2-year-old boy with PFIC 2 – case report

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Progressive Familial Intrahepatic Cholestasis type II (PFIC 2) is a rare disorder which is caused by defect in bile secretion and present with intrahepatic cholestasis, usually in infancy and early childhood, resulting in end stage liver cirrhosis. About 15% of children with PFIC 2 could be prone to develop HCC.

The genetically proven PFIC 2 patient, 2-year-old boy with liver cirrhosis, during qualification to transplantation, was admitted to CMHI with suspicion of developing liver tumour. An abdominal ultrasound examination revealed diffuse focal lesions in the liver. The computed tomography (CT) with a contrast supply confirmed the presence of intensified changes in the liver. The results of imaging studies corresponded with increased AFP levels (30 000 μg/l) in a laboratory test. The patient had been qualified for liver biopsy initially, but he died of massive bleeding from oesophageal varices before the examination. Post mortem histopathological examination revealed a multifocal primary HCC with numerous metastases to the lungs and the right adrenal gland.

Liver cirrhosis may lead to HCC development even in the early years of life. Patients with PFIC 2 require close surveillance with regular alpha-fetoprotein estimation and radiological examination. Currently used treatment by an external biliary drainage reduces the development of cirrhosis and the risk of HCC.

[47] Liver manifestations of enteroviral infections in children: a report of two cases

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Introduction: Enteroviral infections are usually self-limiting, without severe complications. Severe infections, such as: encephalitis, sepsis, myocarditis or liver involvement, have been reported mainly in early infancy, in older children seem to be extremely rare. We present two children with the enteroviral infections who developed hepatic complications.

Case reports: An 18-month old girl with septic shock and coexisting liver failure in the course of enteroviral infection. The disease started with nonspecific symptoms and high fever, then severe stomatitis and hemorrhagic exanthema occured. After two days the girl developed the cardiovascular and respiratory failure, therefore required intensive therapy. Acute inflammatory markers were elevated – CRP 56 mg/l, procalcitonin 160 ng/ml. Markers of hepatic dysfunction were present – GOT 1481 U/l, GPT 896 U/l, INR 1.734. After excluding other causes of infection, the diagnosis of enteroviral sepsis was suspected and confirmed (positive PCR result in blood and pharyngeal swab). Initiation of IVIG therapy caused spectacular improvement of patient's general condition.

A 2-year old boy with classical symptoms of hand, foot and mouth disease and coexisting hepatosplenomegaly (liver +5 cm and spleen +7 cm below the costal margin). The liver function was normal, without symptoms of inflammation. Typical causes of hepatomegaly (as well as cardiac disfunction) were excluded.

Although the child's condition improved, the liver enlargement persisted for the next 4 months.

Conclusions: Enteroviruses may be a rare cause of acute hepatic dysfunction and liver enlargement. In severe enteroviral infections IVIG treatment should be considered.

[48] Infectious complications in patient after liver transplantation

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Introduction: The risk of infectious complications in organs recipients is higher than in general population.

Case report: Here a case of a 60-year-old female after liver transplantation (LTx) in 2015, due to HCV liver cirrhosis and hepatocellular carcinoma (HCC) is presented. In 2016 HCV was eradicated (DAA therapy). Two years after LT she was admitted to the Department with fever and symptoms of respiratory tract infection. Physical examination revealed generalized petechia (skin and mucous membrane). The total count of platelets was 1×10^3 µl. We diagnosed gastrointestinal hemorrhage. No improvement after separated FFP transfusion was observed and platelets count was zero. The PCR test confirmed influenza A virus infection. After 3 weeks of steroid therapy increased in platelets count was observed. She was discharged with PLT 55×10^3 µl with the recommendation of continuous low dose of steroids. She was hospitalized again 5 days later because of high fever and thrombocytopenia (PLT 5×10^3 µl). The diagnosis was *E. coli* sepsis. During antibiotic therapy, she developed severe diarrhea caused by *C. difficile* toxin, post steroid diabetes, and mental disorders. The bone marrow biopsy and laboratory test excluded primary thrombocytopenia. Due to elevated tacrolimus concentration, the dose was significantly reduced. After therapy she was discharged from the department with normal platelets level.

Conclusions: In the patient after LTx during multiple life-threating infections we did not observe any dysfunctions of liver.

[49] 14-year-old girl with PFIC-2 – case report

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14-year-old girl with hepatosplenomegaly and itch was admitted to our outpatient clinic. When she was 2.5 years old celiac disease was diagnosed and hepatosplenomegaly with unknown origin was noticed. 10 years later because of itch she was diagnosed with atopic dermatitis. Moreover she was diagnosed in Endocrinology Clinic (short stature) and Metabolic Clinic. In our hepatological outpatient clinic clinical presentation (itch, hepatosplenomegaly) and laboratory tests (normal gamma-glutamyl transpeptidase [GGTP] level despite elevated bile acids) raised the suspicion of PFIC. The diagnosis was finally confirmed by genetic test (ABCB11 mutation – PFIC-2). She was treated with ursodeoxycholic acid (UDCA), but due to the severe pruritus, elevated bile acids, after 8 months, partial external biliary diversion (PEBD) was performed with good result (clinical and laboratory). Because of poor quality of life after 8 years ileal bypass was performed, but after 6 months itch and elevated bile acides occurred and she was treated with UDCA again with good result. When she was 25 years old, she got pregnant. In second trimester she developed pruritus, which gradually worsened with no response to UDCA treatment. Pruritus gradually decreased after delivery, finally resolved 6 months after delivery healthy child. After 6 years she was consulted with our clinic because of hepatic tumor. There was a high suspicion of cholangiocarcinoma. The further fate of patient is not known.

[50] The quality of life improvement after effective hepatitis C treatment with directly acting antivirals

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New interferon free therapeutic options for HCV infection demonstrate excellent safety profile and clin-

ical trials showed quality of life (QoL) improvement. However this effect was not studied in real world conditions.

We evaluated QoL during the follow-up period after treatment with direct acting antivirals (DAA) in patients who achieved sustained virologic response.

Patients, with mean age 49.4 ± 12.1, mainly infected with genotype 1 were assigned treatment with either Ombitasvir/Paritaprevir/Ritonavir ± Dasabuvir ± Ribavirin (n = 24), or Ledipasvir/Sofosbuvir ± Ribavirin (n = 10). All participants completed 12 question form at the end of treatment (EOT) and week 24 follow-up (FU) visits.

According to patients judgement during the treatment period mean QoL score improved by 113 ± 19%. Maximal QoL improvement at the EOT and FU visits reached 200%, whereas maximal worsening of 42% and 58% respectively. There were no statistically significant differences between QoL scores related to both regimens at EOT and FU. Mean QoL scores measured at EOT were 27 ± 23% higher (better QoL) in patients without cirrhosis than in cirrhotics (p = 0.02). Patients treated with addition of ribavirin compared to those without ribavirin demonstrated at EOT and FU mean QoL scores lower by 42 ± 22% (p = 0.0003) and 12 ± 16% (p = 0.01) respectively. Mean QoL scores improvement at EOT and FU was higher in females (115 ± 20% and 129 ± 19% respectively) than in males (84 ± 27% and 107 ± 23%).

Concluding, we confirmed improvement in QoL during the treatment with DAA and follow-up period. QoL improvement was more apparent in females, patients without cirrhosis and those treated without ribavirin.

[51] Liver fibrosis and steatosis in children with chronic liver diseases – comparison between histology and transient elastography (Fibroscan)

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Introduction: Recently transient elastography (Fibroscan®) has been applied in chronic liver diseases for non-invasive assessment of fibrosis and steatosis. We aimed to evaluate the degree of liver stiffness (fibrosis) and steatosis using Fibroscan in relationship to liver histology in children with chronic liver diseases.

Material and methods: We included 33 children with mean age 11.5 yrs with chronic liver diseases (15 – autoimmune hepatitis, 7 – other hepatitis, 5 – Wilson's disease, 6 – others).

Liver biopsy was performed in all patients. Histology was described semiquantitatively e.g. modified NAFLD scoring system by Kleiner *et al.*: steatosis (0-3), fibrosis (0-4), inflammation (0-3) and necrosis. All patients underwent Fibroscan examination with both: small (S2) and medium (M) probes to assess liver stiffness (E) and steatosis (Controlled Attenuation Parameter, CAP).

Results: On liver biopsy assesment the selected cohort of patients presented with variable fibrosis (grade 3-4 in 14 pts), mild steatosis (grade 1-2 in 8 patients), inflammation (grade 2-3 in 9 pts) and necrosis (1 pt). Fibroscan showed slightly elevated liver stiffness 7.6 kPa (4.8-14.3) (S2 probe) and 6.8 kPa (5.2-14.3) (M probe). Patients presented with median steatosis (CAP) of 199 dB/m (165-228) (median, lower, upper quartile). We found strong correlation between liver fibrosis on histology and liver stiffness by Fibroscan: r = 0.74 for S2 probe and r = 0.66 for M probe respectively. Liver steatosis was also significantly related to CAP (r = 0.5). Inflammation was inversely related to steatosis as assessed by CAP (r = –0.35).

Conclusions: Liver stiffness assessed by both: small (S2) and medium (M) probes of Fibroscan® shows good correlation to liver fibrosis on histology in children with chronic liver diseases. Liver steatosis measured by CAP reliably reflects degree of liver steatosis on histology.

[52] Follow-up of liver steatosis and fibrosis in children with Wilson's disease using transient elastography (Fibroscan)

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Introduction: Liver damage in Wilson's disease ranges from simple steatosis, steatohepatitis to severe fibrosis. Transient elastography (Fibroscan® Echosens) has been applied in many chronic liver diseases for non-invasive assessment of liver stiffness/fibrosis and steatosis. We aimed to evaluate the change of liver stiff-

ness/fibrosis and steatosis and liver function over time in children with Wilson's disease using Fibroscan.

Material and methods: We included 33 children with mean age of 11.5 yrs with Wilson's disease, treated with either zinc or d-penicillamine. At the baseline and after a mean period of 1.5 yrs all patients underwent Fibroscan examinations with medium (M) probe to assess liver stiffness (E) and steatosis (Controlled Attenuation Parameter, CAP). Repeated laboratory liver function tests were performed at the same time.

Results: At baseline, our patients presented with slightly elevated liver enzymes ALT-49.5 U/I (27.5-69), AST-34.5 U/I (25.5-45.5), GGTP-26 U/I (19.5-35.5) and well preserved liver function INR – 1.1 (1.05-1.16) [median, lower, upper quartile]. Initial Fibroscan examination showed normal median liver stiffness 4.4 kPa (M probe) (4.0-5.4) and slightly elevated liver steatosis CAP-257 dB/m (235-283) [median, lower, upper quartile]. After a period of 1.5 years we found decrease, but not statistically significant, in ALT, AST and INR in our patients. Only GGTP was significantly lower than the baseline results ($p = 0.02$). Similarly we have not observed marked difference in liver steatosis (CAP) or liver stiffness by Fibroscan when compared baseline and repeated measurements.

Conclusion: Liver stiffness/fibrosis and steatosis seem not to significantly improve in the short-term follow-up observation period of children with Wilson's disease, as based on the Fibroscan measurements. Transient elastography (Fibroscan®) can be easily used in children with Wilson's disease for monitoring of liver stiffness/fibrosis and steatosis.

[53] Level of alfa-fetoproteine (AFP) in patients with hepatitis C treated direct antiviral agents (DAA)

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Hepatitis C viruses has a potent oncogenic activity and it can induce hepatocellular carcinoma (HCC), which can be screened with AFP levels measurement. Aim of the study is the analysis of AFP level in patients with hepatitis C treated with direct antiviral agents (DAA). The AFP level was determined before the treatment, at the end of the treatment (EOT) and 24 weeks after treatment completion (FU24). The analysis was done in 34 patients aged 21-71 (mean 53.3) and mostly infected with genotype 1. All patients had share wave elastography (SWE); liver cirrhosis (F4) was diagnosed in 16 patients (47%), F3 in 6 (18%), F2 in 7 (21%), F0-F1 in 5 (15%). Patients were treated accordingly to HCV genotype and liver fibrosis with Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir ± Ribavirin or Sofosbuvir/Ledipasvir ± Copegus.

Before the treatment, high level of AFP was detected in 10 patients (29.4%) including 7 with cirrhosis (mean AFP 39.9 ng/dl). After the treatment we noted a sharp decrease in AFP level, and in only 3 patients still demonstrated slighty elevated AFP levels (11.6-15.8 ng/ml), with mean AFP 9.2 ng/dl at EOT and 9.45 ng/dl at SRV24 ($p < 0.01$). Elasticity in decreased slightly during treatment (mean SWE at baseline 21.7 kPa, EOT – 21.1 kPa, FU24 – 18.2 kPa. All patients achieved a sustained virologic response at FU24 visit.

Concluding, after a succesful treatment in patients with HCV related advanced liver fibrosis AFP level decreased significantly. Long-term follow-up can confirm possible reduction of HCC risk in this population.

[54] The course of primary sclerosing cholangitis or primary autoimmune cholangitis in children. Single center experience

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Introduction: Primary sclerosing cholangitis (PSC) and autoimmune sclerosing cholangitis (ASC) are orphan pediatric diseases. The study aimed to charactrerise these entities.

Material and methods: This is a retrospective review of the patients with PSC/ASC.

Results: We identified 39 patients (M – 25/F – 14) with PSC (18) or ASC (21) diagnosed at the age of 11 ± 3 years. Bile duct involvement at presentation of the disease was found in 28 out of 34 cholangiography studies (MRCP – 27, ERCP – 7) and in 26 out of 33 liver biopsies. 23 patients had coexisting IBD, 2 patients had celiac disease and 1 patient had rheumatoid arthritis. Liver function tests, total protein and IgG did not differ between PSC and ASC patients. Patients with PSC had higher GGTP than those with ASC (413 ± 259 vs. 166 ± 100 U/l, $p < 0.01$). The proportion of ANA positive patients was higher in ASC than in PSC

(45% vs. 80%, $p = 0.04$). No differences in SMA and LKM distribution were noted. Patients were observed for 3-12 years (5.3 ± 3). 12 patients required therapeutic ERCP (PSC – 6, ASC – 6). 15 patients developed portal hypertension (PSC – 7, ASC – 8). 11 patients had LTX (PSC – 7, ASC – 4). There were no differences in the time between the onset of PSC/ASC and portal hypertension (3.1 ± 2.3 vs. 3.5 ± 2.2) or LTX (4.9 ± 2.2 vs. 6.5 ± 1.3). Therapeutic ERCP was done earlier in PSC than ASC patients (2.5 ± 1.9 vs. 4.2 ± 3.3, $p = 0.044$).

All patients received UDCA and those with ASC prednisone and azathioprine.

Conclusions: The therapeutic approach to PSC and ASC differ however the course and outcome are very similar.

[55] Life quality in teenagers with autoimmune liver diseases

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Introduction: Autoimmune liver disease may influence different aspects of patient's life quality.

Aim of the study was to assess life quality in children treated for autoimmune liver diseases.

Material and methods: Chronic liver disease quality of life questionnaire (Gut 1999; 45: 295-300) was performed in 46 consecutive patients (M – 23, F – 23, age 10-18, mean ± SD: 15 ± 2.2 years) consulted on outpatient basis for AIH ($n = 33$), PSC ($n = 4$) or AIH/PSC ($n = 9$). 7 patients had exacerbation of liver disease with high ALT activity while 39 had a remission of the disease. Total score and scores for individual domains (abdominal symptoms – AS, fatigue – F, systemic symptoms – SS, activity – AC, emotional functions – EF and worry – WO) were calculated and compared with disease status.

Results: No differences in any domain of QOL between patients with remission or exacerbation of AIH were observed (AS: 18 ± 3 vs. 17 ± 3; F: 24 ± 6 vs. 24 ± 6; SS 30 ± 4 vs. 30 ± 4; AC: 1 ± 3 vs. 18 ± 2; EF: 44 ± 8 vs. 47 ± 7; WO: 30 ± 5 vs. 33 ± 1; total score: 164 ± 22 vs. 169 ± 18. There were no differences in total and individual domains of life quality index according to type of autoimmune disease or sex.

Conclusions: Fatigue decreases quality of life of teenagers with autoimmune liver diseases. The status of the disease, sex or type of the disease do not influence the life quality of teenagers with autoimmune liver diseases.

[56] Fibrosis screening in patients with type 2 diabetes – own experiences

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Introduction: Our population lives in a diabetogenic environment. 9 out of 10 newly diagnosed type 2 diabetics (DM2) has excess body weight. Approximately 70-80% DM2 patients are likely to have NAFLD – non-alcoholic fatty liver disease.

Aim of the study: Detect liver fibrosis in owerweight or obese patients and in patients with DM2 type who in 2016 visited the Internal Clinic in Bardejov Spa for the differential diagnostics of liver diseases.

Material and methods: All patients were tested on the device Fibroscan 502 touch and underwent ultrasound scan of the abdominal cavity.

Results: During 2016 we examined a total of 383 overweight or obese patients (194 men/189 female). 167/383 (78 M/89 F) had DM2, 20/383 had impaired glucose tolerance (IGT) (11 M/9 F). A total of 187 patients (48.8%) had DM2 or IGT. The presence of liver fibrosis stage 1-4 (F1-F4) was found in 151/187 patients (80.7%) with DM2. The presence of severe fibrosis (F2-F4) was found in 108/187 patients with DM2 (57.8%). The presence of liver fibrosis stages 1-4 (F1-F4) was found in 99/196 overweight or obese patients (50.5%). The presence of severe fibrosis (F2-F4) was found in 52/196 overweight or obese patients (26.5%).

Conclusions: Detection of advanced fibrosis or cirrhosis is essential for the future of a patient with type 2 diabetes. In all patients with DM and especially with elevated liver function tests the cause of liver damage should be determined and patients should be controlled regularly.

[57] Autoimmune liver diseases in adults, who have been diagnosed in childhood

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Introduction: Autoimmune liver diseases (ALD) often occur in adolescence and the long-term treatment is required.

Aim of the study was to assess the health status, treatment and life situation in adult former patients of Department of Pediatric Infectious Diseases in Wroclaw with ALD.

Material and methods: 50 patients, aged 18-39 years, were invited to contact. They were asked about medical care and they were offered to perform lab tests and elastography.

Results: We received feedback from 35 patients: 4 patients died; 23 took part in the study, 2 responded the questionnaire only. Among 23 patients (16 females) aged 18-39 years. ALD were primarily diagnosed between 8 and 16 years of age. Current examination was performed 6 to 24 years. following the diagnosis. The treatment was completed in 4 patients at the age 18; in 4 the treatment was completed in adulthood. Liver transplantation was required in 3 people. The treatment was continued in 14/23 patients. Liver cirrhosis was diagnosed in one patient, while fibrosis was confirmed in 40%; thrombocytopenia was found in 30% of patients, elevated aminotransferases and GGTP levels in 43% and 52%, respectively; gamma-globulin level was high in 43%. 56% female patients have children, the liver disease was exacerbated in 5 patients during pregnancy.

Conclusions: The prognosis in patients with ALD is poor, connected with high risk of death or liver transplantation. The quality of care about adult patients with such diseases diagnosed in childhood is inadequate and there is a need to improve.

[58] Real World Evidence of the Effectiveness of Paritaprevir/r + Ombitasvir, ± Dasabuvir, ± Ribavirin in Patients with Chronic Hepatitis C – An Observational Study in Poland (interim report)

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Introduction and aim of the study: Ombitasvir/paritaprevir/ritonavir and dasabuvir (3-DAA) ± rib-

avirin (RBV) or ombitasvir/paritaprevir/ritonavir (2-DAA) + RBV in RCTs has been shown to be safe, well tolerated and efficacious in patients with HCV genotype 1 and 4 infection. This study aims to describe the effectiveness and safety profile of treatment with aforementioned regimens in real world setting in Poland.

Material and methods: HCV GT1- or GT4-infected patients received 3-DAA ± RBV or 2-DAA + RBV according to current clinical practice and guideline recommendations, in 17 centers in Poland. Presented data have been collected between November'2015 and January'2017. Participating sites recorded information on SVR24/SVR12, drug discontinuation rates, frequency/nature of adverse events, co-medication, comorbidities and adherence to therapy.

Results: 394 out of 395 enrolled patients were included in this analysis: 50.3% male; median age – 57 years, in majority (88.6%) GT1b, 31.7% cirrhotic, and 58.4% treatment-experienced. 60.9% patients had at least one comorbidity, the most frequent were: CVD – 32.2%, DM – 14.5% and hypothyroidism 6.1%. At least one co-medication was taken by 44.9% of patients. The SVR12 and SVR24 rates among those who reached post-treatment week 12 or/and 24 were: 98.2% (332/338), 98.1% (313/319) respectively. 99% (101/102), 98.9% (90/91) in cirrhotic, 97.9% (231/236), 97.8% (223/228) in non-cirrhotic. Overall, relapse and breakthrough occurred in 0.5% of patients each. Adherence > 95% was reported in 98.2% of patients, and no unintended error in use was described. Seven (1.8%) patients discontinued prematurely, 6 (1.5%) due to adverse events. Treatment emergent adverse events (AEs) occurred in 17.8% (70/394) of patients, and serious AEs occurred in 4.1% (16/394).

Conclusions: Effectiveness, safety, tolerability and adherence to Paritaprevir/r + Ombitasvir ± Dasabuvir ± Ribavirin in daily routine clinical practice in Poland replicates results achieved in RCTs with those regimens.