Issue #2
June 2024

ipnet NEWS LETTER

This newsletter is intended to keep the medical and patient community in touch with Porphyria developments

FROM IPNET PRESIDENT

Sverre Sandberg

Dear Friends and Colleagues – Ipnet Members,

I am pleased to inform you that the transition from Epnet to Ipnet is progressing very well.
The number of Epnet members during the ICPP in Sofia was 79, and the number of Ipnet members has now increased to 95. We have gained new members from all over the world, bringing the total number of full members to 28.
Ipnet will now elect a new Executive Board for 2025-26. We are delighted to have excellent candidates for all the positions on the Board, and as I write this, an electronic voting process is underway. The results will be communicated to you all as soon as the voting is finalized.
We will present the new Board in person during the General Assembly in Pamplona. I encourage all of you to participate in the General Assembly on Monday, September 23, from 17:30 to 20:00.
The General Assembly will not be boring 😊 as you will learn about new Ipnet activities, hear reports from all the working groups, and have the opportunity to engage in interesting discussions.
Before the summer, Ipnet will launch a call for members to organize the International Congress of Porphyrins and Porphyrias (ICPP) 2026.
The ICPP is the largest conference on this topic and is held every two years. All Ipnet members are welcome to apply to organize this conference. The organizer of ICPP 2026 will be announced at the General Assembly.

I look forward to seeing and discussing with you all in Pamplona!

Best regards from

Sverre Sandberg
Ipnet president

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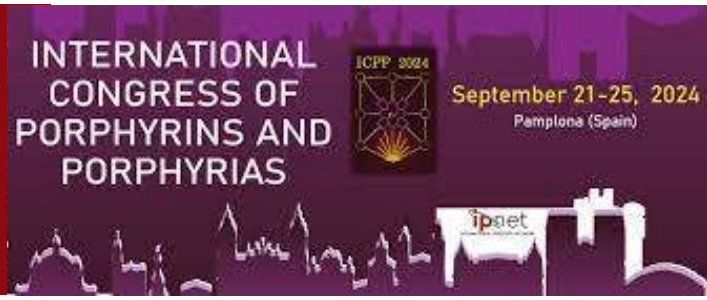
SAVE THE DATE - ICPP 2024 PAMPLONA

Link: http://ICPP2024.com



Ipnet is excited to announce that registration is open for the upcoming International Congress of Porphyrin and Porphyrias (ICPP2024), taking place from September 21-25, 2024, at the University of Navarra, in Pamplona, Spain. This pivotal event brings together global experts to discuss the latest advancements in research, treatment, and support for these diseases.

CONFERENCE HIGHLIGHTS

- Keynote Talks by International Experts: presenting groundbreaking research and significant case studies.
- Poster exhibitions: showcasing the latest studies and discoveries.
- Industry and Startup Presentations: for the first time, slots are available for companies to present new products or ongoing clinical trials.

SPECIAL INITIATIVES

- Ipnet's Meet & Greet event: designed to bring together young and emerging scientists and clinicians in the field and foster collaborations
- Information Sessions for Patients' Associations: both in-person and live video-streaming talks related to global patient advocacy updates, and advances in therapy and management of porphyrias.
- Practical Workshops: aimed at patients and their caregivers in the Spanish-speaking community.

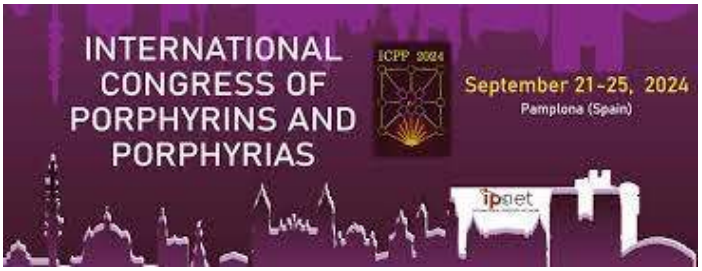
To register and learn more about the program, visit our website at https://icpp2024.com/. The deadline for abstracts submission has been extended until June 23, 2024. Take advantage of reduced registration rates before June 30, 2024.
Do not miss the opportunity to be part of this transformative event! Register today and contribute to the advancement of science and support of porphyrias.

See you all in Pamplona!
Best regards from

Sverre Sandberg
Ipnet president

Antonio Fontanellas Roma
President of ICPP 2024

Please keep looking at ICPP website and do not miss any update



PATIENTS CORNER

International Porphyria Patient Network (IPPN)

The concept of the IPPN was seeded in 2016 at a patient meeting in Rotterdam as reaction of the porphyria patient community to the challenges encountered during the European approval process of afamelanotide, the first effective and safe treatment for patients suffering from erythropoietic protoporphyria. We identified a core priority in the need to ensure that actual patients affected by porphyria (and not proxy patient representatives) must be involved in the assessments of the efficacy, safety, and benefit of any new treatments addressing our condition.

To that aim, we formally constituted the IPPN in 2018 with the objectives of cross-border support and counselling of patients suffering from porphyria and porphyria patient associations in scientific, medical, and healthcare policy matters as well as to safeguard their interests in regulatory, national, and supranational approval processes of related therapies. The promotion of contributions by porphyria patients with a medical and scientific background towards an improved scientific understanding of the porphyrias developed as a key feature of the IPPN over the years, critically supporting our focus around the approval of and access to safe and effective treatments for the porphyrias. As IPPN we have constituted ourselves as a small and agile international group of individuals who are patients or caregivers with a professional background in science, medicine, economics, and other relevant expertise.

We initiate and conduct our own research projects which we publish in peer-reviewed journals and share with the patient and medical expert community (to date, we have published over 10 articles, letters and opinion pieces, as detailed on our website: porphyria.network/IPPN/publications/.

In addition, we support national organisations and individual patients in accessing treatments by, for example, acting as stakeholders in national benefit assessment proceedings. Most notably, we have been involved as formal stakeholders in England's National Institute for Health and Care Excellence (NICE) assessments of afamelanotide and givosiran and, together with other stakeholders such as the British Porphyria Association (BPA) and the British Association of Dermatologists (BAD), have successfully appealed against the negative cost-effectiveness assessments of afamelanotide by NICE. To date, we have funded our activities exclusively out-of-pocket, minimising any potential dependence of third parties, and we remain fully focused on patients' best interests.

Falchetto Rocco
IPPN President

Barman - aksozen Jasmin
IPPN Vice President

IPNET WORKING GROUPS

Ipnet has several active working groups: see details at https://porphyrianet.org/en/content/Ipnet-working-groups. Any person of Ipnet full member group can apply to be part of a specific working group contacting the chair of the WG and submitting the motivations and competences to be admitted. The chairs of each working group will report their ongoing activities at the international Congress during the general assembly. The Ipnet executive board may decide to stop a WG if and when the program of the WG is completed or when no further progress can be made.
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The Acute Porphyria International Support Group

Is now able to offer support to healthcare professionals looking after patients with suspected acute porphyria in countries where porphyria laboratory testing and specialist care are not available.This may include arranging for biological samples from the patient to be sent to a specialist porphyria laboratory in Europe or North America for diagnostic testing without charge.
The referring clinician should complete the webform on the Ipnet website https://new.porphyrianet.org/apis-form providing anonymised patient details, reasons for suspecting acute porphyria and full contact details.
Please note we are unable to accept referrals directly from patients. We ask that patients share the information above with their doctor.

WG-GVC Gene Variant Classification Interview with Michela Barbaro

The Ipnet newsletter team has been in touch with Michela Barbaro, the chair of WG-GVC to provide the porphyria community with an update on their work in progress. The group is currently working towards curating a database for gene variants associated with acute porphyrias.

Background

Acute porphyrias are a group of four rare genetic disorders, each resulting from a pathogenic variant of the HMBS, CPOX, PPOX or ALAD gene. These genes encode specific enzymes within the heme biosynthetic pathway that, when dysfunctional, lead to accumulation of neurotoxic porphyrin precursors. In fact, a subset of those affected experience acute attacks that without timely recognition and appropriate treatment may become life threatening and cause neurological damage.

The aim

The WG-GVC, with their expertise in the field, has undertaken the ambitious task of providing and maintaining an up-to-date list of all known acute porphyria gene variants and their ACMG classification. This comprehensive list will be published on the Ipnet webpage.

The rationale

To date, the number of known gene variants score into the hundreds and most pathogenic variants are family specific. The critical task of distinguishing the pathogenic variants from the benign presents as an ongoing task, especially for rare missense variants. The challenge of publishing papers containing novel variants, coupled with the absence of specific clinical and biochemical data in publicly available databases (such as ClinVar), hinders the sharing and comparison of patient data. Consequently, making interpretation of gene variants much more difficult. WG-GVC hopes that the work they have undertaken will establish a solid foundation for the future and simplify the reporting of novel variants.

The tool at hand

The European Porphyria Registry (EPR) now includes variants submitted by the Porphyria Centres in Paris, Stockholm, Rotterdam, and Cardiff. Michela explains that they will use data from a specialized EPR module and apply a porphyria-specific version of the American College of Medical Genetics and Genomics (ACMG) classification criteria. This approach will classify acute porphyria gene variants into five distinct categories: pathogenic, likely pathogenic, likely benign, benign, and variant of unknown significance (VUS).

Progress and the plan ahead

The WG-GVC will initially focus on classifying variants of the HMBS gene from the literature, as well as those uniquely identified by the Porphyria Centres submitting data to the EPR. Michela reports that the guidelines for data submission to EPR module are being tested by colleagues at the porphyria centre in Milan, Italy. These guidelines will be used initially by the corresponding members of the group to submit acute porphyria gene variant data. Furthermore, a porphyria specific manual for how to apply the ACMG is being developed. Michela explains that the classifications will entail revision by two independent reviewers within WG-GVC who will reach a consensus for each variant. After classification of all known variants of HMBS gene has been completed the WG-GVC intends to proceed with variants of the CPOX and PPOX genes.

Safety of Drugs for Porphyria Patients Working Group (WG-DRUGS) Interview with Dr. Janneke Langendonk

The Safety of Drugs for Porphyria Patients Working Group (WG-DRUGS) was set up in 2023, with Dr. Janneke Langendonk (Porphyria Center Rotterdam, Erasmus University Medical Center, The Netherlands) being appointed as chair. The Working Group exists of twelve members with different areas of expertise, including physicians, pharmacists and pharmacologists.

What are the key objectives of the WG-DRUGS?

The ultimate goal of the WG-DRUGS is to provide guidance to health care professionals on drug use for patients with acute hepatic porphyria, including Acute Intermittent Porphyria (AIP), Variegate Porphyria (VP), Hereditary Coproporphyria (HCP), and ALA Dehydratase Deficiency Porphyria (ADP). To this end, we aim to publish new recommendations on drug use in the acute hepatic porphyrias and further develop and expand the existing Ipnet Drug Database, hosted by NAPOS. We also are making an overview of different methods used to classify drug safety in porphyria, with all their strengths and limitations.

Why is it important to have a database on Drug Safety?

Medication use is one of the known triggers of an acute porphyric attack. Although some experts argue that attacks triggered by medication are relatively rare, this can also related to the fact that much is already known on drug safety. Clinicians are therefore often able to avoid prescribing (potentially) porphyrinogenic drugs. The Ipnet Drug Database has played an important role in this. Keeping the database up-to-date and continuing to expand the work that has already been done, is vital to keep ensuring the safety and well-being of patients living with acute hepatic porphyrias.

Can you explain a bit more about how the safety of a specific drug is evaluated during a meeting of the WG-DRUGS?

We have started evaluating ‘new’ drugs that are commonly used, such as antidiabetics or anticoagulants, or drugs that health care professionals have asked specific questions about. During this process, a drug monograph is prepared by the
pharmacologists from the teams of NAPOS and Cardiff, containing all the information about therapeutic characteristics, metabolism and kinetics, as well as an assessment of the available evidence on safety. This includes (pre-)clinical research, case reports and unpublished clinical experience. Monographs are then discussed during the Working Group meeting. It is important to note, however, that the evidence is not always complete, so that even after extensive evaluation some degree of uncertainty may remain.

How can health care professionals get in touch with the WG-DRUGS, for instance when they have a question about a specific drug?

On the website of the Ipnet Drug Database, it is possible to send in a question or remark, via the “contact us” button, which can be found at the bottom of the webpage. Of course, it is also possible to approach one of the Working Group members directly.

YOUNG INVESTIGATOR IN THE SPOTLIGHT

On June 7th 2023, Debby Wensink successfully defended her thesis, titled: “Living with erythropoietic protoporphyria: Bridging the gap between research and clinical practice”.

Who is Debby Wensink?

Debby obtained her medical degree at Erasmus University Medical Centre in 2017. At the end of that year, she started her PhD trajectory under the supervision of Dr. Janneke Langendonk, at the Porphyria Expert Center Rotterdam. Currently, she is doing her residency in Internal Medicine at Amphia Hospital Breda.

What does the thesis add?

- EPP negatively impacts employment rate and social aspects of wellbeing. Patients were found to have a higher prevalence of type D personality, which is associated with depressive symptoms, anxiety and chronic stress.
- Using real-world data of a Dutch cohort of 117 adult EPP patients, it was confirmed that afamelanotide increases the duration of time spent outside and white light exposure, improved quality of life, and results in less severe phototoxic reactions.
- Both actigraphy, to measure total white light exposure, and time-to-prodome are suitable clinical endpoints, that could be used in future clinical trials with novel treatments in EPP.
- In Dutch patients with EPP (without liver disease), the prevalence of liver steatosis and liver stiffness is comparable with that of the general population. Acute cholestatic hepatitis remains a rare complication of EPP, that cannot be predicted using ultrasound elastography.

For those who wish to read the full version of the thesis, please follow the link below: https://pure.eur.nl/en/publications/living-with-erythropoietic-protoporphyria-bridging-the-gap-betwee

OBITUARIES

Joseph R. Bloomer, MD, FACP, FAASLD, a distinguished physician-scientist and pioneer in the study of porphyria passed away on December 22, 2021. Dr. Bloomer was deeply committed to collaborative research to advance the diagnosis and treatment of porphyria. His collaborative research with colleagues identified enzyme abnormalities and gene mutations in porphyria, developed methods to diagnose erythropoietic prototoporphyria, and showed the relationship between protoporphyrin and the liver. During his exemplary career, Dr. Bloomer's research resulted in the publication of 156 original manuscripts and 68 book chapters and reviews. He was a past president of the American Association for the Study of Liver Diseases (AASLD), and received the ASSLD Distinguished Service Award in 2009 in recognition of his leadership and advancements in liver disease. Dr. Bloomer was a highly respected clinician, teacher, and researcher. His contributions to the study of liver disease will continue to have a far-reaching impact.

Professor Dr. med. Manfred O. Doss, an outstanding scientist and teacher, born July 2, 1935 in Planitz/Saxony died on November 18, 2022 in Marburg/Lahn.Manfred Doss dealt with the topic of porphyrias over a period of five decades and made significant, pioneering contributions to clinical diagnostics, therapy and patient management.He wrote a large number of original publications and case reports, and curated numerous important symposiums for the international porphyria community. From 1965 to the present, more than 4,500 acute and chronic porphyrias were diagnosed at his porphyria center. The work of this center continued in Karlsruhe and Chemnitz following his retirement in 2000 and was supported by him with valuable advice until his death.In 1979 he succeeded in discovering the recessively inherited acute porphyria, subsequently named after him as Doss porphyria (http://www.doss-porphyrie.de/), which is mimicked by lead intoxication. In 2007, Doss porphyria was recognized as the world's first description of a "conformational disease" by Eileen Jaffe and Linda Stith from the Fox Chase Cancer Center in Philadelphia, PA.We thank Manfred O. Doss for a far-reaching, inspiring foundation, indispensable perfection, permanent support and decades of friendship.

SCIENTIFIC UPDATE ON PORPHYRIAS

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