PROGRAM & ABSTRACT BOOK

JOINT

14TH ISFA WORLD CONGRESS

4TH E-ISFA EUROPEAN CONGRESS

BERLIN | JUNE 1–3 · 2023

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Program Thursday, 1 June 2023

	SAAL 6	SAAL 5	SAAL 4
08h30 – 08h55	**Opening Ceremony**		
09h00 – 10h20	**Apheresis around the world I:** Country specific aspects	**Lipid disorders and CVD I:** Lipid disorders – it all starts with the measurement	
10h20 – 10h45	Coffee Break, Exhibition & Poster Viewing		
10h45 – 12h05	**Apheresis around the world II:** South East Asian perspectives	**Registries:** Registries as research tools in apheresis	10h45 – 12h00 **Apherese-Weiterbildung** in deutscher Sprache Teil 1
12h05 – 12h30	Exhibition & Poster Viewing		
12h30 – 13h45		**Lunch Symposium***	**Lunch Symposium***
14h00 – 15h15	**Apheresis around the world III:** Current updates & issues (from the American Society for Apheresis – ASFA)	**Autoimmune diseases I:** Neuroimmune diseases and immuno-modulation	14h00 – 15h30 **Apherese-Weiterbildung** in deutscher Sprache: Teil 2
15h15 – 15h45	Coffee Break, Exhibition & Poster Viewing		
15h45 – 17h30	**Apheresis around the world IV:** Apheresis therapy in Japan – JSFA Workshop	**Apheresis in critical care medicine**	16h00 – 17h45 **Apherese-Weiterbildung** in deutscher Sprache: Teil 3
17h30 – 19h30	SAAL 1 **Welcome Reception & Poster Session**		
17h45 – 18h45	SAAL 7 **ISFA Board Meeting**		
19h30 – 20h30	SAAL 5 **General Assembly ISFA**		

Program Friday, 2 June 2023

	SAAL 6	SAAL 5	SAAL 4	SAAL 7
08h30 – 09h50	**Apheresis around the world V:** Country specific aspects	**Guest WS:** Association of German Dialysis Centers (DN e.V.)		09h00 – 12h00 **Apherese-Weiter-bildung** in deutscher Sprache: **Anwender-workshop**** Teil 1
09h50 – 10h20	Coffee Break, Exhibition & Poster Viewing			
10h20 – 12h10	**COVID-19 I:** Apheresis in COVID-19 and its com-plications	**Lipid disorders and CVD II:** Apheresis targeting microcircu-lation and inflammation		
12h10 – 12h30	Exhibition & Poster Viewing			
12h30 – 13h45		**Lunch Symposium***		13h00 – 15h30 **Apherese-Weiter-bildung** in deutscher Sprache: **Anwender-workshop**** Teil 2
14h00 – 15h20	**COVID-19 II:** Treatment approaches in COVID and its consequences	**New guide-lines and developments:** Technical regulations and develop-ments	**Lipid dis-orders and CVD III:** Workshop German Lipid League	
15h20 – 15h45	Coffee Break, Exhibition & Poster Viewing			
15h45 – 17h30	**Lipid disorders and CVD IV:** Treatment modalities in clinial practice	**Autoimmune diseases II:** Apheresis in rheuma-tologic and inflammatory bowel disease	**Apheresis Service and Education** (in English language)	
18h45 – 23h00	**Congress Dinner**			

Program Saturday, 3 June 2023

	SAAL 6	SAAL 5
08h30 – 10h15	**Autoimmune diseases III:** Apheresis for renal diseases	**Lipids and CVD V:** Pleiotropic and other expected windfall gains
10h15 – 10h45	Coffee Break, Exhibition & Poster Viewing	
10h45 – 12h30	**Future perspectives of apheresis therapy:** The future perspectives of apheresis	**Pediatric apheresis:** Apheresis in children and adolescent patients
12h30 – 13h00	**Closing & Awards**	

*LUNCH SYMPOSIA

THURSDAY, JUNE 1
12h30 – 13h45

SAAL 4
Lunch Symposium
Daiichi Sankyo
Optimised lipid Deutschland GmbH management with Bempedoic acid

SAAL 5
Lunch Symposium
Miltenyi Biotec B.V. & Co.KG
The numerous values of immunoadsorption

FRIDAY, JUNE 2
12h30 – 13h45

SAAL 5
Lunch Symposium
Fresenius Medical Care
New insights and practical experiences for unmet needs

**ANWENDERWORKSHOP
(in German language)

FREITAG, 2. JUNI 2023 | 09h00 – 15h30

Die folgenden Firmen stellen ihre Maschinen für eine intensive Gruppenarbeit zur Verfügung. AnwenderberaterInnen freuen sich auf Fragen und Austausch mit den Pflegenden.

- B. Braun Deutschland GmbH & Co.KG
- DIAMED Medizintechnik GmbH
- Fresenius Medical Care GmbH
- KANEKA MEDICAL EUROPE N.V. German Branch
- Miltenyi Biotec B.V. & Co.KG

1 June, 2023

8:30 a.m. – 8:55 a.m.

Saal 6

OC | Opening Ceremony

Chairs:
Bernd Hohenstein (Villingen-Schwenningen, Germany)
Wolfgang Ramlow (Rostock, Germany)

Congress Opening by

Bernd Hohenstein, ISFA (DE)
Wolfgang Ramlow, E-ISFA (DE)
Ulrich Julius, Honorary Congress President E-ISFA (DE)
Horst Klinkmann, Honorary Congress President ISFA (DE)

9:00 a.m. – 10:20 a.m.

Saal 6

OS1 | Apheresis around the world I: Country specific aspects

Chairs:
Shamanna S. Iyengar (Bangalore, India)
Oliver Moranne (Nimes, France)

1 June 2023

OS1-01 9:00 a.m.

Organization and national activities of therapeutic apheresis in Austria

Prof. Kurt Derfler

ATHOS Institute, Vienna, Austria

OS1-02 9:20 a.m.

Organization and national activities of therapeutic apheresis in Japan(#94)

PhD/MD Ken Yamaji

Juntendo University, Internal Medicine and Rheumatology, Tokyo, Japan

In Japan, there are 36 diseases for which therapeutic apheresis is covered by insurance, including hematologic, hepatic, bowel, neurologic, rheumatic, dermatologic, metabolic, cardiovascular, infectious, and transplant-related diseases. Modalities include plasmapheresis such as PE, DFPP, and PA, hemoadsorption, cytapheresis, and CART. In the past, more than 110,000 cases of therapeutic apheresis were performed annually, but in recent years, due to the COVID-19 pandemic and advances in pharmacotherapy in various areas, the number has been declining, although about 90,000 cases are still performed annually.
Here, we will discuss the current status of therapeutic apheresis in Japan by collecting data from the National Database of the Ministry of Health, Labour, and Welfare (MHLW).

OS1-03 9:40 a.m.

Organization and national activities of therapeutic apheresis in the USA

PhD/MD Amber Sanchez

University of California San Diego, San Diego, USA

OS1-04 10:00 a.m.

Apheresis activities in a low resource country Nigeria: a five years report of a single center (#13)

Prof. Nosakhare G. Bazuaye[1], Nancy I. Ojiehmangbe[2]

[1] igbinedion university teaching hospital/celltek healthcare medical center, Hematology, benin, Nigeria; [2] celltek healthcare medical center, stem cell transplant, benin, Nigeria

Introduction: Apheresis which provides blood components and therapeutic clinical intervention is very important in modern supportive care of patients. However there are very few centers with apheresis units in low resource countries like Nigeria leading to avoidable mortalities from the complications of use of whole blood. We present a five years report of apheresis activities in a private stem cell transplant medical center from July 2017 to June 2022 despite several documented challenges.

Methodology: A private Apheresis unit was set up in a stem cell transplant center with two apheresis machines (initially COBE SPECTRA then OPTIA with Hemonetics). Irradiation of collected leucodepleted single donated platelet concentrates was done using linear accelerator radiotherapy machines .Fresh frozen plasma collected wae stored at – 20^{0}C while platelets were stored vibrating at 25^{o}C .

Results: A total of 324 apheresis sessions (Optia 288 (89.2 %) and Hemonetics 36(10.8 %) was performed over a 5 years period. Single donor platelet concentrates was 209 (64.5 %), automated red cell exchange 81 (24.9 %) with OPTIA and COBE spectra, plasmapheresis 21 (6.6 %), Peripheral stem cell collection 13(4.0 %) with OPTIA. Also a total of 186 fresh frozen plasma was collected during sessions of platelet collections. Red cell exchange sessions was mainly for Sickle cell disease patients with 58(71.6 %) as males and most common indications was recurrent/refractory Vaso occlusive crises 32(39.5 %), others were priapism 13 (16.0 %), chronic leg ulcers 11 (13.6 %), post hip replacement 10 (12.3 %), acute chest syndrome 9 (11.1 %), and pre-stem transplant 6 (7.5 %). Donors for platelets was mainly males 152 (72.8 %), irradiated platelet concentrates for stem cell transplant patients and other indications was 118 (56.6 % of the total platelet collected). Peripheral stem cells collection was a total of 13 sessions, 8(61.4 %) sessions for four patients with Multiple myeloma and donors for sickle cell disease patients undergoing stem cell transplantation 5(38.6%). Indications for therapeutic plasmapheresis was Guillain-Barre syndrome 19(90.5 %) and bleeding dyscrasia in Multiple myeloma 2(9.5 %).

Conclusions: Apheresis activities in low resource countries like Nigeria is still very low due to several documented challenges.There is need for private public partnership to improve supportive and therapeutic care which will reduce mortality and morbidity in Nigerian Hospitals.

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9:00 a.m. – 10:20 a.m.

Saal 5

OS2 | Lipid disorders and CVD I: Lipid disorders – it all starts with the measurement

Chairs:
Winfried März (Weilheim, Germany)
Patrick M. Moriarty (Kansas City, USA)

1 June 2023

OS2-01 9:00 a.m.

Dyslipidemia – it all starts with a correct measurement

Prof. Winfried März

Synlab, Weilheim, Germany

OS2-02 9:20 a.m.

Lipoprotein(a) – from genetics to phenotype (#97)

PhD/MD Johanna F. Schachtl-Riess, PhD/MD Stefan Coassin, Prof. Florian Kronenberg

Medical University of Innsbruck, Institute of Genetic Epidemiology, Innsbruck, Austria

Lipoprotein(a) (Lp(a)) concentrations are a major independent risk factor for coronary artery disease and are mainly determined by variation in the *LPA* gene. Up to 70% of the *LPA* coding sequence is located in the hypervariable kringle IV type 2 (KIV-2) region. This region is hardly accessible by conventional genotyping technologies but recent studies have shown that it contains the functional variants 4733G>A and 4925G>A that greatly impact Lp(a) concentrations and protect from coronary artery disease [1,2]. This talk will focus on these and other relevant genetic variants [3], how they help to elucidate important aspects about the role of Lp(a) in coronary artery and other diseases and conclusions for the clinics [4].

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1 June 2023

OS2-03 9:40 a.m.

Evidence for a strong pro-inflammatory potential of lipoprotein(a)

Prof. Jeffrey Kroon

Amsterdam UMC, Amsterdam, Netherlands

OS2-04 10:00 a.m.

Lipoprotein-apheresis and its effect on HDL functionality

Prof. Patrick M. Moriarty

Kansas University, Kansas City, USA

10:45 a.m. – 12:05 p.m.

Saal 6

OS3 | Apheresis around the world II: South East Asian perspectives

Chairs:
Sasitorn Siritho (Bangkok, Thailand)

OS3-01 10:45 a.m.

Systematic Review of TPE practices in Central Neuroimmunological Disorders: Evolving concepts in South East Asia (#101)

Dr. Sasitorn Siritho[1,2]

[1] Bumrungrad International Hospital, Department of Neurology, Bangkok, Thailand; [2] Siriraj Hospital, Mahidol Bangkok, Department of Medicine, Bangkok, Thailand

Therapeutic plasma exchange (TPE) use is increasing worldwide, and one-third is related to the neuroimmunological disorder, perhaps associated with the mechanism of TPE that removes circulating pathogenic autoantibodies, immune complexes, and inflammatory cytokines, involved in modifying proinflammatory mediators and co-stimulatory signals linked to T and B cell-mediated autoimmunity.[1]

A regional SEA TPE Consortium (SEATPEC) for neurological disorders was established in 2018 to enhance regional collaboration via information and technology exchange to improve the delivery of the best TPE knowledge in SEA. To date, there was no existing ongoing TPE registry in the region.[2]

Most SEA countries adopted published international guidelines such as the American Association of Neurologists (AAN) [3] and the American Society for Apheresis (ASFA)[4] in performing TPE for autoimmune neurological disorders. The spectrum of immune-mediated neurological disorders in SEA is very similar in most countries. NMOSD, MS, idiopathic transverse myelitis, and autoimmune encephalitis are the most commonly encountered CNS disorders. TPE practices in Central Neuroimmunological Disorders in SEA are also no different from other parts of the world, with acute neuromyelitis optica spectrum disorder relapses being the most common indications.[5] However, the use of TPE in SEA varies among different countries due to limited healthcare funding and various restrictions in reimbursement, including poorly equipped healthcare facilities, no availability/high cost of disease-modifying treatment/targeting treatment.[2] TPE technology is considered a more cost-effective and sustainable treatment alternative. In addition to standard TPE, there are alternative methods of performing TPE in some countries, such as limited plasma exchange (LPE)[6], modified plasma exchange (MPE)[7], and small volume plasma exchange (SVPE).[8] Most neurology centers in major SEA cities rely on the TPE services and facilities supported by hematology, nephrology, and intensive care teams.[9]

SEA neurologists usually perform 5 TPE sessions, with 1 to 1.5 plasma volume, and exchanges via the central catheter. They used a combination of normal saline and 5% albumin as replacement fluid. Two-thirds used TPE as an add-on treatment in steroid-refractory cases or as a first-line treatment for severe attacks. They suggested assessing the efficacy of TPE by the interval to the next attack, post-TPE relapse rates, and TPE-related complications.[9]

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OS3-02 11:05 a.m.

Uniting the world through TPE: SEATPEC challenges & potential future collaborations (#90)

Dr. Fu Liong Hiew[1], Dr. Shanthi Viswanathan[2], Dr. Amy May Lin Quek[3], Dr. Metha Apiwattanakul[4], Dr. Brigido Simao Dias De Deus[5], Dr. Riwanti Estiasari[6], Dr. Nghia T.T Hoang[7], Dr. Saysavath Keosodsay[8], Dr. Dhayalen Krishnan[2], Dr. Ohnmar Ohnmar[9], Dr. Paul M Pasco[10], Dr. Rabani Remli[11], Prof. Mya Mya Aye Seinn[12], Dr. Ros Sina[13], Dr. Sasitorn Siritho[14], Dr. Kevin Tan[15], Dr. Norazieda Yassin[16], Dr. Tianrong Yeo[15]

[1] Sunway Medical Centre, Division of Neurology, Department of Medicine, Sunway, Malaysia; [2] Hospital Kuala Lumpur, Department of Neurology, Kuala Lumpur, Malaysia; [3] National University Hospital System, Division of Neurology, Department of Medicine, Singapore, Singapore; [4] Prasat Neurological Institute, Department of Neurology, Bangkok, Thailand; [5] Hospital Nacional Guido Valadares, Neurology Department, Dili, Timor-Leste; [6] Cipto mangunkusumo Hospital, Department of Neurology, Jakarta, Indonesia; [7] Military Hospital 175, Department of Neurology, Ho Chi Minh City, Vietnam; [8] Laos General Hospital, Department of Neurology, Laos, Laos; [9] Yangon General Hospital, Department of Neurology, Yangon, Myanmar; [10] Philippine General Hospital, Department of Neurosciences, Manila, Philippines; [11] National University of Malaysia, Department of Neurology, Kuala Lumpur, Malaysia; [12] Ar Yu, Department of Neurology, Yangon, Myanmar; [13] Calmette Hospital, Neurology Department, Phnom Penh, Cambodia; [14] Bumrungrad International Hospital and Siriraj Hospital, Department of Neurology, Bangkok, Thailand; [15] National Neuroscience Institute, Department of Neurology, Singapore, Singapore; [16] Jerudong Park Medical Centre, Department of Neurology, Brunei, Brunei

Southeast Asia (SEA) comprises 11 members countries with a population of over 600 million and an average GDP per capita of less than USD5000. The management of patients with various central and peripheral autoimmune neurological diseases in SEA is challenging due to many factors, including poorly equipped healthcare facilities, limited funding1, and restricted availability of immunotherapies such as IV Immunoglobulin 2,3. While alternative disease-targeted therapies are available in a few countries, these are limited to special indications and approvals4. Therapeutic Plasma Exchange (TPE) technology is cost-effective and sustainable treatment alternative to expensive immunotherapies in most parts of SEA4,5,6. The main challenge is to improve education and access to TPE in this region.

In 2018, a regional SEA TPE Consortium (SEATPEC) for neurological disorders was established1. SEATPEC aims to enhance regional collaboration to disseminate TPE knowledge for delivery of TPE services in SEA. This consortium is an independent body made up of key-opinion leaders (KOL) with interest in TPE from SEA countries, supported by international experts as advisors. It is a multi-national SEA working group moving towards increasing the awareness, accessibility, education, and research for multimodality TPE within the region.

Since its establishment, multiple clinical expert meetings in various SEA countries have been held in collaboration with TPE technology providers and experts in the field of neurology. Research collaboration among SEATPEC members have produced numerous key publications in the use of TPE for neuroimmunological disorders in SEA including consensus guidelines for the use of multimodality (standard and alternative) TPE2-7. SEATPEC has also engaged regional neuroscience societies which help to endorse educational events and publications, as well as assisted in the distribution and promotion of SEATPEC activities.

Participation of SEATPEC in ISFA/E-ISFA congress 2023 provides a timely opportunity for us to engage the global apheresis communities. This helps to enhance knowledge on innovative ways of performing TPE on the background of a growing number of TPE indications. More importantly, there is a need to form long-term meaningful connections with the global apheresis community in various aspects such as TPE technology transfer, educational programs, and research.

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OS3-03 11:25 a.m.

Therapeutic plasma exchange (TPE) and its challenges in Vietnam

(#104)

PhD/MD Trong-Nghia T. Hoang[1], PhD/MD Nhu-Y T. Huynh[1], PhD/MD Loc D. Huynh[1], PhD/MD An D. Vu[2], PhD/MD Cam D. Truong[3], PhD/MD Viet Q. Tran[2], PhD/MD Shanthi Viswanathan[4]

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Therapeutic plasma exchange (TPE) is a method that removes pathognomonic inflammatory mediators, including autoantibodies, complement components, and cytokines [1]. In Vietnam, TPE is indicated in peripheral nervous system disorders (GBS, CIDP, MG, paraproteinemic polyneuropathies) and central nervous system disorders (MS, NMOSD, ADEM, autoimmune encephalitis). Compared with CNS disorders, peripheral neuropathy is a more common indication of TPE. In 175 Military Hospital, GBS and MG crisis accounts for most plasma exchange indications for neurological disorders.

Although TPE is demonstrated as an efficient treatment, there are many challenges for Vietnamese patients with immune–mediated neurological disorders to access TPE, including difficulties in early diagnosis, high treatment costs, insurance uncover, and lack of medical resources. In Vietnam, There are no standard protocols for diagnosis of MS and other demyelinating diseases, diagnosis biomarkers (oligoclonal bands, anti–AQPR4, anti–MOG, neuronal autoantibodies) are not available, and clinicians are not familiar with MS resulting in misdiagnosis or under–diagnosis. As a result, only at the late stage of the disease do the patients obtain the right diagnosis. The expense of TPE remains high, about USD 4,000 – 5,000 for all TPE sessions, while the average monthly income of Vietnamese people is just USD 200 per capita. Furthermore, Vietnam does not have a national guideline for treating a demyelinating disease or autoimmune encephalitis to get coverage of treatment from insurance.[2]

In Vietnam, TPE was often operated on in ICU and by intensive care doctors without dedicated neurology TPE unit. There needs to be more medical staff in monitoring patients during TPE sessions because the ratio of patients to trained medical staff remains high. During and after covid–19 pandemic, the provision of medical materials faces many difficulties in Vietnam. Many medical centres lack filter sets of TPE devices. Therefore, patients who are indicated TPE have not been promptly treated. Colloid replacement solution, mainly albumin, is scarce and expensive.

Further regional and international collaboration and studies will help reduce the barrier to accessing TPE in Vietnam.

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1 June 2023

OS3-04 11:45 a.m.

Introduction to SEATPEC, best practices and TPE guidelines in SEA

(#98)

Dr. Dhayalen Krishnan[1], Dr. Shanthi Viswanathan[1], Dr. Metha Apiwattanakul[2], Dr. De Deus Brigido Simao Dias[3], Dr. Riwanti Estiasari Riwanti[4], Dr. Fu Liong Hiew[5], Dr. Nghia T.T Hoang[6], Dr. Keosodsay Say[7], Dr. Ohnmar Ohnmar[8], Dr. Paul M. Pasco[9], Dr. Amy May Lin Quek[10], Dr. Rabani Remli[11], Dr. Seinn Mya Mya Aye[12], Dr. Sina Ros[13], Dr. Sasitorn Siritho[14], Dr. Kevin Tan[15], Dr. Norazieda Yassin[16], Dr. Tianrong Yeo[15]

[1] Kuala Lumpur Hospital, Department of Neurology, Kuala Lumpur, Malaysia; [2] Prasat Neurological Institute, Department of Neurology, Bangkok, Thailand; [3] Hospital Nacional Guido Valadares, Department of Neurology, Dili, Timor-Leste; [4] Universitas Indonesia, Jakarta,Cipto mangunkusumo Hospital, Department of Neurology, Jakarta, Indonesia; [5] Sunway Medical Centre, Kuala Lumpur, Malaysia; [6] Military Hospital 175, Department of Neurology, Ho Chi Minh, Vietnam; [7] Laos General Hospital, Department of Neurology, Laos, Laos; [8] Yangon General Hospital, Department of Neurology, Yangon, Myanmar; [9] Philippine General Hospital, Department of Neurosciences, Manila, Philippines; [10] National University Hospital System, Division of Neurology, Department of Medicine, Singapore, Singapore; [11] National University of Malaysia, Department of Neurology, Kuala Lumpur, Malaysia; [12] Ar Yu Hospital, Department of Neurology, Yangon, Myanmar; [13] Calmette Hospital, Department of Neurology, Phnom Penh, Cambodia; [14] Bumrungrad International Hospital and Siriraj Hospital, Department of Neurology, Mahidol, Thailand; [15] National Neuroscience Institute, Department of Neurology, Singapore, Singapore; [16] Jerudong Park Medical Centre, Department of Neurology, Brunei, Brunei

In 2018, the regional South East Asian Therapeutic Plasma exchange Consortium (SEATPEC) for neuroimmunological disorders was established to improve awareness and enhance regional collaboration via information and technology exchange to improve the delivery of therapeutic plasma exchange (TPE) within SEA.[1] The Consortium, initially made up of 10 member countries covering a population of 600 million is an independent body made up of key-opinion leaders with interest in TPE from SEA countries (except Cambodia and Timor Leste at that time), supported by international experts as advisors. Later members from Cambodia and Timor Leste joined as well.

The objectives of the consortium were to gather insights from SEA regions on disease burdens, local practices, and unmet needs of TPE in neurological diseases, to develop and improve the delivery of TPE services, and the establishment of a regional TPE database in the future.[1-2]

Several meetings were held among SEATPEC members annually (2018-2023) to improve TPE education, services and identify challenges involved in delivery of the service. These meetings identified measures to improve the accessibility, service and efficacy of TPE regionally.[1-2] Online surveys, physical and virtual meetings were conducted to gather important information on TPE practices and challenges.[1-4]

The commonest indications for TPE in SEA were acute relapse of NMOsd and MG in crisis.[1,3,4] In 2021, a consensus recommendation was developed on the use of TPE for adult neurological diseases within SEA.[4,5] It encompasses the diagnostic and treatment workflow including TPE methods adopted and adapted by the SEATPEC committee for patients with neuroinflammatory disorders to the local regional situation.

Common challenges with TPE identified included the high costs of the procedure, limited access to TPE due to logistics and lack of trained personnel.[3,4] Reimbursement for TPE regionally is limited. Furthermore, consumables in terms of membrane filters or centrifuge sets, equipment and replacement fluids accounted for the direct and indirect costs, the latter of which is not reimbursed at many centers. Other obstacles identified included the lack of awareness,

education and technical ability to develop peripheral vascular access for TPE which needs more capacity building. To conclude, through SEATPEC member countries hope to improve the care of neuroimmunological diseases regionally and collaborate with global apheresis organizations in the future.

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10:45 a.m. – 12:05 p.m.

Saal 5

OS4 | Registries: Registries as research tools in apheresis

Chairs:
Ulrich Julius (Dresden, Germany)
Volker J. Schettler (Goettingen, Germany)

1 June 2023

OS4-01 10:45 a.m.

CACOV – an apheresis registry for severely ill acute COVID patients

Prof. Christian Schumann

MVZ, Kempten, Germany

OS4-02 11:05 a.m.

The German Long-Covid Apheresis Register – design and first experiences

Prof. Bernd Hohenstein

Nephrological Center, Villingen-Schwenningen, Germany

OS4-03 11:25 a.m.

The German Lipoprotein Apheresis Register – a specific analysis of Lp(a) apheresis patients

Wanja Bernhardt

Centre for Hypertension, Kidney and Metabolic diseases, Hannover, Germany

OS4-04 11:45 a.m.

A multicenter study of safety and incidence of adverse reactions associated with therapeutic apheresis in Thai patients (#18)

Dr. Phandee Watanaboonyongcharoen[1,9,10], Dr. Metha Apiwattanakul[2], Dr. Wanjak Pongsittisak[3], PhD/MD Saharat Aungsumart[2], Dr. Sukit Raksasuk[4], Dr. Thatsaphan Srithongkul[4], Dr. Parichart Permpikul[5], Dr. Sasitorn Siritho[6], Dr. Natavudh Townamchai[8,9], Dr. Pimpun Kitpoka[7], PhD/MD Kriengsak Vareesangthip[4], On behalf of Thai Society for Apheresis

[1] Chulalongkorn University, Department of Laboratory Medicine, Bangkok, Thailand; [2] Neurological Institute of Thailand, Department of Neurology, Bangkok, Thailand; [3] Vajira Hospital, Navamindradhiraj University, Nephrology and Renal Replacement Therapy Division, Department of Internal Medicine, Bangkok, Thailand; [4] Siriraj Hospital, Mahidol University, Division of Nephrology, Department of Medicine, Bangkok, Thailand; [5] Siriraj Hospital, Mahidol University, Department of Transfusion Medicine, Bangkok, Thailand; [6] Siriraj Hospital, Mahidol University, Division of Neurology, Department of Medicine, Bangkok, Thailand; [7] Ramathibodi Hospital, Department of Pathology, Bangkok, Thailand; [8] Chulalongkorn University, Division of Nephrology, Department of Medicine, Bangkok, Thailand; [9] Chulalongkorn University, Renal Immunology and Renal Transplant Research Unit, Bangkok, Thailand; [10] King Chulalongkorn Memorial Hospital, Transfusion Medicine Unit, Bangkok, Thailand

Background: Therapeutic apheresis (TA) has been used for treating patients with various indications. However, adverse reactions associated with TA could be related to anticoagulants, replacement fluids, venous access, or the procedure. This study aimed to evaluate safety and incidence of adverse reactions associated with TA.

Methods: In this multicenter study, we enrolled patients who experienced TA from January to December 2022. The adverse reactions were defined as those events occurring during or within 24 hours of the procedure. Symptoms and signs of adverse events were graded in severity: Grade I (slight): no intervention required; Grade II (moderate): intervention required, the procedure may be prolonged but is usually completed; Grade III (severe): the procedure has to be interrupted and abandoned; Grade IV (fatal): the patient has expired due to the therapy.

Results: Of 114 patients with 523 TA sessions, 77 (67.5%) were female and 37 (32.5%) were male. The median age was 41.5 years (range 5 to 89 years). There were 74 patients (64.9%) with neurology disease, 18 patients (15.8%) with gastrointestinal disease, 11 patients (9.6%) with rheumatology disease, 6 patients (5.3%) with hematology disease, 3 patients (2.6%) with endocrinology disease, and 2 patients (1.8%) other diseases. To perform TA, double lumen apheresis catheter was used in all patients. Majority of the patients (97/114, 85.1%) were performed simple plasma exchange, followed by high volume plasma exchange (16/114, 14%), and leukapheresis (1/114, 0.9%). The median number of TA was 5 sessions (1-16 sessions). We detected 8.8% (46/523) of adverse reactions; hypocalcemia (15/46, 32.6%) and hypotension (15/46, 32.6%) were the most frequent reactions. Forty-three percent (20/46) of adverse reaction was detected on the first session and 87% (40/46) were classified as grade II severity. Grade III severity were classified in 3 patients as follow: the first patient with catheter-related infection, the second patient with hypocalcemia and severe allergy to fresh frozen plasma, and the last patient with hypotension. No fatal complication was observed.

Conclusion: TA is relatively safe without fatal complication. As hypocalcemia and hypotension were the most common reactions, calcium premedication and closely monitoring vital signs could improve the safety of TA.

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12:30 p.m. – 1:45 p.m.

Saal 5

LS 1 | Lunch Symposium Daiichi Sankyo – Optimised lipid management with Bempedoic acid

Chairs:
Bernd Hohenstein (Villingen-Schwenningen, Germany)
Heinz Voeller (Berlin, Germany)

1 June 2023

LS 1-01 12:30 p.m.

Welcome and introduction

LS 1-02 12:35 p.m.

The relevance of LDL cholesterol for cardiovascular prevention

Anja Vogt

LMU, Munich, Germany

LS 1-03 1:00 p.m.

Bempedoic acid for cardiovascular risk reduction in patient with lipid dissorders

Volker Schettler

Center of Nephrology, Dialysis and Apheresis, Goettingen, Germany

LS 1-04 1:25 p.m.

Discussion and Q&A

LS 1-05 1:40 p.m.

Summary and conclusion

12:30 p.m. – 1:45 p.m.

Saal 4

LS 2 | Lunch Symposium Miltenyi Biotec – The numerous values of immunoadsorption

Chairs:
Andreas Kronbichler (Innsbruck, Austria)

1 June 2023

LS 2-01 12:30 p.m.

From Alzheimer's Disease to post-COVID – new insights into the role of disease-relevant autoantibodies

Harald Prüss

Charité – Universitätsmedizin Berlin, Berlin, Germany

LS 2-02 1:05 p.m.

Treatment of CIDP using immunoadsorptions

Johannes Dorst

Universitätsklinikum Ulm, Ulm, Germany

2:00 p.m. – 3:15 p.m.

Saal 6

OS5 | Apheresis around the world III: Current updates & issues (from the American Society for Apheresis – ASFA

Chairs:
Bernd Hohenstein (Villingen-Schwenningen, Germany)

1 June 2023

OS5-01 2:00 p.m.

Growing variations in collections for further manufacturing

Joseph (Yossi) Schwartz

Moffit Cancer Center, Tampa, FL, USA

OS5-02 2:25 p.m.

Vascular access – issues & resolutions

Betty Doggett

Carter BloodCare, Laird Hill, USA

OS5-03 2:50 p.m.

ASFA Guidelines for Therapeutic Apheresis – 2023

Nicole Aqui

(Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA

2:00 p.m. – 3:15 p.m.

Saal 5

OS6 | Autoimmune diseases I Neuroimmune diseases and immunomodulation

Chairs:
Reinhard Klingel (Cologne, Germany)
Dhayalen Krishnan (Kuala Lumpur, Malaysia)

1 June 2023

OS6-01 2:00 p.m.

The role of apheresis therapy in MS and NMOSD

Wolfgang Köhler

Leipzig University, Leipzig, Germany

OS6-02 2:20 p.m.

Immunomodulatory effect associated with therapeutic plasmapheresis

Olivier Moranne

CHU Caremeau Nimes, Montpellier, France

OS6-03 2:40 p.m.

Efficacy and safety of long-term immunoadsorption therapy in patients with myasthenia gravis (#45)

Dr. Miriam Lanska[1], Prof. Milan Blaha[1], Dr. Hana Matulova[2], Dr. Iveta Novakova[3], Prof. Pavel Zak[1]

[1] University Hospital and Faculty of Medicine, 4th Department of Internal Medicine - Hematology, Hradec Kralove, Czech Republic; [2] University Hospital and Faculty of Medicine, Department of Neurology, Hradec Kralove, Czech Republic; [3] General University Hospital, Clinic of Neurology, Prague, Czech Republic

Introduction: Myasthenia gravis (MG) is a heterogeneous autoimmune disease characterized by a post-synaptic neuromuscular transmission disorder that causes fluctuating motor weakness and fatigue. Treatment is based on a combination of cholinesterase inhibitors with immunomodulatory or biologic therapy. In some refractory patients, the effect of long-term treatment with immunoadsorption of IgG has been described. Immunoadsorption (IA) is well known to selectively remove immunoglobulins and immune complexes from plasma. We describe the results IA treatment at our apheresis center.

Methods: we summarized the IA results between January 1, 2001 and February 1, 2023. We treated 13 patients (p.), 3 men, and 10 women (median 46 years, range 22-76 years). For IA, we used initially a separator Cobe Spectra, later a Spectra Optia device (Terumo BCT, Lakewood, USA), and as a secondary device we used an Adasorb device (Medicap, Germany). Initially we used Adsopak columns (Pocard, Russia), in 2016 we started to use Globaffin columns (Fresenius Medical Care, Germany). We used a combination of ACD-A and heparin for anticoagulation. The adverse effects of the procedure, apheresis parameters, and reasons for discontinuation of treatment were

monitored. The efficacy was monitored by a decrease of IgG after IA. The outcome of the patients was evaluated by neurologists.
Results: we performed a total of 1337 IAs (median 60 IAs per p.). The median duration of IA treatment was 56 months (M) in the whole cohort. Treatment was discontinued in 6 p. (median duration of IA was 93.5 M). The reason for discontinuation of IA was: improvement of the disease (3 p.), worsening of the general condition (1 p.), sudden death (1 p.) and non-compliance (1 p.). 7 patients are still treated with IA, the median duration of the treatment is 79.3 M (range 5-260 M). The interval between IA is very individual from 10 days to 4 weeks, depending on the activity of the disease. The median of treated plasma volume was 3655 ml, median procedure time was 157 min, the mean decrease of IgG was 52%. Among the adverse events we observed mostly problems with venous access, mild hypocalcemia, 1 shunt thrombosis and 2 serious complications, 1 aspiration and 1 hypotension requiring ICU care.CONCLUSION: Immunoadsorption is the treatment of choice for patients with refractory myasthenia gravis. It is a well-tolerated and safe procedure, which significantly improves the quality of life of these patients.

OS6-04 2:55 p.m.

Therapeutic Plasmapheresis: A safe and effective periodic treatment for chronic inflammatory demyelinating polyneuropathy. (#17)

Dr. Virginia Athanasiadou, Dr. Eva P. Andronikidi, Dr. Styliani Plavoukou, Dr. Dimitris Panokostas, Prof. Eirini Grapsa

National and Kapodistrial University of Athens, Nephrology Clinic / Aretaieio Hospital, Athens, Greece

Introduction: Therapeutic plasmapheresis (TPE) is a first line treatment for chronic inflammatory polyneuropathy (CIDP) according to the guidelines of the American Society for Apheresis (ASFA).
Case Presentation: A 75-year-old female diagnosed with CIDP over 20 years ago presented acute onset toxicity following rituximab infusion and was successfully treated with chronic periodic TPE.
The patient's symptoms first appeared in the form of progressing weakness and mobility limitation that did not respond to medication [intravenous immunoglobulin (IVIg), azathioprine (AZA) and methylprednisolone] leading eventually to severe deterioration of motor and sensory functions. She started TPE and gradually recovered mobility and sensory function. In order to prevent relapses, the patient was treated with one session of TPE per month and remained clinically stable. In 2004, due to a severe relapse, rituximab (375 mg/m2) was added alongside plasmapheresis. The patient remained on periodic administration of rituximab for 2 years and was asymptomatic for 10 years. On relapse, rituximab was administered but induced acute onset toxicity (palmar erythema, fever, severe deterioration of motor function). Rituximab infusions were interrupted and the patient received TPE as monotherapy. She had 3 sessions per week via peripheral veins, using continuous-flow centrifugal apheresis system (OPTIA) and human albumin 5% as a replacement fluid. Following the 3th session the patient started to regain mobility and fully recovered after 7 sessions. To this date she is on periodic TPE and her condition is stable.
Discussion: TPE success in treating immune-mediated diseases seems to be due to its ability to regulate immune mechanisms. TPE modifies the structure of the immune complex by altering the antigen/antibody ratio (removal) and regulates immune complex solubility through complement activation. TPE can also modulate cellular immunity by changing the ratio of type 1 (Th1) and type 2 (Th2) T-helper cells in the peripheral blood. Th2 cells induce humoral

immune response by facilitating antibody production from B cells. Studies have shown that TPE shifts the Th1/Th2 balance resulting in Th1 predominance and stimulates T-suppressor cells, possibly through modulation of cytokine levels or other components of humoral immunity.

Conclusion: TPE on a periodic basis is safe, prevented our patient from permanent motor and sensory disability and significantly improved her quality of life.

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3:45 p.m. – 5:30 p.m.

Saal 6

OS7 | Apheresis around the world IV Apheresis therapy in Japan – JSFA Workshop

Chairs:
Ken Yamaji (Tokyo, UK)

1 June 2023

OS7-01 3:45 p.m.

Updated Topics in PE, DFPP and plasma adsorption using the membrane separation. (#95)

PhD/MD Ken Yamaji

Juntendo University, Internal Medicine and Rheumatology, Tokyo, Japan

In the past, more than 110,000 cases of therapeutic apheresis were performed annually in Japan, but this number has been decreasing due to the COVID-19 pandemic and remarkable progress in pharmacotherapy, but there are still about 90,000 cases of therapeutic apheresis performed annually. Modalities include plasmapheresis such as PE, DFPP and PA, hemoadsorption, cytapheresis and CART, but plasmapheresis using the membrane separation method accounts for about 40% of all therapeutic apheresis cases.
Here, we will discuss updated topics on PE, DFPP, and PA using membrane separation methods.

OS7-02 4:10 p.m.

A novel low-density lipoprotein/fibrinogen apheresis 'Rheocarna' for patients with chronic limb-threatening ischemia (#107)

Dr. Shuzo Kobayashi

Shonan Kamakura General Hospital, Nephrology, Kamakura, Japan

Background: Low-density lipoprotein (LDL) apheresis is a treatment option for patients with unhealed chronic limb-threatening ischemia (CLTI) after surgical or endovascular revascularization. The newly developed AS-25 (product name: Rheocarna™) is a direct hemoperfusion-type column designed to adsorb both LDL-C and fibrinogen specifically, unlike conventional LDL apheresis.
Methods: We conducted a prospective, single-arm, multicenter study to evaluate the efficacy and safety of LDL/fibrinogen apheresis using AS-25 in CLTI patients with nonhealing ulcers and poor options for surgical or endovascular revascularization treatment options. The primary endpoint was the ulcer healing rate of a target lesion of interest within 6 months, as compared with a performance goal of 29% using historical control data.
Results: We enrolled 61 patients with CLTI who had nonhealing ulcers after revascularization or were ineligible for revascularization. Of the patients enrolled, 50 (82%) were undergoing hemodialysis. Within 6 months, 45.9% of the patients achieved ulcer healing significantly higher than the historical control data. No significant safety concerns were observed.
Conclusions: We found that AS-25 was safe and effective in healing ulcers and preventing major amputation in CLTI patients with poor options for conventional revascularization, including many hemodialysis patients in Japan.

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OS7-03 4:35 p.m.

The development history of Toraymyxin and the update of clinical data of PMX-DHP (#110)

PhD/MD Tomoki Tanaka

Shiga University of Medical Science, Department of Critical and Intensive Care Medicine, Shiga, Japan

Sepsis is defined as a severe infection that results in organ dysfunction due to a dysregulated host response. The inflammatory response to infection is enhanced by pathogen-associated molecular pattern molecules, such as endotoxin, a lipopolysaccharide component of the outer membrane of Gram-negative bacteria. Toraymyxin® (Toray Medical Co., Ltd., Japan), a polymyxin B-immobilized fiber blood purification column, was developed as a medical device to be used in conjunction with direct hemoperfusion to selectively adsorb endotoxin from the blood. In 1994, Toraymyxin® was approved by the Japanese National Health Insurance system for the treatment of endotoxemia and septic shock. Since then, Toraymyxin® has been used internationally.

The efficacy of polymyxin B-immobilized fiber column direct hemoperfusion (PMX-DHP) for septic shock has been evaluated in several randomized controlled trials (RCTs), including the EUPHAS[1], ABDOMIX[2], and EUPHRATES[3] trials, but has yet to be clearly proven. The Surviving Sepsis Campaign Guideline 2021 recommends against using PMX-DHP for sepsis and septic shock based on the results of these RCTs. However, the subgroup analysis of the EUPHRATES trial showed that PMX-DHP improved the mortality of septic shock patients with an endotoxin activity assay level of 0.6-0.9. Reports from Japan suggest that PMX-DHP improves the mortality of patients with septic shock who meet certain criteria (requirement for continuous renal replacement therapy[4], a norepinephrine[5], or a Sequential Organ Failure Assessment (SOFA) score of 7-12[6]). These results suggest that we need to carefully select patients who may benefit from PMX-DHP. Additionally, many observational studies suggest that appropriate use of PMX-DHP includes selecting the right patients, using it at the right time, and for the right duration. As evident from these findings, it is necessary to clarify a strategy to maximize the effectiveness of PMX-DHP.

The presentation will provide attendees with the development history of Toraymyxin® and summarize PMX-DHP research, especially from Japan, to introduce the most effective strategy of PMX-DHP.

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OS7-04 5:00 p.m.

Recent trends of apheresis treatment for inflammatory bowel disease

(#108)

PhD/MD Makoto Naganuma

Kansai Medical University, Third Department of Internal Medicine, Division of Gastroenterology and Hepatology, Hirakata, Japan

Apheraesis therapy involves the selective removal of leukocytes and is used to induce remission for patients with inflammatory bowel disease, such as ulcerative colitis (UC) and Crohn's disease (CD) Several studies have indicated that apheresis therapy are well tolerated and safe and are useful to induce clinical remission in patients with UC. Previously, it was considered that therapeutic effect of apheresis is somewhat slow, therefore, clinical trial for an intensive schedule of apheresis therapy was conducted and it has been shown to provide significantly better clinical efficacy of intensive apheresis therapy than a weekly schedule.As well, it is important to note that apheresis is effective even in cases in which conventional treatments, such as steroid therapy, have not been effective. Recent meta-analysis indicated that the efficacy of apheresis therapy was comparable to that of conventional therapy and safety of apheresis was better than steroid therapy. Furthermore, because clinical efficacy is frequently obtained in patients who did not receive steroid, attempts have also been made to use apheresis as a treatment at earlier stage after diagnosis in some institutions.

Long-term prognosis of apheresis therapy had been unknown because apheresis therapy was not previously permitted as the maintenance therapy to prevent clinical recurrences. Therefore, multicenter, randomized control study has been conducted to show clinical efficacy of apheresis to maintain clinical remission. The cumulative remission rate at 12 months tended to be higher in the apheresis than in control group. The rates of endoscopic remission of 42.5% and 25.9%, respectively at 12 months were significantly higher in the apheresis than the control group. Based on these results, apheresis therapy is currently approved as a maintenance therapy in Japan. The fact that apheresis can now be used as maintenance therapy is thought to be useful for patients who value safety.

3:45 p.m. – 5:30 p.m.

Saal 5

OS8 | Apheresis in critical care medicine

Chairs:
Jan Kielstein (Braunschweig, Germany)
Wladimir Szpirt (Copenhagen, Denmark)

OS8-01 3:45 p.m.

Recent developments in the field of extracorporeal albumin detoxification (ECAD) for Liver Support (#111)

Priv.-Doz. Jan Stange

University of Rostock, Nephrology, Rostock, Germany

In patients with decompensated cirrhosis, endogenous accumulation of toxins leads to overload of albumin as a toxin carrier and a reduction in albumin binding function, which is associated with lower survival. Measures of extracorporeal albumin detoxification (ECAD) have been developed to reverse patients' albumin overload with toxins. However, it has been repeatedly reported that ECAD with MARS® does not effectively improve albumin binding functions. Measurements in the albumin dialysis circuit indicated that the cause was an inadequate recycling process by the adsorbents of a commercial albumin already overloaded with stabilizers as dialysate. ALBUNIQUE® aims to ensure that the next generation of ECAD delivers a constant stream of highly purified dialysate albumin by introducing the Hepalbin® Adsorbent Technology.

Open Albumin Dialysis (OPAL®), using new membranes and ALBUNIQUE® technology, was compared to MARS® in a multicenter, randomized cross-over study to assess whether these changes lead to significant improvement in albumin binding function, a surrogate biomarker of survival.

Thirty subjects with chronic liver disease were initially randomized to either OPAL® or MARS® and then switched to the other system. Patients' albumin binding function was measured by dansylsarcosine binding and ESR.

Albumin binding capacity, detoxification efficiency, and binding efficiency were not improved by MARS but improved significantly with OPAL®. Bile acid reduction was significantly higher with OPAL®. Physiologically, the individual treatments were essentially equivalent in terms of response to intractable pruritus and hepatic encephalopathy, although the immediate response was more pronounced with OPAL®. Patients' plasma toxicity to hepatocytes and macrophages improved significantly with OPAL® but not with MARS®. An exploratory analysis showed that OPAL® provided a clean albumin dialysate until the end of treatment (8 hours). Recent analysis confirmed that the Hepalbin® MaxiCycler can maintain albumin dialysate efficacy for at least up to 24 hours, so it can be used as continuous veno-venous albumin detoxification therapy with citrate anticoagulation in the intensive care unit (ALBUNIQUE® for ECAD on Fresenius multiFiltrate CiCa®).

ECAD as a measure to extend survival time by detoxification in patients with progressive jaundice and secondary organ complications should be revisited for its full potential to bridge to transplant or recovery.

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OS8-02 4:03 p.m.

Extracorporeal immune cell therapy in sepsis

Gerd Klinkmann

University Medical Center Rostock, Rostock, Germany

OS8-03 4:21 p.m.

Cytokine adsorption in sepsis and septic shock – still under debate

Steffen Mitzner

University Medical Center Rostock, Rostock, Germany

OS8-04 4:39 p.m.

How to combine multiple extracorporeal systems in critical care

Amber Sanchez

University of California San Diego, San Diego, USA

OS8-05 4:57 p.m.

TPE in septic shock: to remove and replace

Sascha David

Zurich University Hospital, Zurich, Switzerland

2 June, 2023

8:30 a.m. – 9:50 a.m.

Saal 6

OS9 | Apheresis around the world V: Country specific aspects

Chairs:
Kurt Derfler (Vienna, Austria)
Amber Sanchez (San Diego, USA)

2 June 2023

OS9-01 8:30 a.m.

On the way to establish a lipid apheresis program in India by Lipid Association of India (LAI)"(#102)

Dr. Shamanna S. Iyengar[1], Dr. Chandrasekhar Shivaram[1], Dr. Gopala Sastry Sridhara[1], Dr. Kantharaj Ambuja[1], Dr. Murgod Roopa[1], Dr. Hemantha Kumara[1], Dr. Raman Puri[7]

[1] ManipalHospital, Cardiology, Bangalore, India; [2] ManipalHospital, Transfusion Medicine, Bengaluru, India; [3] ManipalHospital, Cardiology, Bengaluru, India; [4] ManipalHospital, Transfusion Medicine, Bengaluru, India; [5] ManipalHospital, Biochemistry, Bengaluru, India; [6] ManipalHospital, Biochemistry, Bengaluru, India; [7] Apollo Hospital, Cardiology, Delhi, India

Familial hypercholesterolemia continues to be underdiagnosed and undertreated. We felt the need to establish a lipid apheresis program in India after the Lipid Association of India (LAI) collected cases of Homozygous FH(HoFH) and recognized the dismal response to the available pharmacologic therapy and poor outcome in these patients(1).
In a study evaluating evolocumab in patients with HoFH in India (2), those with higher LDL-C (≥500 mg/dL) at baseline did not achieve adequate lipid-lowering with evolocumab compared with those who had LDL-C <500 mg/dL at baseline, indicating minimal or no residual LDLR activity.
Isolated case reports of lipid apheresis have been there in India (3,4,5). Regular lipid apheresis program was initiated in Manipal Hospital, Bangalore by the Cardiology and Transfusion Medicine departments with support from LAI, hospital administration and the biochemistry department.
Lipoprotein apheresis(LPA) was done using Fresenius Comtec Cell separator and Plasmapheresis kit (Fresenius Kabi Pvt Ltd, Bad Homburg, Germany) and Evaflux model 5A20, code: 100205, Cascade double membrane filter (Kawasumi Lab, Inc., Tokyo, Japan).
Between Jan 21 and March 23, 5 HoFH patients underwent LPA (6). 14 sessions were carried out safely. These patients had shown no response to life style intervention, statins, ezetimibe and evolocumab. 4 of them had elevated Lp(a). LDL-C reduction was 73% and Lp(a) 72% after each session. For the first time LPA was used in a pregnant lady who had already undergone CABG, and delivered a healthy looking baby.
Peripheral vein access was utilized in all except in one where AV fistula was used. Hypotensive and hypocalcemic episodes were managed easily. LPA is effective, safe and reportedly has pleiotropic effects. (6,7)
Problems: 1) Financial toxicity- This could be managed with contributions from charitable minds and free services were offered to the extent possible 2) Reluctance to accept and continue the procedure. 3) Nonavailability of drugs like evinacumab. 4) Venous access issues, and 5) Nonavailability of LDL-C filters
Future: LAI is collaborating with an International agency to establish LPA centres in different parts of the country so that accessibility and affordability improve.
Conclusion: LPA program has been established. It is safe and effective in reducing atherogenic lipids including Lp(a).There is more to be accomplished to have a wider reach.

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OS9-02 8:50 a.m.

GUIDELINES ON THE USE OF THERAPUTIC APHERESIS IN CLINICAL PRACTICE IN KUWAIT (#91)

Dr. Ahmad J. AlSarraf

Sabah AlAhmad Cardiac Center, Kuwait, Kuwait

LDL apheresis is a nonsurgical therapy that removes low-density lipoprotein (LDL) cholesterol from a patient's blood. During LDL apheresis, the plasma portion of the blood, which contains cholesterol, is separated and run through a machine that removes the LDL. The Apheresis Program at Sabah AlAhmad Cardiac Center (SACC) is the only therapeutic LDL apheresis program in Kuwait.

People who have high LDL levels who can't take medication can benefit from LDL apheresis. At SACC, The following patients should be considered for the treatment:

- Homozygote familial hypercholesterolemia (FH) patients
- Heterozygote FH patients if their LDL cholesterol level is:
  - >7.8 mmol/L (primary prevention)
  - >5.2 mmol/L (secondary prevention) despite maximum tolerated drug therapy
- Patients with progressive CVD (clinically and on imaging) despite optimal control of all other risk factors and lipoprotein (a) ≥ 60 mg/dL
- Patients with LDL cholesterol > 4.0mmol/l with progression of CAD

Anyone aged 14 and older or weight more than 40 kg can be treated with LDL apheresis.

Studies have shown that LDL apheresis can lower LDL cholesterol approximately 70 percent after a single treatment. The liver will continue to produce LDL following treatment, but it will take approximately two weeks to return to baseline levels.

To maintain lowest possible LDL levels over time, patients will typically require treatment every two weeks. Continuing a healthy diet and cholesterol lowering medications can help increase the time in between treatments.

Low blood pressure is the most common adverse reaction associated with LDL apheresis. Other uncommon side effects include nausea, flushing, lightheadedness and discomfort at the needle site. Side effects are more common in patients taking ACE inhibitors.

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OS9-03 9:10 a.m.

Cross sectional analysis of apheretical therapies in Italy (#113)

PhD/MD Luigi Vernaglione, This contribution has been possible thanks to the data coming from the Apheresis Registry of the Italian Society of Nephrology created by Dr. Stefano Passalacqua

ASL BRINDISI, Nephrology "A. Perrino" Hospital Brindisi, Brindisi, Italy

The purpose of this talk is to present data coming the Apheretical Registry of The Italian Society of Nephrology between 1995 and 2015. The following items will be illustrated:
1) number of patients treated and treatment performed both in general and in single italian Regions;
2) number of patients divided by gender and in the different years;
3) number of patients treated in each year subdivided for range of age;
4) number of treatments subdivided by apheretical systems and techniques
5) number of treatments subdivided by indication classes between specialties and in-speciaties (both in general and in pts subdivided by gender;
6) Clinical and technical complications of apheresis
7) Citapheresis percentages;
8) analysis of vascular accesses utilized;
9) Personnel employed in apheresis clinics.

OS9-04 9:30 a.m.

Organization and national activities of therapeutic apheresis in France

Olivier Moranne

Montpellier, France

8:30 a.m. – 9:50 a.m.

Saal 5

OS10 | Guest workshop: Association of German Dialysis Centers (DN e. V.)

Chairs:
Georg Schlieper (Hanover, Germany)
Wladimir Szpirt (Copenhagen, Denmark)

2 June 2023

OS10-01 8:30 a.m.

Is there a role for immunoadsorption in Post Covid?

Dr. Georg Schlieper

Dialysis Centre Hanover, Hanover, Germany

OS10-02 8:55 a.m.

The German Lipoprotein Apheresis Registry (GLAR) - Summary of the tenth annual report (#31)

Prof. Volker J. Schettler[1], Dr. Christian Peter[2], Thomas Zimmermann[3], Prof. Ulrich Julius[5], Priv.-Doz. Wanja Bernhardt[6], Dr. Franz Heigl[7], Prof. Peter Grützmacher[8], Iris Löhlein[11], Prof. Reinhard Klingel[9], Prof. Bernd Hohenstein[10], Dr. Wolfgang Ramlow[4], Dr. Anja Vogt[12], Priv.-Doz. Georg Schlieper[6]

[1] Center of Nephrology Göttingen GbR, Apheresis and Dialysis, Goettingen, Germany; [2] akquinet tech@spree GmbH, Rostock Division, Rostock, Germany; [3] BioArtProducts GmbH (B.A.P.), Rostock, Germany; [4] Apheresis Center Rostock (ACR), Rostock, Germany; [5] University Hospital Carl Gustav Carus at the Technische Universität Dresden, Department of Medicine III, Dresden, Germany; [6] Center for Nephrology, Hypertension, and Metabolic Diseases, Hanover, Germany; [7] Medical Care Center Kempten-Allgäu, Kempten, Germany; [8] AGAPLESION MVZ Markus Hospital, Frankfurt, Germany; [9] Apheresis Research Institute, Cologne, Germany; [10] Nephrological Center Villingen-Schwenningen, Villingen-Schwenningen, Germany; [11] German Society of Lipidology and resulting affections (DGFF), Frankfurt, Germany; [12] Universität München, Medizinische Klinik und Poliklinik 4, Munich, Germany

Background: In 2012 the German Lipoprotein Apheresis Registry (GLAR) was launched. Real-world data on lipoprotein apheresis (LA) treatment are now available for a time period of 10 years. All patients were treated with the maximum tolerated lipid-lowering therapy including statins, ezetimibe, bempedoic acid and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, including monoclonal antibodies or antisense drugs.

Methods and results: During the time period 2012-2021, 91 German apheresis centers collected retrospective and prospective observational data of a total of 2212 patients receiving regular LA treatment due to high Low-Density-Lipoprotein-Cholesterol (LDL-C) levels and/or high Lipoprotein(a) (Lp(a)) levels suffering from progressive atherosclerotic cardiovascular disease (ASCVD). More than 55,000 LA sessions have been documented in the registry in this period. In 2021, all patients treated with LA showed a high immediate median reduction rate of LDL-C (68.2%, n=1040) and Lp(a) (72.4%, n=943). Patient data were analyzed for the incidence rate of major coronary events (MACE) 1 and 2 years before the beginning of LA treatment (y-2 and y-1) and prospectively up to ten years on LA treatment (y + 1 to y + 10). During the first two years of LA treatment (y+1 and y+2), a MACE reduction of 71% was observed and continued to be low during y+3 to y+10, when all LA patients were analyzed. LA patients with only increased Lp(a) levels (Lp(a) > 60 mg/dl (> 120 nmol/l) and an LDL-C < 100 mg/dl (< 2.6 mmol/l)) had a higher MACE reduction (80%; n=434) in the first two years of LA treatment compared to LA patients with only increased LDL-C-

levels (LDL-C > 100 mg/dl (> 2.6 mmol/l); Lp(a) < 60 mg/dl (< 120 nmol/l)) (59%; n=188). Adverse events of LA remained low (about 5%) over the 10 years and mainly represented vascular access problems (1.0%). No side effects resulted in termination of LA therapy.

Conclusions: The current analysis of GLAR data showed that regular LA treatment resulted in very low incidence rates of cardiovascular events in patients with high LDL-C and/or high Lp(a) levels, progressive ASCVD, despite maximally tolerated lipid lowering medication, including PCSK9 inhibitors. In addition, LA was safe with a low rate of adverse effects over a 10-year period. The number of enrolled patients and the observation period make GLAR the largest LA registry worldwide.

OS10-03 9:20 a.m.

From sepsis to COVID – apheresis therapy in critical care medicine

Prof. Jan Kielstein

Klinikum Braunschweig, Braunschweig, Germany

10:20 a.m. – 12:10 p.m.

Saal 6

OS11 | COVID-19 I: Apheresis in COVID-19 and its complications

Chairs:
Bernd Hohenstein (Villingen-Schwenningen, Germany)
Julia Weinemann-Menke (Mainz, Germany)

2 June 2023

OS11-01 10:20 a.m.

Observational study of repeat immunoadsorption (RIA) in Post Covid ME/CFS patients with elevated ß2 adrenergic receptor autoantibodies

(#115)

Annika Elisa Stein[1], Cornelia Heindrich[1], Kirsten Wittke[1], Birgit Sawitzki[1], Anne Krueger[1,2], Markus Toelle[1,2], **Carmen Scheibenbogen**[1]

[1] Charité – Universitätsmedizin Berlin, Institute for Medical Immunology, Berlin, Germany; [2] Charité – Universitätsmedizin Berlin, Department of Nephrology, Berlin, Germany

The evidence for an autoimmune etiology in postinfectious ME/CFS is growing. We observed that in ME/CFS triggered by COVID, similar to ME/CSF after other infections, there is a close correlation of levels of ß2 adrenergic receptor (ß2R) autoantibodies with symptom severity (PMID: **36238301)**. We have already performed two proof of concept Immunoadsorption (IA) studies in postinfectious ME/CFS with elevated ß2R antibodies, which resulted in improvement in most patients (PMID: **32751659)**. The aim of our ongoing observational study is to assess improvement of functional ability (SF36-PF) in 20 patients with Post COVID ME/CSF with elevated ß2R antibodies undergoing antibody depletion. IA is performed with the TheraSorb® column in the approved use. Patients who improve after the 1st IA will receive two additional IAs in case of relapse. Results from the first 10 patients will be presented. This observational study will provide the basis for a RCT with sham apheresis and a RCT combining IA with B-cell depletion therapy. Potential biomarker of response will be assessed within the NKSG platform https://cfc.charite.de/klinische_studien/nksg/.
The study is funded by BMBF.

OS11-02 10:50 a.m.

H.E.L.P. Apheresis for Children with Long COVID (#103)

Dr. Beate R. Jaeger[1], M.Sc./M.A. student Hayley E. Arron[1,2], M.Sc./M.A. Renata M. Booyens[1]

[1] Praxis Dr med. Beate Jaeger, Mülheim an der Ruhr, Germany; [2] Stellenbosch University, Physiological Sciences, Stellenbosch, South Africa

The increased prevalence of Long COVID cases has resulted in a growing public health emergency. Although more minor flu-like symptoms of Long COVID have been described, Long COVID is also often associated with more debilitating, chronic symptoms including cognitive dysfunction, brain fog, chest pain, insomnia, heart palpitations, and hypersensitivity to stimuli. It was first hypothesised that elderly patients and those with previous comorbidities would be impacted most by Long COVID. However, many Long COVID sufferers appear to be younger in age and previously athletic prior to their COVID-19 infection. Owing to this, a whole new Long COVID patient group has emerged, with more children suffering from severe Long COVID symptoms that prevent them from attending school and enjoying their every-day lives.

At the beginning of 2021, Dr Beate Jaeger began treating severe Long COVID patients with Heparin-induced Extracorporeal LDL Precipitation (H.E.L.P.) apheresis, and less severe cases with triple anticoagulant therapy. The theory behind the use of this treatment in Long COVID patients is explained thoroughly in Jaeger *et al.*[1] To date, Dr Jaeger has treated at least over 300 patients with H.E.L.P. apheresis, and has seen promising diagnostic and clinical improvements in most patients, including reductions in procoagulant markers such as fibrinogen, D-dimer, and C-reactive protein (CRP). Furthermore, many patients (some even bedridden after their acute COVID-19 infection) have been able to resume their work and usual exercise regime.

Since the number of children with Long COVID is increasing, we propose that treating these children with H.E.L.P. apheresis and triple anticoagulant therapy is a viable option. Our study group will consist of patients born after the year 2000 that were previously diagnosed with Long COVID. These patients will be treated with H.E.L.P. apheresis or triple anticoagulant therapy, depending on the disease severity. We will report on diagnostic outcomes, focusing on microscopic data such as fibrin amyloid-like microclots, endothelial damage, and procoagulant markers before and after H.E.L.P. or anticoagulant therapy. Furthermore, we will also report on clinical outcomes such as improvement of symptoms and ability to attend school. We have already observed many positive outcomes in these sick children. Since there is no standardised treatment for Long COVID, this research is of the utmost importance for Long COVID sufferers.

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OS11-03 11:10 a.m.

Is apheresis therapy an option for neuroinflammatory Post-vaccination syndrome?

Dr. Harald Matthes

Havelhöhe Community Hospital, Berlin, Germany

OS11-04 11:30 a.m.

Panel Discussion - pro and contra

10:20 a.m. – 12:10 p.m.

Saal 5

OS12 | Lipid disorders and CVD II: Apheresis targeting microcirculation and inflammation

Chairs:
Wanja Bernhardt (Hanover, Germany)

OS12-01 10:20 a.m.

Apheresis to improve rheology – indications and results(#112)

PhD/MD Luigi Vernaglione, This contribution has been possible thanks to the collaboration of Dr. Alfonso Ramunni and the nephrologists of "A. Perrino" Hospital of Brindisi

ASL BRINDISI, Nephrology, Brindisi, Italy

HDL carry LDL away from arteries in order to avoid that the latter sticks artery walls building-plaques. After 2 years of treatment with apheresis and statins pts present a lower prevalence of aorto-tibial lesions in comparison with the baseline[1]. In a US population stratifyed for age and gender between 1999-2000 the females exhibited higher prevalence of Peripheral Artery Disease (PAD) in all age –ranges but 60-69 where PAD resulted significantly more prevalent in males[2]. Mortality in pts with PAD is higher than in normal subjects and that the presence of symptoms and their severity inversely correlates with mortality[3]. The effectiveness of traditional therapy of PAD is quite scarce: 1 year aftercritical limb ischemia 25 % of pts die, 20% present ulcers, 30% undergo amputation and 25% do not have signs[4]. For uremic pts this situation is more complex because inflammation, oxidative stress and endothelium inbalance between nitric oxide and endothelin interact in enhancing the severity of PAD. For this three bad companions apheresis is the golden bullet. Even when macrocirculation is restored by stenting RBCs clotting could be always represented in microcirculatxion. That because fibrinogen induces strong aggregation of RBCs. Moreover IgM, LDL, and fibrinogen form bridges between RBCs due to their size exceeding the maximum space of electrostatic repulsion of RBCs themselves. HDL prevent bridge formation by occupying RBCs binding sites. Remnant lipoproteins alter the RBCs shape impairing their deformability ad inducing clotting in small vessels. Fibrinogen and a2-macroglobulin interact in determinism of RBCs aggregation[5]. Their apheretical removal is quite mandatory. Three apheretical techniques are mostly indicated in PAD; considering the reduction of plasma viscosity after treatment of 3000 ml of plasma DFPP was the most effective[6]. The supremacy of DFPP can be explained by the additional elimination of alfa-2 macroglobulin and IgM. Ramunni et al. published a paper focused on the use of apheresis in the treatment of PAD in 2 pts[7]. Lipid profile and fibrinogen were worse in the first pts at the first session. After 14 sessions the lipid profile of pts 1 was significantly improved while was stable in the 2nd one. After stopping sessions the pts 1 needed another cycle instead of pts 2 that remitted quite completely. Thus lipid profile at the baseline predicts duration of apheretical efficacy as confirmed by my personal experience in Brindisi over 7 pts.

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2 June 2023

OS12-02 10:40 a.m.

Double filtration plasmapheresis (DFPP) to improve microcirculation

Dusit Lumlertgul

Faculty of Medicine, Chiang Mai, Thailand

OS12-03 11:00 a.m.

C-reactive Protein –from laboratory parameter to key player of inflammation (#87)

Prof. Jan Torzewski

Clinic Association Allgaeu, Cardiovascular Center Oberallgaeu-Kempten, Kempten, Germany

Since its discovery by Tillet and Francis in 1930, C-reactive protein (CRP), the prototype human acute phase protein, has emerged from a laboratory marker to a potential key player in inflammation. As CRP has appeared much earlier in evolution than antibodies and nonetheless partly utilizes the same biological structures, it is likely that CRP has been the first antibody-like molecule in the evolution of the immune system. Like antibodies, CRP may cause autoimmune reactions in a variety of human pathologies.
Consequently, therapeutic targeting of CRP may be of utmost interest in human medicine. Over the past three decades, however, pharmacological targeting of CRP has turned out to be extremely difficult. Currently, the easiest, most effective and clinically safest method to target CRP in humans may be the specific extracorporeal removal of CRP by selective apheresis. The latter has recently shown promising therapeutic effects, especially in acute myocardial infarction and cardiogenic shock.
This presentation summarizes the bench-to-bedside history of CRP and the pros and cons of applying CRP apheresis to patients suffering from various diseases, with a focus on its use in cardiovascular medicine.

2 June 2023

OS12-04 11:20 a.m.

First-in-Man: Plasmapheresis with a novel blood separation device in hypertriglyceridemia and acute pancreatitis. (#36)

Rosita Bihariesingh[1], Ra Bansie[1], Arno Nierich[1,2]

[1] Academic Hospital Paramaribo Suriname, Department of Anesthesiology, Paramaribo, Germany; [2] HemoClear BV, Clinical Department, Zwolle, Netherlands

Introduction:
Hypertriglyceridemia can account for up to one third of cases of acute pancreatitis (HTG-AP) and also results in more severe cases (1).Therapeutic plasmapheresis (TPE) can be effective treatment options in severe HTG-AP (2). Despite the proven beneficial effects of TPE and a grade I recommendation in guidelines, TPE is scarcely available in low and middle income countries (LMICs) such as Suriname based on logistic, financial and technical reasons(3). We hence describe three cases of HTG-AP treated with a novel TPE method which can be of benefit in LMICs such as our country.

Methods:
3 patients were admitted to our ICU with HTG-AP treated with a novel TPE low-cost gravidity driven membrane blood separator modality without the need of hardware[4]. This method already proved to be safe (4,5) and the working mechanism and clinical set-up are illustrated in Figure 1. Serial measurement of plasma triglycerides and cholesterol were performed and the clinical course was documented.

Results:

	Case 1	CASE 2	CASE 3
Age	32	33	29
Gender	f	f	m
Type 2 Diabetes Mellitus	yes	yes	no
Alcohol	no	no	yes
Cholesterol (mmol/l)	22.23	22.45	13.82
Triglycerides (mmol/l)	72.1	24.02	33.5

Table 1: Baseline characteristics

Treatment	CASE 1	CASE 2	CASE 3
Triglycerides After TPE sessions (mmol/L)	5.7	8.1	10
% decrease in Triglycerides After TPE sessions	79	67	71

Number of TPE sessions	5	3	2
Average plasma volume exchange (ml)	1100	1250	1300
Complication of TPE sessions	no	no	no
Start of TPE after admission (h)	24	24	24
Intensive Care Unit (days)	10	5	5
Hospital (days)	14	5	8
Triglycerides at Discharge (mmol/l)	6.3	8.1	7
Outcome	Discharge	Discharge	Discharge

Table 2: Treatment outcome of TPE

Conclusions:
Lowering of TG values in HTG-AP can be achieved with this novel TPE treatment option within reach in our LMIC's setting. A decrease in cholesterol values was also observed. Further research is needed as to whether this novel TPE method can be used for other indications e.g. familial hypercholesterolemia especially in LMIC where standard TPE as well as newer but expensive pharmacological interventions can be scarce.

References
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[2] Kayikcioglu M. LDL Apheresis and Lp (a) Apheresis: A Clinician's Perspective. Curr Atheroscler Rep. 2021;23(4).
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[5] Bihariesingh R, Bansie R, Froberg J, Ramdhani N, Mangroo R, et al. Mortality Reduction in ICU-Admitted COVID-19 Patients in Suriname after Treatment with Convalescent Plasma Acquired Via Gravity Filtration. Anesth Clin Res [Internet].
2021 Apr 19 [cited 2021 May 17];1–12.
https://doi.org/10.1101/2021.04.14.21255104

OS12-05 11:35 a.m.

A Fifteen-years analysis of therapeutic apheresis practices in state of Kuwait. (#9)

Dr. Mohamed Gaber Lotfy A. Sedky, Dr. Reem A. Al-Radwan, Dr. Hanan M. Alawadhi, Dr. Osama I. Sharawi, Dr. Ahmed E. Elganzory

Kuwait Central Blood Bank, Therapeutic Apheresis Unit, Kuwait, Kuwait

Background: Therapeutic apheresis (TA) is a general term for all extracorporeal blood purification procedures in which components of blood are separated through an extracorporeal device to treat a disease. Our therapeutic apheresis unit began its activity in 1983. We performed a total of 9265 TA procedures of different modalities on 990

patients, as we are the sole centre of apheresis in the state of Kuwait.This study aims to present our TA practices over the last fifteen years with the emphasis on how to adhere strictly to American Society for Apheresis (ASFA) indications.[1]

Methods: We conducted a retrospective analysis of data regarding TA procedures over the last fifteen years performed by our therapeutic apheresis unit through electronic medical database from June 2007 to July 2022. The data included demographics, clinical indications, and procedural detail. We also show how we adhere strictly to ASFA indications by applying both the diagnostic and TA modality codes for these indications on our electronic database during the whole study interval.

Results: A total of 5972 TA procedures were performed on 517 patients (302 males, 215 females, with a mean age of 34.62 ± 18.47 years). The procedures were 68.5 %, Plasma exchange (TPE), 14 % erythrocyte exchange, 2.6 % leukocytapheresis, 14.5 % Cascade filtration plasmapheresis with secondary plasma device (SPD), and 0.4 % Platelet depletion(PLD). The categorical indications included 8 % category I , 90 % category II, 2 % category III, and 0 % category IV. The most common indication was Sickle cell disease (35 %). The procedure failure rate was 0.1 %. Patient-related adverse events were reported in 2.1 % of procedures. No case mortality was reported.

Conclusion: Therapeutic apheresis (TA) as primary or adjunctive therapy proved itself in a broad spectrum of diseases. It is progressively developing, safe, and effective treatment modality.[2],[3] Physicians should keep track of new developments on this modality to implement the appropriate indications into clinical practice.

References

[1] Padmanabhan A , Connelly-Smith L , Nicole Aqui N , Balogun R et al.Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue . J Clin Apher. 2019 Jun;34(3):171-354.

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12:30 p.m. – 1:45 p.m.

Saal 5

LS 3 | Lunch Symposium Fresenius Medical Care - New insights and practical experiences for unmet needs

Chairs:
Christophe Ridel (Fresnes, France)

2 June 2023

LS 3-01 12:30 p.m.

The French experience: Rheopheresis in dialysis patients

Dr. Christophe Ridel

Fresnes, France

LS 3-02 12:55 p.m.

Immunoadsorption for dilated cardiomyopathy: Design, rationale and current status of a multicenter study

Prof. Marcus Dörr

Universitätsmedizin Greifswald, Greifswald, Germany

LS 3-03 1:20 p.m.

Objective biomarkers and treatment of autoimmunity in post-COVID

2:00 p.m. – 3:20 p.m.

Saal 6

OS13 | COVID-19 II: Treatment approaches in COVID and its consequences

Chairs:
Steffen Mitzner (Rostock, Germany)

2 June 2023

OS13-01 2:00 p.m.

Plasma exchange utilizing convalescent plasma in severe COVID patients

Prof. Wladimir Szpirt

Rigshospitalet, Copenhagen, Denmark

OS13-02 2:20 p.m.

How to evaluate apheresis efficacy in patients suffering from Long COVID?

Dr. Sebastian Koball

(University Medical Center Rostock, Rostock, Germany

OS13-03 2:40 p.m.

First clinical results after HELP apheresis in Long COVID Syndrome

(#59)

Dr. Gunnar J. Bücker[1], Dr. Marcella Bürkner[1], Dr. Lutz Fricke[2], Prof. Christel Weiß[3]

[1] Nephrology group practice, Osnabrück, Germany; [2] Nephrology group practice, Bochum, Germany; [3] University of Heidelberg, Department of Medical Statistics, Mannheim, Germany

Long COVID Syndrome (LC) is a new and complex disease lacking an established treatment so far. First reports portray HELP apheresis (HELP) as a promising therapy in LC. Since 2021, we have offered HELP in two practices and treated 120 patients so far. Our objective was to evaluate patients` response to HELP in LC. **Method:** The patients‘ response to the HELP has been evaluated by means of a questionnaire checking for symptoms *before* and *after* apheresis, as well as the *current* state of symptoms. The intensity of symptoms was depicted in a five-tier Likert scale ranging from 1 (bad, very pronounced) – 5 (very good, asymptomatic). Inclusion criteria: LC, at least 2 sessions of apheresis in 2022. Exclusion criteria: pre-existing ME/CFS, Post Vac-Syndrome. The questionnaires were issued to 64 patients (Osnabrück 48, Bochum 16). In total 31 responses (OS 26, BO 5) have been analysed so far.Statistical significance was assessed by Friedman test and Wilcoxon test for paired

samples. A test result was considered as statistically significant for p less than 0.05. Subsequently, the median of results is presented.

Results: The patients were aged between 18 and 78 years, with an average of 41 years. 18 of 31 participants are female.The overall rating increased from a score of 2 (range 1 – 3) before apheresis to 3 (1-5) after apheresis and to 4 (1.2-5) currently. Comparison of symptoms *before* and *after* HELP shows a significant and sustained alleviation of symptoms ($p < 0,0001$). Further improvement *after* HELP compared to the patient's *current* situation was not statistically significant.The evaluation of specific symptoms resulted in similar observations: patients' general condition, walking restriction, dyspnoe, chest pain, POTS, PEM, brain fog, insomnia, fatigue and depression improved significantly. The median number of treatments per patient was 5 (2-7). The median duration of symptoms before treatment was 10 months (2-23), follow-up after apheresis was 6.5 months (1-10). Side effects were limited to 1 out of 144 treatment sessions, which resulted in a patient suffering from low blood pressure. 83 percent of the patients would recommend the treatment.Two relapses were noted after a new COVID infection. No worsening of symptoms has been reported after the procedure.

The given findings show a high response rate with significant clinical improvements and long-lasting results. Thus, HELP seems to be a promising and safe treatment option for patients suffering from LC.

References
[1] Jaeger,B, Arron,H, Kakal-Moll,W, Seidel,D: The potential of heparin-induced extracorporeal LDL/fibrinogen precipitation (H.E.L.P.)-apheresis for patients with severe acute or chronic COVID-19 2022 Front Cardiovasc Med Volume 9 - 2022 | https://doi.org/10.3389/fcvm.2022.1007636

OS13-04 3:00 p.m.

Removal of circulating antibodies to adenoassociated virus vectors by immunoadsoption

Prof. Julia Weinemann-Menke

Universitätsmedizin Mainz, Mainz, Germany

2:00 p.m. – 3:20 p.m.

Saal 5

OS14 | New guidelines and developments: Technical regulations and developments

Chairs:
Andre Kaplan (Plainvile, USA)

OS14-01 2:00 p.m.

Relevance of sufficient clinical safety and performance data to maintain CE mark of apheresis devices (#76)

M.Sc./M.A. Uwe H. Wallstab

mdXperts GmbH, Cologne, Germany

Since 1993, the marketing of medical devices (MD) in Europe has been regulated [1,2]. Regulation was fundamentally changed with the Regulation (EU) 2017/745 on Medical Device (MDR) [3]. Currently, manufacturers of legacy devices can continue to market their MDs without demonstrating compliance under MDR. However, by the end of the conditional transition period [4] at the latest, manufacturers must reassess their MDs for conformity according to the MDR. The clinical evaluation (CE) is an essential part of the Conformity Assessment Procedure (CAP). The MDCG 2020-06 document provides information for the CE of legacy device [5].

Safety and performance, including clinical benefit, of a MD must be demonstrated within the manufacturer's intended purpose. Consequently, a careful and clearly specified intended purpose that outlines the medical purpose (disease, indication, contraindication) intended patient groups, user, use environment, and operating conditions is significant. Clinical benefit that can be expected from the MD requires that the MD performs as specified.

Clinical data are essential for the CE to be performed according to Annex XIV MDR. In this, the manufacturer must support the compliance with applicable General Safety and Performance Requirements, as defined in MDR Annex I, with relevant clinical data and demonstrate, using relevant concrete parameters for the clinical outcome, that the clinical benefit specified by the manufacturer for the specified intended purpose will be achieved in the intended patient target groups due to the technical or functional characteristics of the MD. In addition, the acceptability of the benefit/risk ratio for the various indications and intended purpose(s) of the device must be demonstrated.

Apheresis Devices correct the concentration of blood components by physical or physicochemical mechanisms as intended. Therefore, clinical data must demonstrate that the concentration of blood components is corrected and that clinical benefit to the patient is achieved directly or indirectly by achieved corrections.

In order to continue to market Legacy Devices, adequate clinical data are required for CE in accordance with the increased requirements of the MDR. Gaps in existing clinical data should be promptly addressed by systematic collection of clinical data, where possible in the context of PMCF studies. A precisely specified intended purpose of the MD is a prerequisite to be able to realize such studies.

References

[1] Council Directive 93/42/EEC of 14 June 1993 concerning medical devices. OJ L 169, 12.7.1993, p. 1–43

[2] Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007 amending Council Directive 90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/8/EC concerning the placing of biocidal products on the market. OJ L 247, 21.9.2007, p. 21–55

[3] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. OJ L 117, 5.5.2017, p. 1–175

[4] Regulation (EU) 2023/607 of the European Parliament and of the Council of 15 March 2023 amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and in vitro diagnostic medical devices PE/1/2023/REV/1. *OJ L 80, 20.3.2023, p. 24–29*

[5] MDCG 2020-6 Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies. European Commission: Document date: 22/04/2020 - Created by GROW.R.2.DIR, Last update: 24/04/2020. https://ec.europa.eu/docsroom/documents/40904

OS14-02 2:20 p.m.

Influence of the column surface on therapeutic apheresis – an old issue, but new developments are rising (#99)

Dr. Tanja Eichhorn, Dr. Vladislav Semak, Dr. René Weiss, PhD/MD student Marie Ebeyer-Masotta, **Prof. Viktoria Weber**

University for Continuing Education Krems, Department for Biomedical Research, Krems, Austria

Blood compatibility is crucial in hemapheresis, where adsorbent polymers are in direct contact with whole blood. Therefore, our work focuses on the interaction of the adsorbent surface and the circulating blood. We aim to understand and optimize the interface between blood and the biomaterials contained in adsorbent columns. The efficiency of adsorption of target molecules, but also the cellular activation at this interface depend on a number of factors, including the chemical composition of the adsorbent polymers, their porosity and surface properties (charge, roughness), as well as their interaction with the “mobile” phase, i.e., anticoagulated human plasma or whole blood [1].

The talk will address different aspects of the blood-biomaterial interface in therapeutic apheresis. It will summarize how cellular activation at the blood-biomaterial interface can lead to the release of extracellular vesicles from blood cells, in particular from platelets, and will discuss the relevance of these extracellular vesicles in coagulation and immunomodulation [2-3]. As a second aspect, different functionalized surfaces and their potential applications will be presented, including heparin-functionalized adsorbent surfaces for the depletion of mediators of immunothrombosis, or beads functionalized with phosphocholine to deplete C-reactive protein [4].

References

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OS14-03 2:40 p.m.

Safety and Performance of the NucleoCapture®Column for Selective cfDNA/NETs Apheresis in Patients with Sepsis (ClinicalTrials.gov Identifier: NCT04749238) (#66)

PhD/MD Andrew Aswani[1,2], PhD/MD Stanislav Abramovsky[3], PhD/MD Marina I. Afanasieva[4], PhD/MD Nikolay S. Pokrovsky[4], PhD/MD Alexy A. Sokolov[4], PhD/MD Irina Adamova[5], PhD/MD Sergey Avtushenko[1], PhD/MD Kirill Surkov[1], PhD/MD Dmitry Genkin[1]

[1] Santersus AG, Zurich, Switzerland; [2] Guy's and St Thomas' NHS Foundation Trust, Dept of Intensive Care Medicine, London, UK; [3] North Western Regional Scientific and Clinical Center, Named after N. N. L. G. Sokolova FMBA of Russia, St Petersburg, Russia; [4] National Medical Research Center of Cardiology of the Ministry of Health of Russia, Moscow, Russia; [5] Pocard Ltd, Moscow, Russia

Background

Cell-free DNA (cfDNA)/Neutrophil Extracellular Traps (NETs) are associated with sepsis. NucleoCapture® (Pocard) apheresis is based on recombinant histone H1.3 selective binding to cfDNA/NETs. We previously demonstrated that NucleoCapture® reduced organ dysfunction and improved survival in a porcine sepsis model. We therefore performed a first in human study of NucleoCapture® in ten patients with sepsis in the ICU.

Methods

We enrolled ten adult ICU patients diagnosed with sepsis according to the Sepsis-3 criteria. We aimed to apply NucleoCapture® treatment in conjunction with the Terumo Optia system once daily for 3-5 days depending on the physician's assessment, in addition to standard of care. Efficacy and safety parameters were measured. We used the NuQ H3.1 nucleosome assay (Volition) to measure cfDNA/NETs.

Results

Ten patients underwent a total of 32 treatments with NucleoCapture®. The majority underwent 3 sequential treatments on Days 1 to 3. Each treatment lasted 4.26 (±0.8) hours and 3.7 (±0.4) plasma volumes were processed, Mean (±SD). No saturation of the column was evident with near complete removal (85-100%) of cfDNA/NETs in the extracorporeal circuit at all time points. This resulted in a reduction in the circulating levels of cfDNA/NETs in patient blood from 861.45 (IQR 295.7-1201.4) ng/ml to 211.5 (102.8-275.6) ng/ml from Days 1-3. There were statistically significant decreases in inflammatory markers (e.g., CRP), organ function biomarkers (e.g., NGAL) and SOFA score (from 5.4 (±2.76) to 3.14 (±2.34), p=0.05) during treatments with NucleoCapture®. The 28-day mortality was 50%. Six patients experienced a total of 12 adverse events, three of which were determined to be serious adverse events (SAEs). The investigators considered the SAEs to be unrelated to treatment with the investigational device.

Conclusions

This first in human study of NucleoCapture® suggests that selective cfDNA/NETs apheresis in sepsis is feasible, safe and has the potential to improve the course and outcomes of the disease. We plan to test this in an upcoming larger pivotal multicentre randomised controlled trial (ClinicalTrials.gov Identifier: NCT05647096).

References

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OS14-04 2:55 p.m.

Development of Next Generation Apheresis using Artificial base DNA Aptamer (#10)

Kensuke Owari, Kazunobu Futami, Piao Haishun, Miyuki Hori, Gen Watanabe

TAGCyx Biotechnologies, Inc., Tokyo, Japan

Background/Purpose: Currently, most of the adsorbents in apheresis columns for Hemoadsorption or Plasma adsorption remove pathogenic factors through polymer charge dependent, non-selective binding. DNA aptamers are single-stranded nucleotides capable of selectively binding to several molecules, much like antibodies. In this study, we investigated the possibility of developing a next-generation apheresis column that can specifically and efficiently remove pathogenic factors via high functional ligands, artificial base DNA aptamers (Xenoligo®)-conjugated polymers.
Methods: Target-specific Xenoligo® was bound to commercially available polymer beads through a linker to prepare Xenoligo®-conjugated beads. Using interferon gamma (IFNγ) as a model target, the conjugated beads were mixed with a solution containing IFNγ and the removal rate was evaluated. Additionally, autoclave was applied as one of the sterilization methods, and the effect on the removability was examined. Next, we altered the target to other protein implicated in actual disease and performed separation experiments in serum. Finally, we examined whether cell separation is possible using Xenoligo® against cell membrane proteins.
Results: The anti- IFNγ Xenoligo® -conjugated beads were able to remove most of spiked IFNγ from the solution. Autoclaving the beads did not impair their removal capacity. Most of the pathogenic protein in serum was also able to be specifically removed by using a Xenoligo®-conjugated beads-filled column without affecting the quantity of other beneficial factors associated with the same disease. We generated cell membrane protein specific Xenoligo® which also has the capability to capture target specific cells, depending on Xenoligo® density on the bead surface.
Conclusion: By creating DNA aptamers that selectively bind to targets associated with disease as a pathogenic target specific ligand and by conjugating it to a polymer, the targets were able to be effectively removed. DNA aptamers possess remarkable stability in storage. Furthermore, our optimized Xenoligo® exhibits high stability in blood, making them ideal as adsorbents in apheresis. The efficacy of current apheresis systems, achieved through non-specific removal of blood factors, can be improved by utilizing Xenoligo®.

References

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[3] Futami et al., 2019, 'Genetic Alphabet Expansion Provides Versatile Specificities and Activities of Unnatural-Base DNA Aptamers Targeting Cancer Cells', Molecular Therapy Nucleic Acids, 14, 158-170.

2:00 p.m. – 3:20 p.m.

Saal 4

OS15 | Lipid disorders and CVD III: Workshop German Lipid League

Chairs:
Oliver Weingärtner (Jena, Germany)

2 June 2023

OS15-01 2:00 p.m.

A nationwide initiative to reach lipid targets

Prof. Oliver Weingärtner

Universitätsmedizin Jena, Jena, Germany

OS15-02 2:25 p.m.

Novel lipid lowerting medications – current status and future perspectives

Prof. Anja Vogt

LMU, Munich, Germany

OS15-03 2:50 p.m.

Cardiovascular events before and during apheresis treatment - a detailed analysis for vascular regions (#89)

Prof. Ulrich Julius

University Hospital at the Technische Universität Dresden, Department of Internal Medicine III, 01307 Dresden, Germany

At the end of 2018, 389 patients were treated in Saxony (federal state of Germany; approximately 10 patients per 100 000 inhabitants; 16 centers) with lipoprotein apheresis (LA). Patients started the extracorporeal treatment at the median age of 56.0 ± 10.7 years (range 16–77 years) and were treated with six different LA methods.
Atherosclerotic cardiovascular events (ASCVE) have been documented before (56 years, range 16 – 77 years) and after (3 years, range 1 month – 26 years) initiation of LA therapy. Before LA therapy, the following ASCVE were most often observed: myocardial infarction, percutaneous coronary intervention with stent implantation, coronary artery bypass grafting, percutaneous intervention with stent implantation in the legs and pelvis, stroke, percutaneous coronary intervention with stent implantation. ASCVE like an acute coronary syndrome, stents into the carotids or the mesenterial arteries, transient ischemic attacks, percutaneous transluminal angioplasty without stent implantation in the legs and pelvis, thromboendarterectomy in the legs and pelvis and the carotids occurred much less often.

The reduction rates of different ASCVE when comparing the time periods before and after the start of the LA therapy were various. Only percutaneous transluminal angioplasty without stent implantation in the legs and pelvis increased slightly.

In conclusion, LA effectively reduces the rates of ASCVE. Especially life threatening ASCVE decreased, though a few patients develop a new myocardial infarction or needed another vascular intervention.

References

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3:45 p.m. – 5:30 p.m.

Saal 6

OS16 | Lipid disorders and CVD IV: Treatment modalities in clinial practice

Chairs:
Tiziana Sampietro (Pisa, Italy)

2 June 2023

OS16-01 3:45 p.m.

Long-term experience of Lp(a) apheresis in outpatient care

Dr. Wanja Bernhardt

Dialysis Centre Hanover, Hanover, Germany

OS16-02 4:05 p.m.

The role of lipoprotein apheresis on hypercholesterolemia and Lp(a) – the Pisa experience

Prof. Tiziana Sampietro

(National Research Council Institute of Clinical PhysiologyInstitute of Clinical Physiology, Pisa, Italy

OS16-03 4:25 p.m.

Comparison of the plasma lipoprotein apheresis systems MONET and Lipidfiltration from Diamed vs. the whole blood apheresis system DALI in the treatment of patients with cardiovascular disease and severe dyslipidemia (#48)

Prof. Ulrich Julius[1], Dr. Heinrich Prophet[2], Astrid Kraeft[3], Manuela Strauss-Gabo[3], Tatiana De los Rios[3], Dr. Wolfgang Ramlow[2]

[1] University Hospital at the Technische Universität Dresden, Department of Internal Medicine III, 01307 Dresden, Germany; [2] Nephrocare Rostock GmbH, Medizinisches Versorgungszentrum Südstadt, 18059 Rostock, Germany; [3] Fresenius Medical Care Deutschland GmbH, Bad Homburg, Global Medical Office, 61352 Bad Homburg, Germany

This was a prospective, multicentric, open and interventional study with a randomized cross-over design. After inclusion the study patients received cross-over treatment with MONET or DALI or with Lipidfiltration (LF) and DALI in randomized order, three treatments with MONET or LF and three treatments with DALI.

Blood samples were collected before and after the apheresis sessions. Additionally, during each treatment blood/plasma samples were collected immediately before and after device at different on-treatment timepoints. These timepoints were calculated for each patient and corresponded to treatment of 1.6-fold whole blood volume (DALI),

and the 1.0-fold plasma volume (LF) or the 1.1-fold plasma volume (MONET), depending on the treatment group. Finally, before/after the patient´s usual treatment time.
19 patients were randomized, 9 in the group MONET vs. DALI and 10 in the group LF vs. DALI.
The tables below show the relative change in the primary parameters between pre- and post-treatment

Treatment group	Outcome	MONET	DALI	Difference MONET – DALI	P
MONET vs. DALI	Total cholesterol	-48.4% (-56.6%; -40.1%)	-49.1% (-57.3%; -40.8%)	0.7% (-5.9%; 7.2%)	0.838
	LDL cholesterol	-64.5% (-85.9%; -43.1%)	-73.5% (-94.9%; -52.0%)	9.0% (-21.9%; 39.8%)	0.567
	Lipoprotein(a)	-74.6% (-134.6%; -14.6%)	-77.4% (-137.3%; -17.4%)	2.8% (-77.4%; 83.0%)	0.945
	Triglycerides	-51.1% (-60.1%; -42.1%)	-40.2% (-49.2%; -31.3%)	-10.9% (-24.4%; 2.7%)	0.115

Treatment group	Outcome	LF	DALI	Difference LF – DALI	P
LF vs. DALI	Total cholesterol	-49.5% (-53.5%; -45.5%)	-52.7% (-56.7%; -48.7%)	3.2% (-1.4%; 7.7%)	0.176
	LDL cholesterol	-66.0% (-72.2%; -59.8%)	-77.2% (-83.4%; -71.0%)	11.2% (5.3%; 17.1%)	0.000
	Lipoprotein(a)	-74.1% (-84.6%; -63.6%)	-67.3% (-77.8%; -56.8%)	-6.8% (-12.7%; -0.9%)	0.025
	Triglycerides	-31.0% (-38.1%; -23.9%)	-24.4% (-31.5%; -17.3%)	-6.6% (-16.0%; 2.9%)	0.171

As in both subsets an LA system based on filtration was compared with a system based on adsorption, as expected notable similarities between the results of the two subsets were observed. All systems investigated (MONET, LF, DALI) were effective in removing total cholesterol, LDL cholesterol, Lp(a) and triglycerides, for which significantly lower levels were consistently observed at post-treatment as compared to pre-treatment. All systems were found to be safe in use.

OS16-04 4:45 p.m.

Quality of life and coping in Dutch homozygous familial hypercholesterolemia patients (#92)

PhD/MD student Janneke Mulder

Erasmus University Medical Center, Internal Medicine, Rotterdam, Netherlands

Purpose: Patients with homozygous familial hypercholesterolemia (HoFH) have a very high risk of premature atherosclerotic cardiovascular disease (ASCVD). Little is known about how HoFH patients experience their condition in daily life and how they cope with. Therefore, our goal was to investigate this in Dutch HoFH patients.
Methods: Adult patients with genetically confirmed HoFH were invited for in-depth interviews [1]. Interviews were transcribed verbatim and analysed according to the principles of grounded theory. In addition, the EuroQol-5D-5L (EQ-5D-5L) and the Threatening Medical Situations Inventory (TMSI) to assess quality of life and coping were administered.
Results: In total, 20 HoFH patients participated in interviews (50% women, median age 38 yrs, 60% with ASCVD, 10% on apheresis). Based on the interviews, a conceptual model with five themes was made with disease perception as central theme. Some patients (n=7, 35%) did not consider themselves to be ill, but did think of others with HoFH as having a disease. In general, patients do not discuss their condition with others outside of their family environment. The most mentioned reason why patients do not discuss their condition in their social environment is the difficulty of explaining HoFH since it is not clearly visible. When confronted with HoFH in daily life, e.g. in case of disease-related events or invasive questions, patients indicated to experience temporary anxiety. Also, half of the patients indicated to find the issue of family planning complicated, women more often than men. Therefore, patients try to live in the moment and try to avoid thinking about the uncertainty of living with HoFH on the long-term. In addition, patients mentioned that dedicated specialist HoFH care helped them to cope with their condition. In the TMSI, most patients showed both monitoring (information-seeking behaviour) and blunting (distractive strategies) coping styles similar to findings from the interview. The EQ-5D-5L showed a median score of 0.839, being only slightly lower than the general Dutch population median of 0.887.
Conclusions: In daily life, HoFH patients use different effective coping mechanisms. The objective elevated risk of ASCVD and premature death is only slightly affecting subjective quality of (daily) life in Dutch HoFH patients. Awareness of quality of life and coping mechanisms can help healthcare professionals to further support and improve the HoFH care given to these patients.

References
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2 June 2023

OS16-05 5:05 p.m.

Development of novel drug for primary chylomicronemia by using antisense (#54)

Prof. Mariko Harada-Shiba[1], Dr. Tadayuki Kobayashi[2], Dr. Fumito Wada[3]

[1] Osaka Medical and Pharmaceutical University, Cardiovascular Center, Takatsuki, Japan; [2] National Cerebral and Cardiovascular Center, Molecular Pathogenesis, Suita, Japan; [3] Liid Pharmaceuticals, Inc, Suita, Japan

Primary hyperchylomicronemia (PHC) is a rare and intractable disease characterized by marked accumulation of chylomicrons in the blood. The levels of plasma triglycerides (TG) levels are above 1000 mg/dL resulting in recurrent acute pancreatitis (1). PHC is caused by defects in the lipoprotein lipase (LPL) pathway due to genetic mutations, autoantibodies and do on. Recently, apolipoprotein C3 (ApoC3) has been shown to be a good therapeutic target against PHC, and a clinical trial of anti-ApoC3 antisense in patients with PHC reported a decrease in TG levels. However, there have been reported some side effects including thrombocytopenia.

We have been involved in the development of antisense for dyslipidemia intractable diseases. We selected antisense sequence targeting human ApoC3 in vitro by the calcium enriched method which can estimate in vivo activity (2). We synthesized our original GalNAc-conjugated antisense (3) which makes it possible to target hepatocytes and found that it reduced ApoC3 mRNA in the liver of humanized mice (mice with human hepatocytes). Thus, we conducted a dosage and administration study using cynomolgus monkeys with the support of the Translational Research Seeds B of Japan Agency for Medical Research and Development. The single dose study was conducted using the doses of 0.5, 1, 3, 20 mg/kg of GalNAc conjugated antisense which was administered subcutaneously. As a result, a dose dependent decrease in TG and ApoC3 in blood was shown which lasted for more than 40 days. After administration of 3 mg/kg of GalNAc conjugated antisense, the liver was harvested after 3, 28, 56 and 91 days and subjected to measure the amount of ApoC3 mRNA. The decrease in ApoC3 mRNA expression in the liver was observed until the day 56th. For the repeated-dose studies, administration of 0.3, and 1.0 mg/kg biweekly and 1.0 and 3.0 mg/kg monthly showed sustained suppression of TG and ApoC3 levels in the blood. There were no adverse effects. We are now conducting pre-clinical studies and planning first in human study.

References

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3:45 p.m. – 5:30 p.m.

Saal 5

OS17 | Autoimmune diseases II: Apheresis in rheumatologic and inflammatory bowel disease

Chairs:
Harald Matthes (Berlin, Germany)

2 June 2023

OS17-01 3:45 p.m.

Apheresis therapy in autoimmune vasculitides - PEXIVAS is not the end(#28)

Dr. Andreas Kronbichler

Medical University Innsbruck, Innsbruck, Austria

The role of plasma exchange in the management of ANCA-associated vasculitis is one of the most controversial topics in nephrology. MEPEX, including patients with a serum creatinine ≥ 5.7 mg/dL, revealed that patients receiving plasma exchange will have a higher likelihood of kidney function recovery at 3 and 12 months. The largest trial in the field, PEXIVAS, included 704 patients and assessed the combined end point end-stage kidney disease and death. After a median follow-up time of 2.9 years, there was no difference between both treatment arms. Pre-defined sub-analysis are published in Abstract forms and aim to assess the impact of PLEX on alveolar hemorrhage. While there is no significant difference, mainly due to limited number of individuals randomized, it seems that plasma exchange is effective to prevent ESKD/death in those with severe respiratory compromised and recruited into the trial. Similarly, sub-studies focusing on kidney function recovery are ongoing and will look at earlier time points. Notably, plasma exchange is an immediated measure and changes on kidney function should be observed earlier than after 3 years. A recent meta-analysis incorporating close to 1,000 patients with AAV found an impact of plasma exchange on ESKD frequency at one year, but at the expense of more severe infections. This lecture will cover recent developments and future directions of plasma exchange in AAV.

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OS17-02 4:05 p.m.

Novel Hemo-adsorbent for Ulcerative colitis in Japan – Immunopure (#44)

Prof. Yoshihiro Endo

Shiga University of Medical Science, Otsu, Japan

There was a remarkable update in Apheresis medical care in Japan in 2020. A novel Hemo-adsorbent, “Immunopure” by NIKKISO, Japan, was approved to be manufactured and covered by Japan Healthcare Insurance (JHI) system as one of the treatments for moderate Ulcerative colitis (UC).

In this presentation, I would like to summarize 3 reports about Immunopure. First, the analysis of the clinical trials in Japan, second, the results of the pilot trials which had been carried in Europe ahead of Japan, and third, the clinical report of Immunopure therapy after listed on JHI approved devices.
Immunopure was the device designed by NIKKISO, a Japanese company. Ahead of the approval in JHI system, the pilot trial was conducted by Dr. Ramlow, the President of E-ISFA. Prof. Danese, the former President of ECCO, and Prof. Kruis, the former professor of University of Munich, gave an additional consideration of steroid-sparing during IBD treatment. They suggested the effectiveness and the safety of this therapy. Furthermore, they suggested the possibility of steroid-sparing during IBD treatment. After getting the result in Europe, clinical trials for moderate UC were collaboratively conducted among 7 institutions in Japan. As a result of the analysis from the trials in Japan, it was shown this device to be safe and clinically efficient in patients with moderate UC. Dr. Waitz from Dr. Ramlow's group assured that this device had similar mechanism to Cellsorba, which had become regrettably discontinued to be on sale. They proved Immunopure selectively and effectively adsorbed and reduced activated platelet-aggregates of platelets, neutrophil, and granulocytes in the outflow line during the therapy.
Immunopure has started to be on the market in Jun. 2020 after listed on JHI devices. According to the manufacturer's report, more than 60 hospitals have utilized this device until Sep. 2022. As Immunopure therapy is usually given 10times in a course, it is supposed that a little over 200 patients got Immunopure therapy. The number of the practices has been increasing every year, and that expected to bring the clinical assessment to us.

OS17-03 4:25 p.m.

Positioning of apheresis for ulcerative colitis ~compared to biologics and JAK inhibitors (#109)

PhD/MD Makoto Naganuma

Kansai Medical University, Third Department of Internal Medicine, Division of Gastroenterology and Hepatology, Hirakata, Japan

Ulcerative colitis (UC) is a chronic intestinal disease with abdominal symptoms, characterized by repeated recurrence and remission, with continuous inflammation. Although the etiology and morbidity of UC are unknown and a fundamental treatment for UC has not yet been established, its pathophysiology has been extensively studied and found to involve host genetic factors, immune system dysregulation, and environmental factors. Although 5-aminosalicylic acid and corticosteroids (CS) are effective, some patients do not achieve clinical remission with these treatments. Therefore, several therapeutic treatments for treatment-refractory UC have been developed, including calcineurin inhibitors, anti-tumor necrosis factor (TNF)-α antibodies, Janus kinase (JAK) inhibitors, anti-integrin antibodies, and anti- interleukin (IL)-12/23 therapy. However, treatment positioning for these agents remains unclear due to differences in clinical background of the patients, such as age, clinical and endoscopic severity, and previous use of CS or biologics. Although recent clinical guidelines on moderate-to-severe UC management described the treatment options of biologics and JAK inhibitors for patients refractory to 5-ASA or CSaccording to the previous use of TNF-α antibodies. However, these treatments were described in parallel and the drug choice should be determined by clinical factors, patient choice, cost, adherence likelihood, and local infusion capacity.

Ttherapeutic effect of infliximab and JAK inhibitors is relatively rapid although that of apheresis is not so rapid. Regarding the safety, while TNF-α antibodies and JAK inhibitors have the potential to induce severe adverse effects, apheresis therapy is considered as a tolerate and safe treatment. Compared to biologics and apheresis, anti-integrin antibodies, vedolizumab, is a relatively safe, so it may be positioned similar to apheresis. Although there is more evidence for outpatient treatment with vedolizumab, apheresis appears to have more evidences in hospitalized patients. In recent years, the effectiveness of therapy combining apheresis with biologics and calcineurin inhibitors has also been reported. in viewpoint of both rapid efficacy and safety, it may be possible to expect a treatment option that giving combination of biologics and apheresis in hospitalized patients to induce clinical remission and then, treating patients with apheresis alone as a maintenance therapy in the near future.

OS17-04 4:45 p.m.

Is apheresis therapy still an option in rheumatic diseases? (#96)

PhD/MD Ken Yamaji

Juntendo University, Internal Medicine and Rheumatology, Tokyo, Japan

No other area of medicine, except for rheumatic diseases, has seen such dramatic advances in pharmacotherapy. Immunosuppressants, biologics, and JAK inhibitors have been developed one after another, resulting in marked improvements not only in prognosis of organ damage but also in prognosis of life, ADL, and quality of life. However, it is also true that there are still intractable conditions that cannot be resolved even with the use of combination therapies that have made great strides in pharmacotherapy.
Is apheresis therapy still an option in rheumatic diseases?
The answer is yes.
Here, we present apheresis therapy for such refractory conditions.

OS17-05 5:05 p.m.

Apheresis treatment leads to increased levels of circulating neutrophil extracellular traps (#62)

Dr. Natalia Jarzebska[1], Dr. Sergey Tselmin[1], Dr. Andrew Aswani[2,3], Prof. Juergen Graessler[1], Prof. Ulrich Julius[1], Dr. Jens Passauer[1], Prof. Stefan R. Bornstein[1,4], Priv.-Doz. Roman N. Rodionov[1,5]

[1] University Hospital Carl Gustav Carus, Technische Universität Dresden, Department of Medicine III, Dresden, Germany; [2] Guy's and St Thomas' NHS Foundation Trust, Department of Intensive Care Medicine, London, UK; [3] Santersus, Zurich, Switzerland; [4] King's College London, School of Cardiovascular and Metabolic Medicine and Sciences, Faculty of Life Sciences & Medicine, London, UK; [5] University Hospital Carl Gustav Carus, Technische Universität Dresden, University Center for Vascular Medicine, Dresden, Germany

Background: Neutrophil extracellular traps (NETs) are net-like complexes consisting of DNA, histones, and granule proteins, which are released by neutrophils to the extracellular space in a special form of programmed cell death (NETosis). They represent an evolutionarily conserved element of the innate immune response and bind pathogens to prevent their spread. However, NETs can also contribute to the development and progression of various diseases, including immune-related and cardiovascular, and are emerging as a new potential therapeutic target. The goal of the study was to investigate whether conventional lipoprotein apheresis methods can be used to remove NETs.
Methods: Blood samples were collected from 52 patients referred for lipoprotein apheresis just before and after a single treatment session and 1 week later. Apheresis was performed using methods based on double-filtration, precipitation or (immuno)adsorption. NETs in plasma were measured using a chemiluminescence immunoassay including labeled anti-nucleosome and anti-histone modifications antibodies.
Results: Surprisingly, all apheresis methods investigated led not to a decrease, but increase in the levels of circulating NETs right after the treatment session. One week later the plasma levels of NETs were back to baseline.
Conclusions: Our results suggest potential benefits of adding an additional NETs-specific filter to remove the excess of NETs before reinfusion of plasma in patients undergoing apheresis. Understanding the mechanisms responsible for the elevated NETs levels after apheresis requires further research, but one possible explanation might be that cell injury in the extracorporeal circuits leads to release of NETs.

3:45 p.m. – 5:30 p.m.

Saal 4

OS18 | Apheresis Service and Education (in English language)

2 June 2023

OS18-01 3:45 p.m.

NHS Blood and Transplant - A Gold Standard Therapeutic Apheresis Service Model (#78)

Claire Gillson, Christopher Dixon

NHS Blood and Transplant, Therapeutic Apheresis Services, National, UK

NHS Blood and Transplant (NHSBT) Therapeutic Apheresis Services (TAS) teams provide adults and children with access to an extensive portfolio of apheresis therapies across a wide range of clinical specialities. Based within NHS Trusts in eight geographical regions across England and Wales, the medical and nursing teams deliver a range of collection and therapeutic procedures using specialist apheresis machines that exchange, remove or collect specific components from within the blood. In addition, TAS support the UK Stem Cell Registries, clinical trials and research programmes.

Working in partnership with hospital clinical teams, TAS puts patients at the centre of how it delivers its services. Working with partners, patient pathways and protocols are developed to ensure patient procedures are safe, effective and efficient.

TAS national infrastructure with regional service provision offers a scale of service which is resilient and is able to provide high quality apheresis services for all patients. NHSBT's Apheresis model includes:

- Therapeutic apheresis unit - located in regional trust
- Dedicated specialist apheresis nursing team - expert in full range of apheresis procedures for adults and children
- Consultant haematologist - providing expert apheresis support for patients and referring clinical teams
- Mobile patients - attend TAS Unit for apheresis procedure
- Sick in-patients - TAS nurses are mobilised to attend the patient's bedside in regional hospitals
- Apheresis machines - NHSBT logistic teams transport equipment to the patient's location for treatment
- On-call services - accessible for 24/7 urgent apheresis access, for example for red cell exchange for sickle cell disease.

TAS front-line staff are supported by Quality, Governance and Education teams ensuring TAS teams have access to quality training programmes and the highest clinical and regulatory standards are met. Also, the Service Development and Business Support teams who collaborate with partners to develop new services which bridge gaps for patient access to apheresis services.

TAS service model enables 12000 procedures to be provided for 2100 patients and donors each year. In our latest patient survey, 94% of patients reported overall satisfaction in service as 9-10 out of 10. In addition, 78% of our referring clinicians scored TAS overall service as 9-10 out of 10. We continue to evaluate our service by regularly seeking feedback from our patients, donors and referring clinical teams.

2 June 2023

OS18-02 4:05 p.m.

Education and Traininig in Apheresis (#83)

Elisabete Gaspar, Sandra Jones, Chrisitne Hood, **Bridget Audsley**

NHS Blood and Transplant, NHS, Barnsley, UK

Therapeutic Apheresis Services is a unique and rapidly expanding service provide apheresis services to NHS Trusts across the UK. The service had undergone high staff turnover resulting in loss of knowledge and specialist expertise. The impact on staff satisfaction and retention highlighted in leaver interviews flagged the need for greater education and training and ongoing support. A new education and training strategy was developed ensuring regulatory compliance, to support new starters and provide continued professional development opportunities for the current nursing workforce.

Investment in a larger education team has enabled development of established successes in training. A continuous improvement scoping event identified the need for a new bespoke training programme. Cohort groups allow greater peer support and shared learning to maintain national standards and reinforce robust regulatory compliance. Development of new procedural competencies, an interactive modular training programme and coordinated manufacturer training streamlines national training methods and delivery. Increased clinical presence allows robust oversight and monitoring of training gaps and support provision. The team has recently expanded to support the roll out of ultrasound guided cannulation to improve the patient experience but reducing the requirement for central venous access to perform procedures.

Streamlining and oversight of recruitment enables a fixed start date and induction, with content refined following feedback. Existing staff have also requested to attend and support training modules. A new digital training package for the care of paediatric patients has enabled staff to develop knowledge and confidence when treating young patient. Responsibilities between education and operations are now clearly defined and both works closely with Quality and Governance teams to ensure teams are supported and deliver the best care to our patients. Support for mentors was increased as a knowledge gap was identified. An annual shared practice day provides a platform for ongoing learning and revalidation.

Robust oversight from an experienced education team has introduced bespoke training creating streamlined practice and regulatory compliance. Creation of a uniquely knowledgeable workforce and further educational opportunities such as access to Masters courses, advanced nurse practitioner roles and extended roles aims to improve staff satisfaction, development and retention.

2 June 2023

OS18-03 4:05 p.m.

Alliances and Challenges of a CommunityBlood CenterMobile Apheresis Program Providing Carefor Donors and Patients during Covid-19 (#3)

Betty M. Doggett, Pamela Malvern, Tamra Capps, PhD/MD Todd Nishimoto, PhD/MD Geeta Paranjape, PhD/MD Laurie Sutor

Carter BloodCare, Clinical Apheresis, Dallas, USA

Purpose:
A team of nurses and technicians from our community blood center provides mobile apheresis as requested for therapeutic procedures and cellular therapy collections. Therapeutic apheresis procedures are done as inpatients in local hospitals, while the cellular therapy collections are done as outpatients in one of our donor center fixed sites, or at one of the hospital clinics. We have performed more than 30,000 procedures since the inception of our program in 1992. With the onset of the SARS-CoV-2 epidemic in early 2020, challenges arose in providing the usual care. Staffing shortages, supply chain disruptions, uncertainties as to the infectious nature of the virus, and general staff concerns about safety and burnout became important concerns. This abstract addresses how our apheresis service successfully adapted to the COVID crisis.
Methods:
Hospital referral forms were updated to include the patient's COVID status. To promote patient and staff safety, adequate levels of personal protective equipment (PPE) needed to be ensured. If hospitals did not have enough for our staff, we needed to bring our own. The individual PPE items included a gown, face shield, mask, shoe covers, and hair bonnet. Each staff member signed out a single-use PPE packet and disposed of items on-site. Also, each staff member was provided with additional N-95 masks, face shields, and goggles for added protection. Staff working in the office followed COVID protocols requiring masks and social distancing, and rotating days working remotely when possible. Staff was given additional education and time with the medical director to address hesitancy to work with COVID patients. Our service opted to do the procedures with the instrument at the bedside, rather than have the machine in the next room. We used the decontamination protocol recommended by the manufacturer to clean the Optia after each patient treatment.
Results:
13 patients with COVID were successfully seen between December 2020 and April 2021 for therapeutic apheresis procedures. These patients qualified as ASFA category 1 or 2 indications. In total, 57 plasma exchanges were completed and one white blood cell depletion was done.
Conclusion:
Careful planning and judicious use of resources allowed continued successful treatment of local patients and donors despite the onset of the COVID-19 pandemic. Personnel safety of our staff was maintained by a combination of PPE, good work practices, and remote work when feasible.

2 June 2023

OS18-04 4:05 p.m.

Effectiveness of therapeutic apheresis (TA): experience and outcomes analysis in an italian center (#65)

Dr. Giuseppe Leonardi[1], Vito Lobefaro[2], Michele Grammatico[1], Alessia Baccaro[1], Giuseppina Ungaro[1], Dr. Cosima Balestra[1], Dr. Flavia Capaccio[1], Dr. Patrizia Covella[1], Dr. Annarita De Giorgi[1], Dr. Brigida Di Renzo[1], Dr. Antonio Flores[1], Dr. Marco Mangiulli[1], Dr. Michi Recupero[1], Dr. Palmira Schiavone[1], Dr. Alessandra Spinelli[1], **PhD/MD Luigi Vernaglione**[1]

[1] "A. Perrino" Hospital, Nephrology, Brindisi, Italy; [2] La Traccia Software House, Softwares, Matera, Italy

Introduction. TA represents an important therapeutic approach in some diseases and its precociousness is decisive in determining the outcome. Although TA is considered a first or second level therapy in many diseases, a knowledge gap often remains in relation to the different triggers or cut-offs for initiation or different methods to be applied. The settings for TA differs among hospitals. In this study, we retrospectively analyzed the TA performed on a large cohort of patients admitted in our unit between 2016 to date taking into account the underlying disease, TA techniques and replacement fluids. We also evaluated the outcomes of the patients.

Materials and methods. A retrospective analysis was performed on 19 patients admitted to our unit in the last 7 years and affected by diseases requiring TA treatment. The mean age was 63.9 ± 10 years. 61% of them were affected by histologically diagnosed active ANCA-related vasculitis, 22% by Haemolytic Uremic Syndrome and 17% by other pathologies (sepsis, glomerulonephritis).

Results. 90% of treatments were plasma exchange (PEX), 5% were Double Filtration Plasmapheresis (DFPP), and 5%, Coupled Plasma Filtration Absorption (CPFA). 88% of the patients were therefore discharged while 22% died during their hospital stay. The replacement fluid was Fresh Frozen Plasma (FFP) in 85% of cases and a 5% albumin solution in saline in 15% of cases. AKI requiring replacement dialysis was also present in 38% of cases. The mean replacement volume was 2750 mL. The mean hospitalization was 33.8 days. After 5 years the survival rate is 55%. A Central Venos Catheter for hemodialysis was used as vascular access in 95% of patients.

Conclusions. In our experience TA still plays a pivotal role in several diseases such as ANCA-related vasculitis. The use of TA allowed for 88% of home discharges; in 38% of cases the underlying disease led to a worsening of renal function requiring chronic hemodialysis treatment. However the diseases requiring TA presented a high 5-year mortality rate (55%).

OS18-05 4:05 p.m.

Vascular access options for therapeutic apheresis

PhD/MD Rasheed Balogun

University of Virgina, Charlottesville, USA

3 June, 2023

8:30 a.m. – 10:15 a.m.

Saal 6

OS19 | Autoimmune diseases III Apheresis for renal diseases

Chairs:
Wladimir Szpirt (Copenhagen, Denmark)

3 June 2023

OS19-01 8:30 a.m.

Apheresis and desensitization before kidney transplantation

Prof. Lionel Rostaing

CHU Grenoble Alpes, Grenoble, France

OS19-02 8:50 a.m.

The role of apheresis therapy in glomerulopathies

Benjamin Savenkoff

CHR Metz-Thionville, Metz, France

OS19-03 9:10 a.m.

Influence of therapeutic plasma exchange treatment on early survival of septic patients: a systematic review and meta-analysis (#46)

PhD/MD Vladimir Kuklin[1], PhD/MD Michail Sovershaev[2], PhD/MD Johan Bjerner[2], Dr. Philip Keith[3], Dr. L. Keith Scott[4], Prof. Wladimir Szpirt[6], Prof. Bernd Stegmayr[8]

[1] Ahus university hospital, Oslo, Norway; [2] Fürst Medical Laboratory, Oslo, Norway; [3] Lexington Medical Center, Lexington, USA; [4] Louisiana State University Health Sciences Center, Shreveport, USA; [5] Ahus university hospital, Oslo, Norway; [6] Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [7] University of Ottawa, Ottawa, Canada; [8] University Hospital, Umea, Sweden

Introduction

The effect of therapeutic plasma exchange (TPE) to reduce lethal outcome by removal of substances involved in the pathogenesis of septic shock remains unclear. Thus, the main aim of the study was to evaluate whether treatment with TPE influences on the early survival in septic patients.

Methods

The National Library of Medicine's Medline, Ovid, Cochrane Library database and clinical trial.gov from January 1966 until October 2022 were searched for terms «therapeutic plasma exchange, plasmapheresis, sepsis, and septic shock». We used the Cochrane Collaboration's tool for assessing risk of bias in the randomized clinical trials (RCT) and ROBINS-I tool for assessing risk of bias in non-randomized studies. The meta-analysis was performed using statistical program of R Core Team (2020): A language and environment for statistical computing. R Foundation for

Statistical Computing, Vienna, Austria, https://www.R-project.org/. Individual trials and summary results were reported as a relative risk (RR) with 95% confidential intervals (CI) of reported mortality in patients assigned to TPE versus controls.

Results

In the meta analysis, we included five randomized clinical trials (RCTs) and sixteen matched cohort studies (MCSs), enrolling a total of 951 adult critically ill septic patients where 557 of them were treated with TPE. Three RCT were rated as good quality with low risk of bias, whereas there was unclear with one RCT and one RCT had a high risk of bias. Eleven of MCSs were rated as a good quality with low risk, where two and three of these MCSs were assessed to have moderate and/or serious risk of bias, respectively. We pooled data about mortality at 14 to 35 days from five RCTs and seven MCSs (n=726) where 332 of septic patients were additionally treated with TPE. The pooled data showed a significant overall reduction in risk ratio (RR 0.50, 95% CI 0.41-0.60, p<0.001, I2 47%) for application of TPE using plasma as replacement fluid compared to the standard intensive care therapy. In subgroup analyses both centrifuge (RR 0.52, 95% CI 0.36-0.75) and membrane filtration techniques of TPE (RR 0.57, 95% CI 0.35-0.91) were associated with significantly reduced mortality.

Conclusion

This meta-analysis shows that TPE, using plasma replacement, helps reduce the risk of early death as adjunct therapy in patients failing standard treatment.

OS19-04 9:30 a.m.

An evolution in treatment of anti GBM nephritis – plasma exchange or imlifidase?

Prof. Wladimir Szpirt

Rigshospitalet, Copenhagen, Denmark

OS19-05 9:45 a.m.

Selective Plasma Exchange in Critical Care (#15)

Haruna Yoshida, Ayumu Tsuruoka, Tomoya Yamashita, Kazuaki Shigemitsu, Hiroshi Rinka

Osaka City General Hospital, Emergency and critical care medical center, Osaka, Japan

[Background]

In recent years, there have been many reports on the efficacy and safety of the selective plasma exchange (SePE) procedure using the Evacure plus EC-4A10 plasma separator, which has a smaller pore size than conventional membrane plasma separators.

[Objective and Methods]
Patients who were treated with SePE in our ICU from February 2018 to January 2023 were included in the study. We retrospectively examined the details of SePE: immunoglobulin G (IgG) removal rate, fibrinogen (Fib) removal rate, safety outcomes, and clinical efficacy based on medical records.

[Results]
We performed 38 sessions of SePE procedures in 10 patients (three cases of autoimmune encephalitis, four cases of rapidly progressive glomerulonephritis with alveolar hemorrhage, one case of myasthenic crisis, one case of acquired hemophilia A, and one case of thyroid crisis) in our ICU and investigated its efficacy and safety.
The median quantity of blood flow was 100 ml/min, the median plasma separation rate was 19.4% of the quantity of blood flow, and the median processed plasma volume was 1.4 times the circulating plasma volume.
The median IgG removal rate per session was 59.3%, and the median Fib removal rate per session was 7.1%.
There were no cases of allergic reactions, bleeding events, decreased blood pressure, or worsening of respiratory condition.
Regarding clinical efficacy, three cases of autoimmune encephalitis, one case of myasthenic crisis, and one case of thyroid crisis were weaned from the ventilator. Four cases of rapidly progressive glomerulonephritis achieved disappearance of hemoptysis and improvement of respiratory condition. In one case of acquired hemophilia A, the inhibitor was removed, and bleeding tendencies were improved.

[Discussion and Conclusion]
Patients with severe coma, respiratory failure, and/or circulatory failure are admitted to the ICU. Many of them are post-operative of major surgeries or show bleeding tendency.
SePE seems to be safer for patients after major surgeries or with bleeding tendency than other therapeutic plasma exchange modalities because of fewer Fib reductions after treatment. It also seems to be a preferred modality if the main purpose of therapeutic plasma exchange is to remove IgG-class autoantibodies.

OS19-06 10:00 a.m.

Evaluation of iron deficiency and mechanisms of potential iron loss in patients undergoing immunoadsorption (#77)

Dr. Noemi E. Ginthör[1], Dr. Tobias Niedrist[2], Priv.-Doz. Alexander H. Kirsch[1], Dr. Werner Ribitsch[1], PhD/MD Andras Deak[1], Dr. Michael Kolland[1], Dr. Andreas Meinitzer[2], Prof. Kathrin Eller[1], Prof. Alexander R. Rosenkranz[1], PhD/MD Katharina Artinger[1]

[1] Medical University of Graz, Clinical Division of Nephrology, Graz, Austria; [2] Medical University of Graz, Clinical Division of Medical and Chemical Laboratory Diagnostics, Graz, Austria

Background: Immunoadsorption (IAS) is a well-established tool for the removal of autoantibodies in a variety of antibody–mediated diseases where conventional therapy has reached its limits and is also used to prepare recipients for AB0-incompatible kidney transplantation. Anaemia has a high global prevalence and is caused in over 80% by iron deficiency. Data on the prevalence of iron deficiency in patients undergoing IAS is scarce and limited mainly to patients treated with lipoprotein apheresis. Direct evidence of iron loss through apheresis is still lacking. The aim of

this prospective observational study was to evaluate the potential role of IAS in the development of iron deficiency due to loss of iron through binding and removal during apheresis.

Methods: Eighteen patients undergoing therapeutic IAS were prospectively included. Serum parameters specific for anemia and iron loss (iron status, Vitamin B12, folic acid, red blood cell count) were measured before and after IAS at initiation as well as one,wo and three weeks after initiation of treatment. The last IAS in this time period was regarded as “last visit”. Eluted solution was evaluated for the abundance of iron, ferritin and transferrin.

Results: Five patients underwent therapeutic apheresis for desensitization before ABO-incompatible kidney transplantation, three patients for underlying neurological diseases and ten patients for post-transplantation complications. All patients undergoing therapeutic apheresis before ABO-incompatible kidney transplantation received at least one dose of i.v. iron. Iron substitution was not followed by a significant rise in serum iron parameters.Patients undergoing therapeutic IAS for other reasons than desensitization before ABO-incompatible kidney transplantation did not receive i.v. iron. In these patients, a 16.6% decrease in serum hemoglobin from initiation to last visit as well as a non- significant decrease in serum iron parameters was found. Ferritin was found in significant amounts after eluting columns with glycine.

Conclusion: We observed anaemia and low iron status in patients undergoing IAS. Our findings show that iron deficiency is common in patients undergoing immunoadsorption and suggest that ferritin is at least in part lost during apheresis.

8:30 a.m. – 10:15 a.m.

Saal 5

OS20 | Lipids and CVD V: Pleiotropic and other expected windfall gains

Chairs:
Dursit Lumlertgul (Chiang Mai, Thailand)

3 June 2023

OS20-01 8:30 a.m.

Health care-relevant retrospective analysis based on real-world data on cardiometabolic risk profile in patients with atherosclerotic-related cardiovascular disease (#61)

Dr. Grit Waitz[1], Dr. Jens Ringel[2], Frank Breuel[1], Dr. Ulrike Wolf[3], Dr. Elke Wecke-Harbarth[3], Dr. Petra Gierloff[4], Thomas Zimmermann[1], Dr. Wolfgang Ramlow[5]

[1] BioArtProducts GmbH, Rostock, Germany; [2] Diamedikum Potsdam, Potsdam, Germany; [3] Nephrologicum Lausitz, Cottbus, Germany; [4] Praxis für Allgemeinmedizin, Kleinmachnow, Germany; [5] Apherese Care Rostock (ACR), Rostock, Germany

Introduction: With early diagnosis, treatment, and education, cardiovascular events could probably be avoided or significantly delayed in many patients at very high cardiovascular risk. However, in daily care, high-risk patients are often disregarded because they have a low level of suffering in early disease stages. Despite the availability of a wide variety of lipoprotein lowering drugs, a high proportion of patients with atherosclerotic cardiovascular disease (ASCVD) show suboptimal controlled lipoprotein levels. The aim of this study approved by an independent ethics committee was to analyze more than 50.000 anonymous electronic patient records from three different outpatient health care facilities in the Berlin-Brandenburg region with regard to the detection of cardiometabolic risk factors with special emphasis on dyslipidemia.

Methods: Data sets of electronic health records were analyzed retrospectively for a period of approx. 24 months (Lipoprotein (a) (Lp(a)) measurements for 60 months if possible) in an anonymized and aggregated manner. Various search algorithms had been developed to improve the detection of cardiometabolic high-risk patients. To achieve this goal, routine laboratory parameters, clinical diagnoses (ICD), billing data, and prescribed medications were evaluated.

Results: Forty four percentof all analyzed patients had one of the following comorbidities: ASCVD, nicotine abuse, relevant proteinuria, drug-dependent diabetes, chronic kidney disease, relevant dyslipidemia, relevant hypertension. Patients diagnosed with relevant ASCVD were more likely to have other comorbidities (80.2%) and a higher number of different comorbidities. A significantly higher proportion of patients with relevant ASCVD and at least one Lp(a) measurement had further comorbidities compared with the group without relevant ASCVD with at least one Lp(a) measurement. However, Lp(a) measurements were performed in only 15.7% of patients with relevant ASCVD. The percentage of patients with relevant ASCVD increased with rising serum Lp(a) concentrations from 23.1% to 34.6%.

Conclusions: The identification of patients with cardiometabolic risk factors can substantially be improved by search algorithms analyzing routinely collected patient data. To further advance awareness and medical care for these high-risk individuals, better diagnosing and documentation of cardiometabolic risk factors is urgently required.

3 June 2023

OS20-02 8:50 a.m.

Lipoprotein apheresis for the treatment of familial hypercholesterolemia in Japan (#55)

Prof. Mariko Harada-Shiba[1], PhD/MD Hisashi Makino[2]

[1] Osaka Medical and Pharmaceutical University, Cardiovascular Center, Takatsuki, Japan; [2] National Cerebral and Cardiovascular Center, Endocrinology and Metabolism, Suita, Japan

Familial hypercholesterolemia (FH) is an inheritable metabolic disease linked to mutations in the LDL receptor or its related genes. FH is characterized by high levels of LDL-cholesterol (LDL-C), xanthomas and premature atherosclerotic cardiovascular diseases (ASCVD). In the homozygous FH (HoFH) patients, atherosclerosis develops from their early childhood. Lipoprotein apheresis (LA) has been shown to be the main therapeutic approach in these patients. Severe heterozygous FH (HeFH) that respond poorly to medical treatments also have had indication of LA. Recently, novel lipid lowering drugs have been developed, some of which have already been on a market. Introduction of inhibitors of PCSK9, evolocumab and alirocumab has made it possible to reduce LDL-C levels in HeFH and some of HoFH patients. Lomitapide, inhibitor of MTP has been indicated to HoFH, which reduced LDL-C levels in HoFH patients (1). Evinacumab, an inhibitor of angiopoietin-like 3 (ANGPTL3) has been developed and on the market in US and Europe, which is still under expanded clinical trial in Japan.

The development of these novel drugs has contributed to the better control of lipids in HoFH and HeFH patients. We have recently published a paper describing worldwide experience of HoFH which summarized 751 HoFH patients (2). Among 751 patients 92% received statins, 64% received ezetimibe, 39% received LA. On-treatment LDL-C levels were lower in high-income countries (3·93 mmol/L) versus non-high-income countries (9·3 mmol/L), with greater use of three or more lipid-lowering therapies.

In Japan, the medical cost of HoFH patients have been covered by the Japanese and local government under the intractable disease low. Anonymous data of 130 HoFH patients were obtained from the Ministry of Health and Welfare. Age averaged 51 y.o., 63% and 96% had cutaneous and tendon xanthoma, respectively. Although they have been treated with statins, ezetimibe and LA, 33.6% had aortic valve disease, 65.2% had coronary artery disease including 36.5% PCI and 23.0% CABG.

LA reduces risks of ASCVD by not only removal of atherogenic lipoproteins but also removal of factors related to atherosclerosis (3). We have experienced some cases who developed ASCVD after cessation of LA although their LDL-C levels were well controlled by recent developed drugs. We need to be very careful in stopping LA.

References

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[3] Yuasa Y, Osaki T, Makino H, Iwamoto N, Kishimoto I, Usami M, Minamino N and Harada-Shiba M. Proteomic analysis of proteins eliminated by low-density lipoprotein apheresis. Ther Apher Dial. 2014;18:93-102.

3 June 2023

OS20-03 9:10 a.m.

Efficacy and safety of LDL apheresis for the treatment of cholesterol crystal embolism (#11)

Prof. Takafumi Ito[1,2]

[1] Teikyo University School of Medicine, Department of Internal Medicine, Nephrology, Ichihara, Japan; [2] Shimane University Hospital, Izumo, Japan

Cholesterol crystal embolism (CCE) is a disease in which cholesterol crystals from atherosclerotic lesions disperse and obstruct peripheral blood vessels, causing organ damage.
Treatment with corticosteroids, RAS inhibitors, HMG-CoA reductase inhibitors, and LDL apheresis (LDL-A) may be used, but none of these methods have been established.
At Shimane University Hospital, LDL-A was first performed for CCE after cardiac catheterization in 2008, with good results. Since then, we have had more cases, so we divided 11 CCE patients who underwent LDL-A at our hospital from April 2008 to March 2018 into two groups, non-dialysis and dialysis groups within one year after CCE onset and examined the clinical differences between them (study control number 20181018-3).
Clinical indices included age, gender, serum creatinine (Cr) level before onset, serum Cr level at diagnosis, serum Cr level at LDL-A initiation, serum Cr level after treatment, eosinophil count at diagnosis, time from trigger event to LDL-A initiation, time from diagnosis to LDL-A initiation, whether serum Cr level was doubled at diagnosis, and doubling of serum Cr level at LDL-A initiation, corticosteroid dosage, presence of RAS inhibitors, presence of HMG-CoA reductase inhibitor administration, and number of LDL-A were examined.
Serum Cr levels before onset, at diagnosis, at the start of LDL-A, and after treatment tended to be lower in the non-dialysis group. The time from trigger event to LDL-A initiation was not significantly different between the two groups, but the time from diagnosis to LDL-A initiation tended to be longer in the non-dialysis group.
Patients with good renal function before the onset of CCE benefitted from LDL-A even if their renal function deteriorated severely.
In this presentation, I will review the epidemiology, diagnosis, and treatment strategies for CCE and present the results of the first prospective multicenter trial evaluating the efficacy and safety of LDL-A use for CCE after cardiovascular surgery conducted under the Japanese advanced medical care system (Ishiyama K, et al. Ther Apher Dial 2022;26:456-464).

3 June 2023

OS20-04 9:30 a.m.

Actual situation at the Dresden Lipoprotein Apheresis in 2023 (#12)

Lena Jochheim[1], Dr. Sergey Tselmin[1], Dr. Ulrike Schatz[1], Prof. Ulrich Julius[1]

[1] University Hospital Carl Gustav Carus at the Technische Universität Dresden, Lipidology and Lipoprotein Apheresis Center, Department of Internal Medicine III, Dresden, Germany; [2] University Hospital Carl Gustav Carus at the Technische Universität Dresden, Lipidology and Lipoprotein Apheresis Center, Department of Internal Medicine III, Dresden, Germany; [3] University Hospital Carl Gustav Carus at the Technische Universität Dresden, Lipidology and Lipoprotein Apheresis Center, Department of Internal Medicine III, Dresden, Germany; [4] University Hospital Carl Gustav Carus at the Technische Universität Dresden, Lipidology and Lipoprotein Apheresis Center, Department of Internal Medicine III, Dresden, Germany

Lipoprotein apheresis (LA) is an effective therapy for reducing the incidence of atherosclerotic cardiovascular events (ASCVE) in patients, who are at high risk for atherogenesis due to severe hyperlipoproteinemia and in whom lipid-lowering medications are either insufficient or not well tolerated.
154 patients (females 34%) are treated with LA in Dresden, Saxony, Germany. These patients will be characterized with respect to age, lipid pattern, medication and ASCVE before and after LA initiation. These data will be compared with the 2018 analysis describing 339 patients (females 32%) from different Saxonian LA units.
48 patients started LA during the years of 2019 to 2022.

Year	2019	2020	2021	2022
Number	13	19	4	12

15 patients discontinued LA during the above mentioned years.

The age of the patients ranges from 36 to 85 years, the median is 64 years. Patients' age of entry into LA ranged from 29-80 years, median 58 years. The duration of LA varied from 0.2 to 21 years, with a median of 6 years. Most of them are treated weekly.
Currently, 8 different kinds of devices, based on different physical mechanisms

- double filtration: Lipid Filtration, MONET, Inuspheresis, Afersmart
- precipitation: HELP
- adsorption (whole blood method): Liposorber D, DALI
- (immuno)adsorption: Therasorb LDL

are used and their efficacy in lowering blood lipids and pleiotropic effects will be compared.
Mean values before and after a single session in January 2023 were:

	Pre LA	**Post LA**	**Relative reduction**	**Interval mean value**
Apolipoprotein B (g/l)	0.68	0.18	74%	
LDL-C (mmol/l)	3.27	0.76	77%	2.59

	Pre LA	Post LA	Relative reduction	Interval mean value
Lipoprotein(a) (nmol/l)	184.49	44.22	76%	127.32
Triglycerides (mmol/l)	2.05	1.01	51%	
HDL-C (mmol/l)	1.39	1.13	19%	
Total cholesterol (mmol/l)	3.98	2.92	27%	
Non-HDL-Cholesterol (mmol/l)	2.59	1.78	31%	

Currently, 54 patients (35%) are additionally treated with PCSK9 inhibitors.

Almost all patients had experienced ASCVE in the coronary, carotid, and peripheral arteries before starting LA treatment. During LA treatment, ASCVE occurred in 58 (38%) of 154 patients.
Our patients have increased in number, comparing with 2018, are being treated mainly for elevated Lp(a) levels. All used devices are effective with respect to lowering Lp(a) and LDL-C concentrations. Nevertheless, we started PCSK9 inhibitor therapy in many patients, in order to improve their metabolic situation.

OS20-05 9:45 a.m.

Effective exosomes reduction in hypercholesterinemic patients suffering from cardiovascular diseases by lipoprotein apheresis: exosomes pheresis (#30)

Sophie Schroeder[1], Prof. Andre Fischer[1,2,3], Prof. Volker J. Schettler[4]

[1] German Center for Neurodegenerative Diseases (DZNE) Goettingen, Department for Epigenetics and Systems Medicine in Neurodegenerative Diseases, Goettingen, Germany; [2] University Medical Center Goettingen, Department of Psychiatry and Psychotherapy, Goettingen, Germany; [3] University of Göttingen, Cluster of Excellence "Multiscale Bioimaging: from Molecular Machines to Networks of Excitable Cells" (MBExC), Goettingen, Germany; [4] Center of Nephrology Goettingen GbR, Apheresis and Dialysis, Goettingen, Germany

BACKGROUND:Extracellular vesicles (EVs) are released by a majority of cells in response to cell activation, injury, or cell death. EVs participate in cell-to cell communication and have also been implicated with atherosclerosis. EVs get co-transported with lipoproteins in blood. In this study, we compared three lipoprotein apheresis procedures (LA) for their efficacy to lower EV concentration in blood.
METHODS AND RESULTS: 46 hypercholesterinemic patients suffering from extreme and very high atherosclerotic cardiovascular diseases (ASCVD) were selected for this study. All specimen were collected before (BA) and at the end of apheresis (EA) and plasma was isolated directly. EVs from plasma were isolated using the ultrafiltration method by Merck and analyzed using a Nanosight LM14C.

EVs were similarly reduced by all LA methods (median: 93.4%;16. percentiles: 84.9% ; 84 percentiles: 97.6%), whereas LDL-C (66%;55%;75%) and Lp(a) (72%;67%;79%) were less effectively reduced. No difference in EVs reduction could be determined, comparing a hemoperfusion procedure (DALI; n=16), a precipitation procedure (HELP; n=7) and double filtration procedure (Thermofiltration; n=23).
CONCLUSIONS:
For the first time, it was shown that EVs could be removed very effectively by different LA procedures and this was independent of the LA procedure used. What impact this exosomes pheresis has on the pathophysiological process of atherosclerosis needs to be shown by further studies.

OS20-06 10:00 a.m.

Prognostic value of plasma lipidome for determining the risk of cardiovascular events in patients with lipoprotein apheresis (#22)

Dr. Romy Walther, Dr. Sergey Tselmin, Prof. Ulrich Julius, Dr. Ulrike Schatz, Priv.-Doz. Roman N. Rodionov, Prof. Stefan R. Bornstein, Prof. Juergen Graessler

Technische Universität Dresden, University Hospital, Department and Outpatient Department of Medicine III, Dresden, Germany

Subject: Lipoprotein apheresis (LA) leads to a considerable reduction of cardiovascular events (CVE) in patients with severe disturbances of lipid metabolism, particular in patients with lipoprotein(a) (LP(a)) hyperlipoproteinemia. As already shown earlier, acute and chronic LA treatment is associated with profound modifications of the plasma lipidome. (1,2)
Methods: In order to investigate whether prognostic parameters could be derived from plasma lipidome, we followed patients without (n=11) and with (n=9) CVE, occurring during the first year after beginning of LA treatment with either DALI (n=12) or MONET (n=8), for 5 LA sessions within two years observation time. Samples for routine clinical chemistry and plasma lipidomics were taken directly before and after LA. Plasma lipidomic profile was analyzed by shotgun lipidomics after extraction with MTBE/methanol with a QExactive mass spectrometer (Thermo Fisher Scientific, Bremen, Germany). In total 650 metabolites of 12 major lipid classes were analyzed.
Results: MANOVA using all values or selectively pre-LA values revealed significant higher plasma concentrations for cholesterol (chol), cholesterol esters (CE), diacylglycerols (DAG), phosphatidylcholines (PC), phosphatidylinositols (PI), and triglycerides in patients without CVE. MANOVA analysis of post-LA values revealed higher values for lysophosphatidylethanolamines (LPE), PC, and PI, but not for chol, CE, DAGs, and TAGs. No group differences by MANOVA were observed for ceramides, PC- and PE-ethers, and sphingomyelins. Stepwise forward binary logistic regression or discriminant analysis using pre-LA values derived plasma concentrations of PI, ceramides, TAGs, and PE as determining factors for correct classification, reaching up to 70%.
Conclusion: Our analysis of LA-induced modulations of plasma lipid classes showed that individual plasma concentrations, in particular of PI, ceramides, TAGs, and PEs, are suitable for correct assignment of LA patients to a group with higher CVE risk, whereas mean plasma concentrations neither their pre- nor their post-LA values are helpful for the discrimination of the CVE risk. Further investigations should include the analysis of selective lipid

metabolites and their interaction with other biomarkers and clinical data to further improve the prediction of the individual CVE risk.

References

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10:45 a.m. – 12:30 p.m.

Saal 6

OS21 | Future perspectives of apheresis therapy
The future perspectives of apheresis

Chairs:
Bernd Hohenstein (Villingen-Schwenningen, Germany)

3 June 2023

OS21-01 10:45 a.m.

Future perspectives in apheresis therapy – lipoprotein apheresis

Patrick Moriarty

University of Kansas Medical Center, Kansas City, USA

OS21-02 11:10 a.m.

Future perspectives in apheresis therapy – critical care medicine

Prof. Jan Kielstein

Universitätsklinikum Braunschweig, Braunschweig, Germany

OS21-03 11:35 a.m.

Future perspectives in apheresis therapy – renal diseases and transplantation

Prof. Lionel Rostaing

CHU Grenoble Alpes, Grenoble, France

OS21-04 12:00 p.m.

Future perspectives in apheresis therapy – immune-mediated conditions

Prof. Reinhard Klingel

Apheresis Research Institute, Cologne, Germany

10:45 a.m. – 12:30 p.m.

Saal 5

OS22 | Pediatric apheresis Apheresis in children and adolescent patients

Chairs:
Julia Thumfart (Berlin, Germany)
Volker Witt (Vienna, Austria)

3 June 2023

OS22-01 10:45 a.m.

Severe chronic fatigue syndrome (ME/CFS) in children – when is immunoadsorption justified?

Prof. Wolfgang Ries

Diako Hospital, Flensburg, Germany

OS22-02 11:05 a.m.

Apheresis therapy for pediatric neurological diseases – a German perspective

Dr. Julia Thumfart

Charité - Universitätsmedizin Berlin, Berlin, Germany

OS22-03 11:25 a.m.

ECP in children and young adults – special needs

Prof. Volker Witt

Paediatric Hospital “St. Anna”, Vienna, Austria

3 June 2023

OS22-04 11:45 a.m.

Erythrocytapheresis prior to allogeneic stem cell transplantation in children with sickle cell disease is a safe and efficient method to lower sickle haemoglobin. (#67)

Dr. Thomas Blom[1,2], PhD/MD Claudia Ootjers[1], Linda Oudshoorn[1], Dr. Alexander Mohseny[3], Prof. Jaap-Jan Zwaginga[1]

[1] Leiden University Medical Centre, Department of Haematology, Leiden, Netherlands; [2] Sanquin Blood Supply, Transfusion Medicine Unit, Amsterdam, Netherlands; [3] Leiden University Medical Centre, Department of Pediatrics/Willem-Alexander Children's Hospital, Leiden, Netherlands

Purpose:
Allogeneic stem cell transplantation (allo-SCT) is a curative treatment for sickle cell disease (SCD). Unfortunately, the SCT trajectory itself can trigger SCD crises due to stimuli, such as central venous catheter insertion, fertility-preserving surgery, and the conditioning regimen before infusion. These crises can lead to significant morbidity and mortality. Erythrocytapheresis mediated lowering of sickle hemoglobin (HbS) levels to a target level below 30%, however, can mitigate these risks. Here we report on our experience with such a pre-transplant strategy in children.
Methods:
In our tertiary care academic medical center (Leiden University Medical Centre), 14 of 17 children with SCD were considered to receive erytrocytapheresis prior to allo-SCT between January 2020 and January 2023. HbS percentages were measured by capillary electrophoresis. Procedures were performed on the apheresis ward using a Spectra Optia Apheresis System (Terumo, Japan). The volume of donor red blood cells (RBCs) was calculated using Terumo BCT RBCX Calculation Tool app. Patients received RBCs that were prophylactically matched according to national guidelines. For vascular access, bilateral peripheral venous catheters were used.
Results:
Out of the 17 children, 14 eventually underwent erythrocytaferesis (female n=7; male n=10). Two children were ineligible due to poor peripheral venous access and one due to an unplanned hospital admission. One procedure was discontinued early in a 16-year-old male due to flow problems, but the second procedure was successful. The median age and weight of the patients were 12 years (range 7-17 years) and 34 kg (range 22-78 kg), respectively. The average pre- and post-apheresis HbS percentage was 64.9% (range 35.5-83.8%) and 23.3% (7.8-33.8%), respectively. A median of 4 RBCs (range 2-8) were exchanged during the procedure, with an average total processed volume of 3051 ml (range 1300-5581 ml). In 4/15 (27%) procedures, the extracorporeal line was primed with RBCs, and 5 top-up transfusions (5/15, 33%) were given directly after apheresis. No adverse events were reported during or after the procedures. Most important, no crises were reported in the pre- and peri- SCT period in these patients.
Conclusion:
Erythrocytapheresis prior to allo-SCT is a safe and efficient method for reducing HbS levels in children with sickle cell disease. The procedure can be feasibly performed on the apheresis ward using peripheral venous catheters.

3 June 2023

OS22-05 12:00 p.m.

Panel discussion – Particularities in pediatric apheresis

12:35 p.m. – 1:00 p.m.

Saal 6

Award | Closing Ceremony & Awards Presentation

1 June, 2023

6:00 p.m. – 7:30 p.m.

Saal 4,Saal 5,Saal 6

PS | Poster Session I Saal 1

PS-01

The role of cetrimide body wash and prophylactic antibiotics in reducing Catheter related blood stream infections in Therapeutic Plasma exchange patients: A Game changer (#75)

Dr. Shanthi Viswanathan

Kuala Lumpur Hospital, Neurology, Kuala Lumpur, Malaysia

Pre-Vascular Access prophlactic Antibiotics to reduce the risk of cathether related blood stream infections.

Viswanathan S, Krishnan D, Fu Liong H
Therapeutic plasma exchange in non acute settings has been performed since 2015 at the Department of Neurology, Kuala Lumpur Hospital, Malaysia in increasing numbers. An initial study in 2019, revealed 1-2 cases of catheter related blood stream infections per year resulting in patient morbidity resulting in a CRBSI rate of 9.1%. [1] In view of this we decided to review the technical aspects of prepration of the patient prior to Cathether insertion and study how prophylactic antibiotics may reduce biofilm seeding and reduce the incidence of CRBSI.

Methods
We prospectively started using prophylactic antibiotics and cetrimide body wash from 2020 to 2023 prior to and for 24 to 48 hours after the catheter was inserted. Prophlactic antibiotics used were intravenous(IV) Fortum 2 g tds and IV cloxacillin 1 g Qid for 2-3 day (given one day before and continued for 24 to 48 hours post insertion. We then followed up patients prospectively from 2021 to 2023 to asess the outcome in terms of number of CRBSI per catheter insertions for patients undergoing TPE

Results:
Over the 2 year period, with the institution of the above measures, the rates of CRBSI reduced dramatically to 0 cases per year.

Conclusion:
In low resource settings, the rates of catheter related CRBSI can be reduced by simple measures of cetrimide body wash and prophylactic antibiotics prior to catheter insertion. The treatment of CRBSI is expensive and causes a burden to the patient and institution. Simple measures like this go a long way in improving TPE service and patient care.

References
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PS-02

Long-term therapeutic plasmpheresis and successful treatment of dysphagia in a patient suffering from myasthenia gravis and chronic kidney disease. (#16)

Dr. Virginia Athanasiadou, Dr. Eva P. Andronikidi, Dr. Styliani Plavoukou, Dr. Dimitris Panokostas, Prof. Eirini Grapsa

National and Kapodistrial University of Athens, Nephrology Clinic / Aretaieio Hospital, Athens, Greece

Introduction: Plasmapheresis (TPE) is a therapeutic option for patients suffering from Myasthenia Gravis (MG) who do not respond to usual medication, according to the guidelines of the American Society for Apheresis (ASFA).
Case Presentation: An 85-year-old female patient with a history of MG and chronic kidney disease (CKD) stage 3a was referred to our department by the treating neurologist for TPE. Until recently her solitary symptoms were ptosis of the left eyelid and mild muscle weakness in the lower limbs for which she received no treatment. She sought neurological consultation when she noticed progressive dysphagia and hoarse voice. She was on pyridosphigmine 60mg x 3/24h for a month but the symptoms worsen and she lost 4Kg due to dysphagia. Fiberoptic endoscopic evaluation of swallowing (FEES) revealed pooling of saliva at the cricopharyngeal level and the piriformis sinus, as well as the presence of residue at the level of the glossoepiglottic fossa that did not clear even with repeated swallows. TPE was performed via a 12 French double lumen dialysis catheter 3 times per week, using continuous-flow centrifugal apheresis system (OPTIA) and human albumin 5% as a replacement fluid. After 6 sessions, the patient reported a minor improvement in symptoms, but not to a satisfactory degree to allow free feeding. Treatment resumed for another 12 sessions. After the 8th session the patient started to feed better and until the 12th session she had gained 1,5Kg. FEES was repeated 2 weeks later and revealed clear improvement in relation with FEES prior to the treatment. There was no pooling of saliva and less residue at the level of the glossoepiglotic fossa that the patient could clear with repeated swallows.
Discussion: A 2021 systematic review and meta-analysis of comparative evidence showed that TPE induced higher response rate in acute MG patient than intravenous immune globulin (IVIG). A 2020 retrospective longitudinal follow-up study pointed out that patients with glomerular filtration rate (GFR) <60ml/min/1,73m² need higher number of TPE sessions in order to clinical improvement and reduce the possibilities of relapses.
Conclusion: Long-term TPE was a life-saving treatment for our patient. The decision to continue the treatment beyond 6 sessions was of great importance in order to alleviate symptoms and improve the quality of life.

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PS-03

Evinacumab reduces EU and US apheresis eligibility in patients with homozygous familial hypercholesterolemia (#24)

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Purpose: Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder associated with extremely elevated levels of low-density lipoprotein cholesterol (LDL-C) due to its impaired clearance from the circulation, which results in increased cardiovascular events and premature mortality. Evinacumab, a fully human monoclonal antibody against angiopoietin-like 3, has demonstrated approximately 50% reductions in LDL-C in patients with HoFH. This post-hoc analysis assessed the effect of evinacumab on the change in lipoprotein apheresis eligibility based on predefined EU and US criteria in patients with HoFH.

Methods: An ongoing, single-arm, open-label, phase 3 study (NCT03409744) enrolled and treated patients aged ≥12 years with HoFH. All evaluable patients (n=106) received intravenous evinacumab 15 mg/kg every 4 weeks. Predefined lipoprotein apheresis eligibility criteria were as follows: EU, LDL-C >160 mg/dL (primary prevention) or LDL-C >120 mg/dL (secondary prevention); US, LDL-C ≥300 mg/dL or LDL-C ≥100 mg/dL for patients with coronary heart disease or peripheral artery disease, respectively.

Results: At baseline, 78.3% (83/106) and 67.9% (72/106) of patients did, and 21.7% (23/106) and 32.1% (34/106) of patients did not, qualify for apheresis using predefined EU and US criteria, respectively. Overall, evinacumab treatment reduced mean (standard deviation) LDL-C by 130.6 (109.3) mg/dL from baseline at Week 56. Of the 83 and 72 patients who initially qualified for apheresis at baseline using EU and US criteria, respectively, over half (58.1% [43/74] and 61.9% [39/63], respectively) no longer qualified for apheresis following 56 weeks of evinacumab treatment (data were missing for nine patients). The observed reduction in the proportion of patients qualifying for apheresis was maintained through to Week 184 (results not shown).

Conclusions: Based on predefined EU and US apheresis eligibility criteria, evinacumab treatment substantially reduced the proportion of patients who would qualify for apheresis.

PS-04

Cytokine modulation in abdominal septic shock via the crucial role of IL-6 signaling in endothelial dysfunction (#2)

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Background: Early recovery from shock improves prognosis in septic shock patients. We determined whether cytokine modulation by Continuous Renal Replacement Therapy (CRRT) following acute care surgery resulted in stable hemodynamics in them.
To investigate our hypothesis, we measured proinflammatory cytokines IL-6, IL-1ra and the coagulation cascade activator plasminogen activator inhibitor-1 (PAI-1) following CRRT with polymyxin B immobilized fiber (PMX-DHP) which has been utilized as an adjuvant treatment option for patients with severe septic shock.
Methods: 66 septic shock patients requiring 2 hours direct hemoperfusion therapy PMX-DHP were included. 36 patients of them also received continuous hemodiafiltration (CHDF) after performing PMX-DHP.Circulatory dynamics and levels of inflammatory mediators, namely IL-6, IL-1ra, and PAI-1 were assessed before, immediately after, and 24 hours initiation of PMX-DHP.
Results: Mean Arterial Pressure (MAP) rose intentionally by PMX-DHP just after enforcement 24 hours later ($p<0.01$). Levels of IL-6, IL-1ra, and PAI-1 significantly decreased after PMX-DHP ($p<0.05$) and this trend was observed up to 24 hours post initiation of PMX-DHP ($p<0.05$). IL-6 modulation by PMX-DHP was enhanced with using CHDF and there was a significant correlation between IL-6 and MAP ($p<0.0001$). In addition, levels of IL-6 and PAI-1 showed a significant correlation.**Conclusions:** Our data showed employing CRRT as cytokine modulators could be an additional therapeutic strategy to improve septic shockoutcomes via the crucial role of IL-6 signaling in endothelial dysfunction.

PS-05

Therapeutic plasma exchange in Paraneoplastic encephalitis - Case report (#21)

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Abstract:

Background: Paraneoplastic syndromes (PS) appear in the context of immune cross-reactivity between malignant and normal tissues or in tumor secretion of hormones, peptides, or cytokines. PS can affect multiple organs, therefore having multiple clinical manifestations. Paraneoplastic neurologic syndromes (PNS) are associated with onconeural antibodies that react against antigens expressed by both the tumor and the nervous system and mostly precede detection of the underlying cancer.
Methods: We report a case of a 80-year-old male who performed a therapeutic plasma exchange (TPE) program after being diagnosed with paraneoplastic encephalitis, with no response to intravenous immunoglobulin. The patient was initially admitted in the emergency room due to complaints of gait imbalance with progressive worsening over 2 weeks. Cranial CT scan was normal but he kept neurologically worsening, presenting with pancerebellar syndrome associated with cognitive deterioration. MRI, ecographic scans and lumbar puncture were normal, except elevated white blood count in cerebrospinal fluid (CSF). Presumption of autoimmune etiology, a 10-day therapeutic trial with immunoglobulin was made with little response. Antibodies anti-Tr/DNER were positive in blood serum and CSF. TPE program was performed: 6 treatments every other day, with an exchange plasma volume ratio of 1-1.5, using human albumin as replacement fluid (Recommendation Grade 2C; Category III; American Society for Apheresis; Guidelines from 2019); There were no adverse reactions. Neurological status remained without improvement. A Thoracic CT scan showed mediastinal ganglionic formations compatible with lymphadenopathy, with high-uptake on PET. Excisional biopsy revealed classic Hodgkin lymphoma and chemotherapy was started.
Results: Although initially the patient didn't respond to treatment, after starting therapy directed to lymphoma his neurological status has been improving.
Conclusion: If PS is suspected in patients with severe neurological impairment, immunosuppression including TPE might be an option to try to halt the process. Patients who present with subacute cerebellar degeneration and anti-Tr antibodies are more likely to respond to TPE. Although the exact mechanism is not well understood, it probably results from reducing circulating IgG antibodies and immune complexes.

PS-06

The effect of Continuous Plasma filtration with Dialysis (PDF) in Patients with Sepsis and Acute Liver Failure with/without Surgical Intervention (#58)

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Background. In 2019, four clinical phenotypes of sepsis were identified; 28-day mortality was highest among the θ phenotype (had more liver dysfunction and septic shock:40%) vs the other 3 phenotypes (P<0.001) [1]. We developed Plasma dia-filtration (PDF) for acute liver failure (ALF) in 2000 [2,3], and Taniguchi has continuous PCF (cPDF) in 2014 [4]. In this study, we evaluated the effect of cPDF in patients among sepsis and ALF with/without surgical intervention.
Materials and Methods. cPDF was performed by the Evaclio EC-2A (Asahi Kasei Medical. CO. LTD., Tokyo, Japan) as the plasma separator, which has a sieving coefficient of 0.3 for albumin. PDF requires flowing dialysate outside the hollow fiber.The flow rates of the blood, dialysate, substitute and additional one were 80ml/min, 400ml/h, 0 to

280ml/h according to the rate of water-elimination and 120ml/h, respectively. The filtration rate was 400ml/h. We used Sublood BS as dialysate and substitute. We added substitute from the additional fluid 120ml/h of fresh frozen plasma with 25% albumin 50ml/8h, considering the loss of albumin by diffusion. As an anticoagulant, Nafamostat Mesilate was used at a rate of 20-35mg/h. cPDF was performed for 24h once or twice on a patient.
Results. Continuous PDF was performed in 17 and 18 patients among sepsis and ALF without and with surgical intervention from 2014 to 2019, and their 28-day survival rates were 65% and 56%, respectively. The age in non-survivor was significantly older than that in survivor (77.1±8.9 vs 71.1±11.5, p<0.05). Plasma and serum levels (average±SD) of PT(%), total bilirubin(mg/dl), CRP(mg/dl), SOFA score and lactate(mg/dl) before cPDF procedure were similar with survivor and non-survivor (43.5±15.1 vs 46.3±14.1, 3.3±2.8 vs 3.3±2.7, 14.1±7.3 vs 16.4±5.3, 13.2±2.5 vs 13.9±3.1, 24.5±18.2 vs 28.1±15.5, respectively). On the next day after cPDF procedure, serum level of CRP significantly decreased in survivor (10.6±6.0), whereas not in non-survivor (15.2±6.3) compared with that before cPDF procedure, and that difference was significant (p<0.05). This finding suggests that cPDF could eliminate cytokines inducing CRP production in survivor, because CRP (MW:105KD) itself cannot be eliminated by cPDF procedure.Conclusion. Continuous PDF has an effect on patients with sepsis and ALF. Reduction of serum CRP level on the next day after cPDF procedure would make an indicator of prognosis in patients with sepsis and ALF.

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PS-07

Selective cfDNA/NETs apheresis with NucleoCapture®in a Porcine Intensive Care Sepsis Model: A blinded randomised controlled trial (#60)

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Background
Cell-free DNA (cfDNA)/Neutrophil Extracellular Traps (NETs) are associated with sepsis. We investigated the removal of cfDNA/NETs from the circulation in a porcine intensive care model of sepsis using NucleoCapture® selective apheresis based on recombinant histone H1.3 binding in a blinded randomised controlled trial.
Methods

We induced sepsis in 18 pigs with a 3-hour intravenous infusion of E. coli. Nine pigs were randomly allocated to treatment with NucleoCapture® selective apheresis for 5 hours. Nine pigs were subjected to apheresis with a sham column. The column was used in conjunction with the Terumo Optia system using regional citrate anticoagulation. The operators were blinded to the column type. We measured cfDNA/NETs using the NuQ H3.1 and H3R8cit nucleosome assays (Volition).

Results

A single pass of septic plasma through the NucleoCapture® column resulted in near complete removal (96-99.1%) of cfDNA/NETs. There was no evidence of non-specific direct adsorption of proteins such as albumin and cytokines.

The baseline levels of circulating cfDNA/NETs measured in the NucleoCapture® and sham treated pigs prior to the experiment were 11.6 (±4.1) ng/ml and 10.2 (±3.5) ng/ml (mean±SD), respectively. Infusion of E. coli. resulted in an increase in cfDNA/NETs levels to 68.6 (±24.5) ng/ml and 71 (±53.1) ng/ml, respectively.

The level of cfDNA/NETs in the sham treated pigs rose continuously during the experiment reaching 361.2 (±190.2) ng/ml. In contrast, NucleoCapture® treatment prevented a continuous rise in cfDNA/NETs with levels plateauing at 149.9 (±152.98) ng/ml ($p<0.05$).

The low cfDNA/NETs levels in the NucleoCapture® treated pigs were consistent with the attenuation of septic shock as evidenced by reduced lactate (4.6 vs 6.9 mmol/l, $p<0.05$), reduced total norepinephrine required (1,172 (±1,832) µg vs 6,360 (±5,017) µg, $p<0.05$) and improved survival (9/9 vs 7/9). There was also a 2-fold increase in urine output in the NucleoCapture® group.

No technical difficulties with the use of the NucleoCapture® column or any problems with anticoagulation were found.

Conclusions

In this blinded randomised controlled study, selective cfDNA/NETs apheresis with NucleoCapture® safely and effectively removed cfDNA/NETs from the circulation of septic pigs, resulting in improved organ function and survival. We aim to progress the investigation of NucleoCapture® to clinical trials in sepsis and other indications.

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PS-08

Selective cfDNA/NETs apheresis with NucleoCapture®in a Prolonged Clinically Relevant Porcine Intensive Care Sepsis Model (#68)

PhD/MD Andrew Aswani[1,2], PhD/MD Dmitry Genkin[1], PhD/MD Kirill Surkov[1], PhD/MD Paul Skorup[4], Robin Varsebroucq[3], Marion Wargnies[3], Julie Candiracci[3], PhD/MD Marielle Herzog[3], PhD/MD Jake Micallef[3], PhD/MD Miklos Lipcsey[4]

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Background

Cell-free DNA (cfDNA)/Neutrophil Extracellular Traps (NETs) are associated with sepsis. We previously demonstrated that NucleoCapture® selective cfDNA/NETs apheresis improved organ function and survival in a 7-hour model of porcine sepsis. We therefore investigated the use of NucleoCapture® in an extended 24-hour clinically relevant porcine intensive care model of sepsis.

Methods

We induced sepsis in two pigs with a 2-hour intravenous infusion of Pseudomonas aeruginosa. Antibiotics were administered at either 6 hours or earlier if the norepinephrine requirement was greater than 0.1mg/kg/min. One pig was subjected to NucleoCapture® apheresis using the Terumo Optia system with regional citrate anticoagulation for 8 hours, followed by a further dose of antibiotics. A second NucleoCapture® treatment was then applied for another 8 hours. The other pig was subjected to the same protocol with sham column apheresis. We measured cfDNA/NETs using the NuQ H3.1 nucleosome assay (Volition).

Results

The baseline levels of circulating cfDNA/NETs measured in the NucleoCapture® and sham treated pigs were 2.52 ng/ml and 1.64 ng/ml, respectively. Infusion of Pseudomonas aeruginosa resulted in an increase in cfDNA/NETs to 82.6 ng/ml and 87.4 ng/ml, respectively.

The level of cfDNA/NETs in the sham treated pigs rose continuously during the experiment reaching 508.9 ng/ml. In contrast, NucleoCapture® treatment caused a sustained decrease of cfDNA/NET levels to 20.9 ng/ml by the end of the experiment.

The suppressed cfDNA/NETs level in the NucleoCapture® treated pig was consistent with the attenuation of septic shock as evidenced by a marked 4-fold reduction in the total norepinephrine requirement: 3,725 µg vs 13,841 µg. The NucleoCapture® treated pig also produced more urine: 3,260ml vs 2,531ml.

Conclusions

In this extended 24 hour clinically relevant model of porcine sepsis, which included the use of antibiotics and intensive care support, prolonged selective cfDNA/NETs apheresis with NucleoCapture® effectively removed cfDNA/NETs from the circulation of septic pigs and resulted in improved physiological indicators. We aim to progress the investigation of NucleoCapture® to clinical trials in sepsis and other indications.

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PS-09

Three cases of long COVID syndrome treated with immunoadsorption - possible profit in the improvement of quality of life (#20)

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Purpose:
In a prospective observational case report, we investigated the disease courses and treatment effects of three patients with long COVID syndrome associated with G-protein-coupled receptor antibodies. Between March 16, 2022, and July 27, 2022, 3 female patients, between 40 and 55 years old were assigned to receive immunoadsorption (IA) using the TheraSorb LIFE 21 apheresis platform and the Ig omni 5 adsorbers (Miltenyi Biotec) for the removal of IgG, IgM and IgA.
Methods:
All patients underwent 5 IA sessions and the 2.0-fold individual total plasma volume was processed each time.
Results of the study:
The removal of IgG was high as shown in the following table.

Patient No.	IgG pre apheresis (g/L)	IgG post 5th apheresis (g/L)	Reduction IgG (%)
A	7.9	< 0.7	> 91%
B	9.2	< 0.7	> 92%
C	8.1	< 0.7	> 91%

An increase of WBC and a decrease of platelets was observed, whereas the hemoglobin level remained stable during apheresis.
Our patients tolerated the IA procedures very well with no signs of bio intolerance such as flushing, fever, or even anaphylactic reactions. Rare occurrences of hypotension, citrate reaction, and punction failure were treated symptomatically and did not lead to cessation of the session.
IA resulted in significant reduction of symptoms in all three patients and none worsened.

In conclusion IA is a safe and efficient method for the removal of (auto-) antibodies in patients with Long-COVID. A clinical benefit could be demonstrated in all three patients of this case report, but large randomized controlled trials are warranted.

PS-10

Therapeutic plasma exchange rescues SLE-associated bilateral optic neuritis: A case report. (#43)

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Introduction: Systemic lupus erythematosus (SLE) with bilateral optic neuritis is less common. Treatment is based on immunosuppressive drugs; however, treatment outcomes are uncertain

Case report: We present a Thai 40-year-old female diagnosed with SLE. She presented with progressive bilateral visual loss (visual acuity: right eye 20/200 and left eye 20/160) and color blindness for one month. The ophthalmoscopic exam showed a pink and sharp disc, a normal cup-to-disc ratio in both eyes. She was investigated by MRI-brain, cerebrospinal fluid (CSF) analysis, and laboratory tests. Anti-AQP4, Anti-MOG, and the oligoclonal band were negative in CSF fluid. The diagnosis SLE associated bilateral optic neuritis was made. Pulse methylprednisolone was immediately started at 15 mg/kg/day for three days, then taper to prednisolone at 1 mg/kg/day. After seven days, the visual acuity was not improved. Therapeutic plasma exchange (TPE) with membrane filtration technique was initiated for five sessions on an alternate day. The plasma volume per session was 2.8 Liters (1.5 times of plasma volume). The replacement fluid was a mixture between 5% albumin and fresh frozen plasma. Prednisolone was still prescribed during TPE treatment. After the second session of TPE, color blindness was improved. The visual acuity then improved to the right eye at 20/50 and the left at 20/32. After finishing the TPE course, visual acuity improved to 20/25 in both eyes and 20/20 in both eyes one month after TPE.

Conclusion: We report a case with SLE and bilateral optic neuritis that failed to methylprednisolone and had an excellent response to TPE.

PS-11

Immunoadsorption in anti-MDA5-positive refratory amyopathic dermatomyositis (#84)

Dr. Anne Sayer-Klink[1], Prof. Peter Oelzner[2], Dr. Diana Schmerler[3], Dr. Agnieszka Hilge[1], Priv.-Doz. Michael Kiehntopf[3], Dr. Silke Rummler[1], Priv.-Doz. Alexander Pfeil[2]

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Introduction: Treatment of anti-MDA5-positive associated amyopathic dermatomyositis (A-DM) is consist of immunosuppressive therapy. Some patients remain resistant to therapy and are affected with poor prognosis. Case reports on the use of the therapeutic plasma exchange are already described as a useful treatment. As an alternative to plasma exchange, we apply immunoadsorption (IA) in severe treatment refractory cases.
Methods: We describe the long-term clinical trends of two patients with anti-MDA5-positive A-DM. Each IA cycle consisted of two ot three immunoadsorptions in with the following intravenous immunglobulins. IA was carried out with effective and highly selective IgG-binding regenerable columns (Globaffin®, Fresenius, Bad Homburg, Germany). Treatment intervals were extended to four weeks. In addition to anti-MDA5, we tested further DM specific autoantibodies in patient serum and eluat to monitor treatment intensity and effectiveness.
Results: Patient A showed a good response to treatment within four months of IA start. Status of disease is stable after 5.8 years after start of IA. Patient B, disease progression was be delayed until 2.5 years.
Conclusion: IA appears to be an effective treatment for anti-MDA5-positive A-DM for disease control and should be taken into account at an early stage in the treatment decisions in therapeutic refractory cases. Case studies in a treatment register could be useful to find parameters to predict the effectiveness of an IA.

PS-12 6:11 p.m.

*Bifidobacterium longum*R0175 Protects Mice against APAP-induced Liver Injury by Modulating the Nrf2 Pathway (#1)

PhD/MD student Shengjie Li, **Prof. Lanjuan Li**

Zhejiang university, school of medicine, Hangzhou, China

Acetaminophen (APAP) overdose is the most common driver of drug-induced liver injury (DILI) worldwide, and the gut microbiome plays a crucial role in this process. In this study, we estimated the effect of *Bifidobacterium longum* R0175 on APAP-induced liver injury in mice and discovered that *B. longum* R0175 alleviated liver injury by diminishing inflammation, reducing oxidative stress levels, inhibiting hepatocyte death and improving APAP-induced microbiome dysbiosis. Further studies revealed that the antioxidative effects of *B. longum* R0175 were primarily due

to activation of the Nrf2 pathway, which was supported by the Nrf2 pathway inhibitor ML385 counteracting these ameliorative effects. *B. longum* R0175 modified intestinal metabolites, especially the key metabolite sedanolide, which could activate the Nrf2 pathway and contribute to the protective effects against APAP-induced liver injury. Moreover, we found that sedanolide exhibited close interrelationships with specific microbial taxa, indicating that this factor may be derived from gut microbes. In conclusion, our work demonstrated that *B. longum* R0175 could reduce oxidative damage, inflammation and hepatocyte death by activating the Nrf2 pathway. Importantly, we identified the microbiota-derived metabolite sedanolide, which was first discovered in the mouse intestine, as a key agonist of the Nrf2 pathway and primary effector of *B. longum* R0175 in APAP challenge. These findings provide new perspectives for APAP overdose therapy and demonstrate the enormous potential of *B. longum* R0175 in alleviating acute liver injury.

PS-13

Akkermansia muciniphila-derived acetate activates hepatic AMPK-SIRT1-PGC1α to alleviate lipid peroxidation in metabolic-associated fatty liver disease (#7)

PhD/MD student Aoxiang Zhuge, **Prof. Lanjuan Li**

Zhejiang University, State Key Laboratory for Diagnosis and Treatment of Infectious Disease, Hangzhou, China

Background: Ferroptosis is an iron-dependent regulated cell death type, and emerging evidence have verified its participation in the progression of the metabolic-associated fatty liver disease (MAFLD), thus inhibiting ferroptosis is a promising target for MAFLD. The gut commensal bacterium *Akkermansia muciniphila* (*A. muc*) exhibits great potential to ameliorate metabolic disorders in MAFLD. Latest studies have demonstrated the anti-oxidative effect of *A. muc*, however, the its anti-ferriotic effect remains unclear.
Purpose: The current study investigated the effect of *A. muc* on MAFLD-related ferroptosis.
Method: We investigated the protective effect of *A. muc* on MAFLD using a murine MAFLD model induced by long-term high fat high fructose diet (HFHFD) feeding. 16s rRNA sequencing and untargeted metabolomics were conducted to identify key microbes and metabolites. Fecal microbiota transplantation (FMT) and germ-free mice were conducted to verify the role of microbiota in the progression.
Result: *A. muc* intervention efficiently reversed HFHFD-induced lipid peroxidation and oxidative damage in the liver. These beneficial impacts were mediated by activation of hepatic AMPK-SIRT1-PGC-1α axis, as evidenced by AMPK deficiency induced by adeno-associated virus (AAV)-shRNA or antagonist Compound C abrogated its amelioration in lipid peroxidation. Further, we observed elevations in the short chain fatty acids upon *A. muc* treatment and identified acetate as key activator of hepatic AMPK. Mechanically, microbiota-derived metabolite acetate is transported to the liver and metabolized to adenosine monophosphate (AMP) which triggers AMPK activation. Further, we confirmed *A. muc* mediates anti-ferroptotic effect by itself in the absence of the other microbes.
Conclusion: These data indicate that *A. muc* exerts anti-ferroptotic effect through producing acetate, which activates hepatic AMPK-SIRT1-PGC-1α axis to strengthen mitochondrial biosynthesis. *A. muc* could be a potential therapeutic approach targeting ferroptosis in MAFLD.

PS-14 6:13 p.m.

mt DNA changes in Platelet prepared by Apheresis (#23)

Dr. Azita Chegini, M.Sc./M.A. Leila Vakili, M.Sc./M.A. Shahram Samiee

The authors confirm contribution to the paper as follows: study conception anddesign: Azita Chegini; data collection: Leila vakili,Azita chegini; analysis and interpretation of results: shahram samiee and Azita Chegini; draft manuscript preparation: Azita Chegini.

High Institute for Research and Education in Transfusion Medicine, Blood research center, Tehran, Iran

Introduction

Mt DNA (DAMPs) plays a key modulatory role in immune cells and may also mediate a variety of adverse transfusion reactions.

Material and Method

The cross-sectional study was performed on 22 (PRP) and 14 (SDP) between February 2019 and 2020. mtDNA DAMPs by quantitative real-time PCR was assessed on days 1, 3, and 5 of platelets storage. The data was entered in REST 2009 software, and the amount of fold change was calculated. Multiple *t* tests were also used.

Results

The mtDNA DAMPs fold change in SDP on days 1–3, 1.3 times, on days 3–5, 1.5 times, and on days 1–5, 2.1 times increased. The fold change on days 1–3, 0.8 times, on days 3–5, 0.6 times, and on days 1–5, 0.49 times decreased in PRP products.

Conclusion

The method of preparation and processing can affect mtDNA DAMPs fold changes.

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PS-15 6:14 p.m.

Problems of achieving the lipid spectrum target levels in patients with familial hypercholesterolemia (#49)

PhD/MD Viktoria A. Korneva[1], PhD/MD Tatiana Y. Kuznetsova[1], Prof. Ulrich Julius[2]

[1] Petrozavodsk State University, Faculty Therapy Department, Petrozavodsk, Russia; [2] University Hospital at the Technische Universität Dresden, Department of Internal Medicine III, 01307 Dresden, Germany

Familial hypercholesterolemia (FH) is a genetic disease, characterized mainly by the increase of low density lipoprotein cholesterol (LDL-C) level and high cardiovascular risk. SCORE-2 is the new scale for cardiovascular risk-stratification, and non–HDL cholesterol (non HDL-C) is used now as the goal for preventive actions.
Aim: toevaluate the achievement of target levels in FH patients according to risk assessment on different scales (SCORE and SCORE-2) by statins and inhibitors of PCSK9 (iPCSK9).
Materials and methods: we have analyzed the treatment results of 203 FH patients, 81 males (39.9%), the mean age was 43.2±2.7 years. In 109 patients (53.6%) a genetic analysis was performed. A definite FH was diagnosed in 114 (56.2%) patients. Non-HDL-C was calculated as “total cholesterol (TC) – HDL-C”.
Results: The mean initial lipid levels were: TC 10.2±0.3 mmol/l, LDL-C 7.1±0.13 mmol/l, HDL-C 1.46±0.1 mmol/l, non-HDL-C 8.4±0.2 mmol/l, TG 1.7±0.3 mmol/l. The treatment of patients was not optimal: 29% did not receive any hypolipidemic medications. Statins were taken in 62% of patients, in 15.2% statin + ezetimibe and in 8.4% statin + ezetimibe + iPCSK9.
A target LDL-C level less than 1.8 mmol/L (70 mg/dL) was seen in 22.6%, and only 5.7% patients achieved a target level less than 1.4 mmol/L (55 mg/dL) on statin therapy. The target levels for LDL–C on iPCSK9 therapy were achieved in 62.5% of FH patients.
On statin therapy, there were no FH patients who achieved the target non-HDL-C level less than 2.2 mmol/l, and only 2% of patients achieved the target non-HDL-C level less than 2.6 mmol/l. On iPCSK9 therapy, after three months non-HDL-C decreased by 77.5%, 42.8% of patients achieved a target level of non-HDL-C less than 2.2 mmol/l. The reason for this were objective difficulties with hypolipidemic therapy. A target level of non-HDL-C less than 2.6 mol/l was achieved in 22.7% of patients with probable FH.
Conclusion: Achieving lipid targets in FH patients is challenging, even with iPCSK9 therapy, and the non-HDL-C indicator is more difficult to achieve than LDL-C. These data point to the necessity to start an lipoprotein apheresis therapy in patients who are at high atherosclerotic risk and do not reach the needed lipid target levels.

PS-16

The development of functional biliary tree organoids with network structures and serotonin expression in decellularized liver scaffolds

(#56)

PhD/MD student Jiaxian Chen[1], PhD/MD student Shiwen Ma[1], PhD/MD student Hui Yang[1], PhD/MD Xi Liang[2], PhD/MD Heng Yao[1], PhD/MD Beibei Guo[1], PhD/MD Deying Chen[1], PhD/MD Jing Jiang[1], PhD/MD Dongyan Shi[1], PhD/MD Jiaojiao Xin[1], PhD/MD student Xingping Zhou[1], PhD/MD student Lulu He[1], PhD/MD Yun Li[1], Prof. Lei Geng[3], **Prof. Jun Li**[1]

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Background and Aims: A functional biliary tree network is essential for bioengineered liver construction, which is a promising alternative to the treatment of liver failure. This study aims to develop a functional biliary tree organoid (FBTO) with network structures in decellularized liver scaffold (DLS) and reveal the key metabolic mechanism of biliary tree generation.
Method: Mouse primary cholangiocytes were transplanted into the rat DLS and cultured for 14 days with recirculating perfusion to construct an FBTO. The developed FBTOs were dynamically characterized by phenotypes and functional features, and the bio-processes of biliary tree generation was revealed by metabolomics.
Results: FBTO was successfully constructed in DLS. Morphological evaluation showed that the primary cholangiocytes implanted into DLS gradually formed biliary tree network with high vitality with 14-day culture. FBTO maintained bile duct specific markers (CK7, CK19, EpCAM) functional markers (GGT, CFTR, AQP1). Immunostaining of acetylated α-tubulin and E-cadherin revealed significant apical-basal polarity of FBTO. Rhodamine 123 transport assay and active collection of cholyl-lysyl-fluorescein showed that FBTO exhibited the biliary secretion and transport functions. Tight junction protein ZO1 staining and bile leakage experiments showed that FBTO possessed the barrier capacity of confining bile components to the lumen. Metabolomics analysis showed that serotonin was specifically expressed during the whole process of FBTO culture, and the tryptophan metabolic pathway where serotonin located may be the key metabolic pathway linked to biliary tree reconstruction.
Conclusion: An FBTO with network structures and serotonin expression was developed in DLS with primary cholangiocytes. It provides a promissing for disease modelling, drug screening and the construction of functional bioengineered liver, paveing the way for future clinical therapeutic applications.

PS-17

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients (#57)

Dr. Patrick M. Moriarty[1], Dr. Steven E. Nissen[2], Dr. A. Michael Lincoff[2], Prof. Kausik K. Ray[3], Prof. John J. Kastelein[4], Dr. Paul D. Thompson[5], Dr. Peter Libby[6], Dr. Leslie Cho[2], Dr. Jorge Plutzky[6], Dr. Harold E. Bays[7], Prof. Diederick E. Grobbee[8], Dr. Michael J. Louie[10], Prof. Stephen J. Nicholls[9], Dr. JoAnne M. Foody[10]

[1] University of Kansas Medical Center, Kansas City, USA; [2] Cleveland Clinic, Cleveland, USA; [3] Imperial College London, London, UK; [4] University of Amsterdam Academic Medical Center, Amsterdam, Netherlands; [5] Hartford Hospital, Hartford, USA; [6] Brigham and Women's Hospital, Boston, USA; [7] Louisville Metabolic and Atherosclerosis Research Center, Louisville, USA; [8] University Medical Center Utrecht, Utrecht, Netherlands; [9] Monash University, Victorian Heart Institute, Clayton, Australia; [10] Esperion Therapeutics, Incorporated, Ann Arbor, USA

BACKGROUND-Bempedoic acid (BA), an ATP citrate lyase inhibitor, reduces low-density lipoprotein (LDL) cholesterol levels and is associated with a low incidence of muscle-related adverse events; its effects on cardiovascular (CV) outcomes remain uncertain.
METHODS -We conducted a double-blind, randomized, placebo-controlled trial involving patients who were unable or unwilling to take statins owing to unacceptable adverse effects (“statin-intolerant” patients) and had, or were at high risk for, CV disease. The patients were assigned to receive oral BA, 180 mg daily, or placebo. The primary end

point was a four-component composite of major adverse CV events, defined as death from CV causes, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization.

RESULTS-13,970 patients underwent randomization; 6992 were assigned to the BA group and 6978 to the placebo group. The median duration of follow-up was 40.6 months. The mean LDL cholesterol level at baseline was 139.0 mg/dL in both groups, and after 6 months, the reduction in the level was greater with BA than with placebo by 29.2 mg/dL; the observed difference in the percent reductions was 21.1 percentage points in favor of BA. The incidence of a primary end-point event was significantly lower with BA than with placebo (819 patients [11.7%] vs. 927 [13.3%]; hazard ratio, 0.87; 95% confidence interval [CI], 0.79 to 0.96; P = 0.004), as were the incidences of a composite of death from CV causes, nonfatal stroke, or nonfatal myocardial infarction (575 [8.2%] vs. 663 [9.5%]; hazard ratio, 0.85; 95% CI, 0.76 to 0.96; P = 0.006); fatal or nonfatal myocardial infarction (261 [3.7%] vs. 334 [4.8%]; hazard ratio, 0.77; 95% CI, 0.66 to 0.91; P = 0.002); and coronary revascularization (435 [6.2%] vs. 529 [7.6%]; hazard ratio, 0.81; 95% CI, 0.72 to 0.92; P = 0.001). BA had no significant effects on fatal or nonfatal stroke, death from CV causes, and death from any cause. The incidences of gout and cholelithiasis were higher with BA than with placebo (3.1% vs. 2.1% and 2.2% vs. 1.2%, respectively), as were the incidences of small increases in serum creatinine, uric acid, and hepatic-enzyme levels.

CONCLUSIONS-Among statin-intolerant patients, treatment with bempedoic acid was associated with a lower risk of major adverse CV events (death from CV causes, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization).

PS-18

Lipoprotein-Apheresis therapy, for patients with an elevated Lipoprotein(a) and progressive cardiovascular diseases, reduces the development of calcific aortic valve stenosis. (#64)

Prof. Patrick M. Moriarty

Kansas University medical Center, Medicine, Kansas City, USA

BACKGROUND: Elevated lipoprotein(a) [Lp(a)] is an independent risk factor for cardiovascular disease (CVD) and calcific aortic valve stenosis (CAVS). A recent study has identified over 50% of patients with an elevated Lp(a), after 14 years of observation, may develop CAVS.

Presently, only Lipoprotein-apheresis (LA) is FDA approved for treating elevated Lp(a) levels and progressive CVD.

OBJECTIVE: To evaluate the clinical significance of Lp(a) reduction with LA therapy and the reduction in CVD and development of CAVS.

METHODS: A retrospective/prospective cohort study at one LA site in the United States evaluated 39 CVD patients with elevated Lp(a) and without CAVS. Patient data was analyzed to demonstrate possible clinical benefit in reducing Lp(a) levels with LA to mitigate risk of major adverse cardiovascular events including CAVS.

RESULTS: Pre-LA patient's mean LDL-C and Lp(a) were 103mg/dL (range 17-278) and 278nmo/L (range 153-596) respectively. LA therapy demonstrated a reduction of mean LDL-C to 31mg/dL and Lp(a) to 66nmol/L. There was an 88% reduction in major adverse cardiovascular events over a mean treatment period of 58 months while no patient developed CAVS.

	Pre-Apheresis	Ongoing Apheresis
Patients	39	39
Mean Duration (months)	64	58
MACE (total)	90	11 (-88%)
MI	13	1 (-93%)
PCI	52	7 (-86%)
CABG	10	1 (-90%)
Stroke/ TIA	15	2 (-87%)
CAVS	0	0

MACE, Major Adverse Cardiovascular Events; **MI**, Myocardial Infarction; **PCI**, Percutaneous Coronary Intervention; **CABG**, Coronary Artery Bypass Graft; **TIA**, Transient Ischemic Attack; **CAVS**; Calcific Aortic Valve Stenosis.
CONCLUSION: LA therapy prevented the development of CAVS and significantly reduce the number of CVD events for patientswith an elevated Lp(a) and CVD.

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10:45 a.m. – 12:00 p.m.

Saal 4

WB1 | Apherese-Weiterbildung in deutscher Sprache: Teil 1

WB1-01 10:45 a.m.

Begrüßung

Prof. Jens Ringel

Potsdam, Germany

WB1-02 10:50 a.m.

Apherese ist nicht gleich Apherese

Prof. Uwe H. Wallstab

Wernigerode, Germany

WB1-03 11:25 a.m.

Apherese mehr als nur Lipidreduktion

Prof. Reinhard Klingel

Köln, Germany

2:00 p.m. – 3:30 p.m.

Saal 4

WB2 | Apherese-Weiterbildung in deutscher Sprache: Teil 2

WB2-01 2:00 p.m.

Ultima ratio bei Lipoproteinstörungen

Jens Ringel

Dialysezentrum Postdam, Potsdam, Germany

WB2-02 2:30 p.m.

Apherese – eine erfolgreiche Geschichte

Dr. Jens Ringel

Potsdam, Germany

WB2-03 3:00 p.m.

Citrat und Heparin während der Apheresebehandlung - Pflegerelevante Besonderheiten (#42)

Jörg Müller

Universitätsklinikum Dresden, Lipoproteinapherese, 01307 Dresden, Germany

Eines der Hauptprobleme aller Aphereseverfahren stellt die Neigung zur Bildung von Gerinnseln im extrakorporalen Kreislauf dar.
Bei der Verwendung von Heparin und Citrat zur Antikoagulation müssen wir Pflegekräfte genau auf Wirkung und Nebenwirkung achten. Dabei legen wir auch einen besonderen Augenmerk auf die Calcium Substitution während der Therapie.
Die Balance zwischen Clotting des Systems und einer vermeidbaren erhöhten Blutungsneigung des Patienten zu finden, ist oft nicht einfach aber lösbar.
Durch tägliches Praktizieren und Hinzuziehen aller gewonnenen Erkenntnisse über die Blutgerinnung können wir so eine optimale Behandlung der Patienten gewährleisten.
Für die Umsetzung werden dazu Lösungen, Strategien sowie viele praktische Tipps aus unserem Apheresezentrum der Universitätsklinik Dresden gegeben.
One of the main problems of all apheresis procedures is the tendency for clot formation in the extracorporeal circuit.

When using heparin and citrate for anticoagulation, we nurses must pay close attention to the effects and side effects. We also pay special attention to calcium substitution during therapy.
Finding the balance between clotting the system and an avoidable increased bleeding tendency of the patient is often not easy but solvable.
By practicing daily and using all the knowledge we have gained about blood coagulation, we can guarantee optimal patient treatment.
For the implementation, solutions, strategies and many practical tips from our apheresis center at the University Hospital Dresden are given.

4:00 p.m. – 5:45 p.m.

Saal 4

WB3 | Apherese-Weiterbildung in deutscher Sprache: Teil 3

WB3-01 3:45 p.m.

Pflegerische Aspekte in der Apheresebehandlung von Long/Post-Covid Patienten

Anja Ramlow

Potsdam, Germany

WB3-02 4:25 p.m.

Pflegerische Aspekte in der Apheresebehandlung von Kindern

Dr. Volker Witt

Wien, Austria

WB3-03 5:05 p.m.

Vorstellung der E-ISFA

Jens Ringel

Dialysezentrum Potsdam, Potsdam, Germany

WB3-04 5:25 p.m.

Verabschiedung

Jens Ringel

Dialysezentrum Potsdam, Potsdam, Germany

2 June 2023

9:00 a.m. – 12:00 p.m. & 1:00p.m. – 3.30. p.m.

Saal 7

WB4-1 | Apherese-Weiterbildung in deutscher Sprache: Anwender-WS

Die nachfolgenden Firmen werden Ihre Maschinen sowie AnwenderberaterINNEN für die Gruppenarbeit an den verschiedenen Maschinen mit Erfahrungsaustausch unter den Pflegenden zur Verfügung stellen.
Der Anwender-WS erfolgt parallel an allen Maschinen.

BBraun

H.E.L.P.-Apherese steht für: H.eparin-induzierte E.xtrakorporale L.DL P.räzipitation.Die H.E.L.P. Therapie ist das bewährte und etablierte B. Braun Verfahren zur Behandlung konventionell nicht ausreichend therapierbarer Fettstoffwechsel-störungen. Die Basis von H.E.L.P. ist die selektive Präzipitation kardiovaskulärer Risikofaktoren. Unsere langjährige Erfahrung in der Praxis – bis heute wurden mehr als 500.000 H.E.L.P.-Behandlungen erfolgreich durchgeführt – zeugen für ein ausgereifte Therapieoption.Im Workshop werden wir Ihnen die Grundlagen des H.E.L.P. Verfahrens sowie den Aufbau und die Funktion des H.E.L.P.-Apheresegerätes Plasmat® Futura vermitteln und die Vorbereitung und Durchführung der H.E.L.P.-Behandlung demonstrieren.Lernen Sie die Vorteile dieser Therapiemöglichkeit kennen und erfahren Sie mehr über dieses hochselektive Therapieverfahren zur Reduktion von LDL-Cholesterin und Lp(a).Wir freuen uns über Ihre Teilnahme an diesem Apherese Anwenderworkshop. Unsere Anwendungsberaterin Frau Tatiana Steffen hat jahrzehntelange praktische Erfahrung und wird Ihnen das H.E.L.P.-Aphereseverfahren anschaulich erläutern sowie Ihre Fragen gerne beantworten.B. Braun Sharing Expertise auf dem ISFA World Congress2023

Diamed Medizintechnik

Beim diesjährigen Anwenderworkshop auf der E-ISFA zeigt DIAMED Medizintechnik ihre langjährig etablierte und sehr zuverlässige Gerätetechnik Octo Nova®. Einzigartig ist die Multifunktionalität der Octo Nova® in allen Bereichen der Therapeutischen Apherese, sowohl in der Klinik als auch in ambulanten Zentren.Im Workshop werden wir die Anwendung und Durchführung unterschiedlicher Therapieverfahren am Beispiel der Lipidfiltration und Immunadsorption demonstrieren. Sowohl die Lipidfiltration als auch die Immunadsorption zeichnen sich neben dem

therapeutischen Nutzen für den Patienten durch eine hohe Verträglichkeit und Sicherheit aus – selbst bei Kindern.Erfahren Sie mehr über die Vorzüge der Gerätetechnik Octo Nova® und überzeugen Sie sich selbst von der einfachen und schnellen Systemvorbereitung sowie der einzigartigen automatischen Startfunktion, welche zu Zeitersparnis und weniger Stress für Personal und Patienten führt.Unsere erfahrenen Vertriebsspezialisten beraten Sie gerne bei speziellen Fragen und freuen sich auf Ihre Teilnahme am Anwenderworkshop.DIAMED – Mit Herzblut und Verstand für das Leben

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Kaneka Medical Europe N.V.

Die Kaneka-Apheresetherapie – so einfach kann es gehen. Schnelles und unkompliziertes Integrieren im Zentrum Einfaches und nur kurzes Training für die BedienungIm Anwenderworkshop können Sie sich einen ersten Eindruck über unser Hämoperfusionsgerät die Lipidsmart sowie den Liposorber® D, in verschiedenen Adsorbergrößen, verschaffen.Haben Sie Interesse oder spezielle Fragen? Besuchen Sie uns an unserem Stand!Unsere kompetenten Fachkräfte stellen ihnen gerne unsere Produktpalette vor und beantworten gerne Ihre Fragen.Mehr Informationen auf unserer Webseite.

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