11th National Clinical Immunology Symposium (NACLIS-11)

2nd International Conference on Primary Immunodeficiencies (ICPID)

PID at the Threshold of 2020. Is It Still a Rare Disease in South East Asia?

20th - 21st November, 2019

Auditorium Hospital Pengajar UPM
Serdang, Malaysia

Organised by:

PERSATUAN ALERGI & IMUNOLOGI MALAYSIA
MSAI

Co-organised with:

UPM
UNIVERSITI PUTRA MALAYSIA
BERILMU BERBAKTI

MyPOPI

IPOPI
INTERNATIONAL
PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

iPPT
INSTITUT PERUBATAN & PERGIGIAN TERMAJU

USM
UNIVERSITI SAINS MALAYSIA

16 CPD points Awarded

Souvenir Programme And Abstracts

CONTENTS

MESSAGE FROM THE PRESIDENT OF THE MALAYSIAN SOCIETY OF ALLERGY AND IMMUNOLOGY (MSAI)

Dear Colleagues and Delegates

Welcome to the 2nd International Conference on Primary Immunodeficiencies (PID), in collaboration with the 11th edition of the National Clinical Immunology Symposium (NACLIS 11). Following the 1st International Conference held in 2013, and with much progress in the recognition of new PID and its management, it was timely to organise the 2nd edition, with the theme "PID at the threshold of 2020. Is it still a rare disease in South East Asia?" Since that 1st Conference too came the official birth of the Malaysian Patient Organisation for Primary Immunodeficiencies or MyPOPI in 2014. This patient organization has grown from strength to strength and particularly active towards increasing awareness of PID in Malaysia and the surrounding region, as well as patient advocacy.

We are very pleased to have international experts in their specific fields within PID amongst the faculty and I hope that their expertise and experience be shared amongst all delegates in this conference. This will lead to viable and sustainable strategies to enhance the PID awareness, with much better tools in diagnosing PID, and maintaining a concrete foundation to build the best possible treatment for these patients in the region. By having all these in place, we will underpin the pursuit of excellence in our approach to managing PID patients in the best possible mode.

"The bigger the challenge, the greater the opportunity."

Dr Amir Hamzah Dato' Abdul Latiff
MBBS, MMed (Paeds), MRCP (Ire), DipRCPath (Imm), AM (Mal), FACAAI, FAAAAI
President
Malaysian Society of Allergy and Immunology (MSAI)

MESSAGE FROM THE FOUNDER OF THE MALAYSIAN PRIMARY IMMUNODEFICIENCY NETWORK (MyPIN)

We bid you a warm welcome to the 11th series of National Clinical Immunology Symposium (NACLIS 11) 2019 in Serdang, Malaysia.

With primary immunodeficiency (PID) within our midst in Malaysia as early as in 1977 in the University Hospital of University Malaya (now known as University of Malaya Medical Centre), a lull of a decade, before a re-emergence in 1986 at General Hospital Kuala Lumpur occurred. Throughout the next 3 decades more PIDs were diagnosed and with it, morbidity and unacceptable mortality.

In 2007 with an addition of another clinical immunologist (Universiti Putra Malaysia, UPM), the time was ripe for like-minded paediatricians and laboratory immunologists in both the universities and the Ministry of Health Malaysia Hospitals to harness their strength within a workable frame work to tackle this ominous health threat. Universiti Sains Malaysia (USM) through Advanced Medical and Dental Institute (AMDI) initiated and funded this venture with sufficient funding towards a full implementation. Thus, came the birth of MyPIN (Malaysian Primary Immunodeficiency Network) replacing an earlier initiative called NPII (National Primary Immunodeficiency Initiative) on June 5, 2007 in Penang. At a second meeting held in Langkawi on October 26, 2007, the deliberation was translated towards the main goals of:

1. To provide coordinated clinical service for PID in Malaysia
2. To provide local data towards the creation of a National centralised Registry for PID in Malaysia

The drawbacks to implement these goals were the lack of awareness of PID worldwide especially in the less developed and developing countries as in Malaysia. As creating awareness is the key towards establishing excellent PID care, all efforts were geared towards such an approach. Creating the human capital in the form of subspecialty training for clinical immunologist was the next emphasis. The product of such a program is to take leadership towards the realisation of improved services including clinical and laboratory diagnostics, clinical translational research and advocacy for the needs of PID patients. The stated requirements for clinical immunologist is 2 per every million population (WHO/IUIS 1997).

As the creation of awareness is deemed central to the above to be assailable, MyPIN went into full gear towards disseminating knowledge and experience to the community and the medical fraternity exploiting all platforms be it printed news and electronic media, publications or conferences and symposiums.

NACLIS series is the optimum avenue for interactive discourse with foreign and local experts on the subject of PID, including with young doctors and clinical specialists. The first NACLIS in 2007 was organised jointly by UKM, UPM and MSAI officiated by the then Director General of Health whose advice was to work on the data if PID is to make significant headway. By 2013, there were records of 168 PID patients in Malaysia extracted as published abstract of ESID Meeting 2014, *J. Clin. Imunol.* 2014;**34**:696-747. The NACLIS series prospered and never looked back.

Prof Dr Lokman Mohd Noh
MBBS (Mal), MRCP UK, FRCP (Edin), Post Doc Immunology (Stanford 1983-85)
Founder
Malaysian Primary Immunodeficiency Network (MyPIN)

11TH NATIONAL CLINICAL IMMUNOLOGY SYMPOSIUM (NACLIS-11) AND 2ND INTERNATIONAL CONFERENCE ON PRIMARY IMMUNODEFICIENCIES (ICPID) ORGANISING COMMITTEE

MSAI Committee

Dr Amir Hamzah Dato' Abdul Latiff

Prof Dr Lokman Mohd Noh

Assoc Prof Dr Intan Hakimah Ismail

Dr Marina Mohd Sham

Dr Intan Juliana Abd Hamid

Dr Siti Mardhiana Mohamad

Dr Mohd Azri bin Zainal Abidin

Dr Sangeetha A/P Siniah

Dr Ilie Fadzilah Binti Hashim

Dr Zarina Thasneem Zainudeen

Mr Bruce Lim

UPM Committee

Dr Thong Pui Ling

Dr Nor Azyati Yusoff

Dr Zurina Zainudin

Dr Melissa Anne Nunis

Dr Husna Musa

Dr Sithra Rengasamay

Siti Hasrizan Hassan

Hatiffah Mohd Suffian Soo

Mas Yati Mohd Lazim

Muhammad Yuzairi Mohammad Yusof

Ainul Azizi Mohd Kamslian

Nurmiza Syakirah Che Sukri

Suhaya Binti Hamzah

Haryati Mohd Raffi

Noor Elisma Ayob

Nur Syazalleyana Mohd Zaki

Nor Ain Binti Azahari

MALAYSIAN SOCIETY OF ALLERGY AND IMMUNOLOGY (MSAI) EXECUTIVE COMMITTEE 2019/2020

PRESIDENT
Dr Amir Hamzah Dato' Abdul Latiff
MBBS, MMed (Paeds), MRCP (Ire), DipRCPath (Imm), AM (Mal), FACAAI, FAAAAI
Fellowship in Clinical Immunology & Allergy (Leeds UK)
Consultant Clinical Immunologist/Allergist
(Adults & Pediatrics) &
Consultant Paediatrician
Allergy & Immunology Centre
Pantai Hospital Kuala Lumpur
Bangsar, Kuala Lumpur

PRESIDENT ELECT
Prof Dr Baharudin bin Abdullah
MBBS (UM), Master of Medicine in Otorhinolaryngology - HNS (USM)
Professor and Surgeon in Department of Otorhinolaryngology-Head & Neck Surgery
Universiti Sains Malaysia
Department of ORL-HNS, School of Medical Sciences, Health Campus USM
Kubang Kerian, Kelantan

VICE PRESIDENT
Mr SP Palaniappan
KMN, PJK, MBBS(Madras), DLO(Eng), FRCS(Edin), AM.
Consultant ENT Surgeon
Gleneagles Penang
Penang

SECRETARY
Assoc Prof Dr Intan Hakimah Ismail
MD (UKM), MMed Paeds (USM), PhD (Melbourne)
Consultant Paediatrician
Clinical Immunologist & Allergist
Head of Department and Head of Immunology Unit
Department of Paediatrics
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
Serdang, Selangor, Malaysia

ASSISTANT SECRETARY
Dr Faizah Mohamed Jamli
MD (UKM), Master of Medicine (Paeditrics), UKM
Consultant Paediatrician
Jabatan Pediatrik, Hospital Serdang
Selangor

TREASURER
Dr Shahjahan Kassim
M.B.B.S (MYSORE); Dip. Derm(London); Msc. Allergy (Imperial College London)
Klinik Dr Shah
Kelana Jaya, Petaling Jaya, Selangor

COMMITTEE MEMBERS
Dr Kent Woo Chee Keen
MD (USA) MD (USA), Diplomate American Board of Allergy and Immunology,
Diplomate American Board of Internal Medicine.
Fellow in Allergy & Immunology (Louisiana State University)
Consultant Allergy & Immunology
Consultant Internal Medicine
Gleneagles Hospital Kuala Lumpur
Kuala Lumpur

Dr Faisal Fadzli
MRCP (Medicine of Childhood) Ireland,Royal College of Physicians of Ireland (RCPI), MB BCh BAO BMedSc, Malaysian Matriculation Certificate (UKM)
Consultant Paeditrician
Tawakkal Specialist Hospital
Kuala Lumpur

Dr Nazirin Ariffin
Consultant Dermatologist
MBBCH, MRCP (UK), Masters in Clinical Dermatology (Lon), Dip in Derm. (Glas)
Pantai Hospital Kuala Lumpur
Allergy & Immunology Centre
Bangsar, Kuala Lumpur

Prof Dr Salina Hussain
MBBS, MS ORL-HNS
Consultant Otorhinolaryngologist
Senior Consultant, Rhinology
Department of Otorhinolaryngology-Head And Neck Surgery
UKM Medical Centre
Kuala Lumpur

MALAYSIAN SOCIETY OF ALLERGY AND IMMUNOLOGY (MSAI) EXECUTIVE COMMITTEE 2019/2020

CO-OPTED MEMBERS

Dr Noormalin Abdullah
Unit Head of Allergy
Allergy and Immunology Research Centre
Institute for Medical Research
Kuala Lumpur

Dr Ang Siang Chie
M.D. (USM), M. Med. (Paediatrics) UM
Consultant Paediatrician
Jesselton Medical Centre
Kota Kinabalu, Sabah

AUDITORS

Dr Zulkefli Hussein
MD (UKM), MS (ORL/HNS) (UKM)
Consultant Ear Nose And Throat Surgeon
Pantai Hospital Penang
Penang

Dr Intan Juliana Abdul Hamid
M.D. (UKM), M.Med. (Paeds) (USM), PhD (Immunobiology) (Newcastle, UK)
Medical Lecturer
Primary Immunodeficiency Disease Group
Regenerative Medicine Cluster
Advanced Medical and Dental Institute
Universiti Sains Malaysia
Penang

NACLIS Conference Secretariat
142, Jalan Ipoh, 3rd Floor, UMNO Selangor Building, 51200 Kuala Lumpur, Malaysia
T : 603-4041 0092 / 603-4041 6336 / 603-4042 7919
F : 603-4042 6970 / 603-4042 7919
E : info@allergymsai.org
W : www.allergymsai.org / www.xyzofallergy.org

INTERNATIONAL FACULTY

Prof Surjit Singh

MD, DCH (Lon.), FRCP (Lon.), FRCPCH (Lon.), FAMS

Head, Department of Pediatrics and Chief, Allergy Immunology Unit, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. Principal Investigator, Indian Council of Medical Research (ICMR) Centre for Advanced Research in Primary Immunodeficiency Diseases. Vice-President, Indian Rheumatology Association (2017-2019). President-Elect, Asia Pacific Society for Immunodeficiencies (2018-2020).

Prof Martin van Hagen

P. Martin van Hagen has been appointed Professor of Clinical Immunology and is currently the head of the section 'Clinical Immunology' within the Department of Internal Medicine of the Erasmus Medical Center Rotterdam, the Netherlands. Besides his appointment in the Erasmus MC he is also a staff member of the Eye Hospital in Rotterdam and Visiting Professor of Immunology of the Chulalongkorn University in Bangkok, Thailand. Prof. van Hagen is an expert in diagnosing and treating patients with immune-mediated diseases. His department takes care for approximately 3000 patients with well-defined rare immune diseases. In 2020 the section Clinical Immunology will be expanded by merging with the section Allergy. Furthermore the section Clinical Immunology has been recognized as a Centre of Excellence by the Dutch Federation of Universities and is part of the European Reference Network.

Except the clinical work Prof. van Hagen has a long-standing interest in translational research in immune-mediated diseases. Prof. van Hagen published about 200 peer-reviewed international papers, 18 peer-reviewed national papers, and 10 book chapters. Additionally he is member of many (medical) advisory boards, such as Vice chair of the Medical Advisory Panel of the International Patient Organization of Primary Immunodeficiencies (IPOPI), Member of the working group 'Chronic Immune diseases' of the Ministry of Health (Horizonscan) and Board member Dutch working group 'Immunodeficiencies' (WID).

Dr Nizar Mahlaoui

M.D., Ph.D.

Dr Nizar Mahlaoui is a pediatrician specialized in immuno-hematology at Necker-Enfants Malades University Hospital (Paris, France). He manages the French National Reference Center for Primary Immune Deficiencies (CEREDIH, chaired by Prof. Alain Fischer).

Dr Narissara Suratannon

Assistant Professor, Division of Allergy and Immunology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. Head, Pediatric Allergy & Clinical Immunology Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. Group Leader, Clinical Immunology Interest Group, Allergy, Asthma and Immunology Society of Thailand.

LOCAL FACULTY

Dr Amir Hamzah Dato' Abdul Latiff

MBBS, MMed (Paeds), MRCP (Ire), DipRCPath (Imm), AM (Mal), FACAAI, FAAAAI

Fellowship in Clinical Immunology & Allergy (Leeds UK)
Consultant Clinical Immunologist/Allergist (Adults & Pediatrics) &
Consultant Paediatrician
Allergy & Immunology Centre
Pantai Hospital Kuala Lumpur, Malaysia
President
Malaysian Society of Allergy and Immunology (MSAI)
2nd Vice-President
Asia Pacific Association of Allergy, Asthma and Clinical Immunology (APAAACI)
Chair
ARIA Malaysia
Board Member
Asia Pacific Society for Primary Immunodeficiencies (APSID)
Editorial Board Member
AP Allergy
European Medical Journal - Allergy & Immunology

Prof Dr Lokman Mohd Noh

MBBS (Mal), MRCP UK, FRCP (Edin), Post Doc Immunology (Stanford 1983-85)

Honorary Consultant Paediatrician (Immunology), Departments of Paediatrics
Women Children Hospital (WCH) Kuala Lumpur
Previously Professor at Dept of Pediatrics and Dept Microbiology-Immunology
UKM Med Centre Kuala Lumpur

Assoc Prof Dr Intan Hakimah Ismail

Associate Professor Dr Intan Hakimah Ismail is a Clinical Immunologist & Allergist as well Consultant Paediatrician and Senior Medical Lecturer at the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia (UPM). She is currently the Heads of Paediatric Department and Clinical Immunology Unit, UPM. She graduated with Doctor of Medicine (MD) from Universiti Kebangsaan Malaysia (UKM), and Master of Medicine in Paediatrics from Universiti Sains Malaysia (USM). She obtained her PhD specialising in Allergy and Clinical Immunology from the University of Melbourne, Australia. She started the Clinical Immunology and Allergy services in UPM and Serdang Hospital since then. She is currently the Secretary of Malaysian Society of Allergy and Immunology (MSAI). Her research interest includes primary immunodeficiencies, eczema, food allergy, gut microbiota and probiotics.

Dr Jeeyaseelan P Nachiappan

MBBS (UM), MRCP (UK)

Head of Department & Senior Consultant
Paediatric Infectious Disease Consultant
Department of Paediatrics
Hospital Raja Permaisuri Bainun
Ipoh, Perak

State Paediatric Clinical services Head
Perak College of Medicine Honorary Lecturer

LOCAL FACULTY

Dr Leong Chee Loon

M.B.B.S.(U.M.) & Master of Internal Medicine (U.M.)

General Physician and Infectious Diseases Consultant
Infectious Disease Unit, Medical Department, Hospital Kuala Lumpur
Adjunct lecturer of Faculty of Medicine MAHSA University for Bedside Teaching Year 5 Medical Students and End of Posting Examination Adjunct Facility Member
Lecturer of Faculty of Medicine Perdana University

Dr Adiratna Mat Ripen

Dr Adiratna Mat Ripen received her MD and PhD from the University of Tokushima, Japan. She currently works at the Institute for Medical Research (IMR) Malaysia, as the head unit of Primary Immunodeficiency (PID). She conducts research primarily in immunology with a special interest in PID. Her skills and expertise include diagnostics in PID, molecular and cellular typing in immune defects and functions, cellular biology, immunology, and immunohistochemistry.

Dr Dayang Zuraini Sahadan

M.D, M.Med (Paed) USM

Paediatric Respiratory Physician
Hospital Serdang, Selangor, Malaysia

Dr Mohamed Najib Mohamed Unni

Dr Mohamed Najib is a Paediatric Hemato-Oncologist & Stem Cell Transplant Paediatrician based at Hospital Wanita dan Kanak-kanak Kuala Lumpur. He has been involved in paediatric stem cell transplants for the past 4 years and has just returned from a 2 year stint at the Paediatric Stem Cell Transplant Unit,Great North Children's Hospital,Newcastle Upon Tyne which is one of the 2 leading centres for Primary Immunodeficiency transplants (PID) in the UK. He has also previously served as Treasurer of the Malaysian Society of Paediatric Haematology and Oncology (MASPHO) and currently sits on the expert panel for Bone Marrow Transplantation of the National Transplant Registry.

Dr Intan Juliana Abd Hamid

Paediatric Immunologist, Institut Perubatan & Pergigian Termaju
Penang, Malaysia

LOCAL FACULTY

Dr Mohd Azri Zainal Abidin

Dr Mohd Azri bin Zainal Abidin is a paediatrician and clinical lecturer in the Department of Paediatrics, Faculty of Medicine and Health Sciences, UPM. He is currently undergoing fellowship training in Clinical Immunology and Allergy field.

Dr Siti Mardhiana Binti Mohamad

Dr Siti Mardhiana Binti Mohamad is currently a medical lecturer and Head of the Immunology Unit, Advanced Diagnostic Laboratory at Advanced Medical and Dental Institute, Universiti Sains Malaysia.

SCIENTIFIC PROGRAMME

DAY ONE

20th November, 2019 (Wednesday)

0700 - 0800	**REGISTRATION**
0800 - 0815	**Negaraku and Doa Recitation**
0815 - 0830	**Welcome Speech by President of MSAI** *Dr Amir Hamzah Abdul Latiff*
0830 - 0900	**Opening Ceremony by Director of HPUPM** *Prof Dr Muhammad Mohd Isa*
0900 - 0945	**Clinical Diagnosis of Patients with PID** *Prof Surjit Singh*
0945 - 1015	**GROUP PHOTO AND TEA BREAK**
1015 - 1100	**When to Suspect Primary Immunedeficiencies in Adults** *Dr Leong Chee Loon*
1100 - 1200	**PID in Malaysia Through 4 Decades: A Pre 2020 Awakening** *Prof Dr Lokman Mohd Noh*
1200 - 1230	**Sharing Session with PID Patients** *MyPOPI*
1230 - 1400	**LUNCH AND PRAYER**
1400 - 1430	**Interesting PID Cases 1** *Dr Mohd Azri Zainal Abidin*
1430 - 1500	**PID Experience and Development of Postgraduate Training in Clinical Immunology in India** *Prof Surjit Singh*
1500 - 1530	**Transition Care of PID: From Paediatric to Adult** *Dr Nizar Mahlaoui*
1530 - 1600	**TEA BREAK**
1600 - 1700	**Establishing Clinical Immunology as a Stand Alone Subspecialty in Developing Countries (FORUM)** *Moderator: Dr Amir Hamzah Abdul Latiff* *Panelists: Prof Dr Lokman Mohd Noh / Dr Jeeyaseelan P Nachiappan / Dr Leong Chee Loon*

SCIENTIFIC PROGRAMME

DAY TWO

21st November, 2019 (Thursday)

0830 - 0900	**Infectious and Non-Infectious Manifestations of PID** *Dr Jeeyaseelan P Nachiappan*
0900 - 0930	**Recurrent Respiratory Illness and PID** *Dr Dayang Zuraini Sahadan*
0930 - 1000	**Vaccination and PID** *Assoc Prof Dr Intan Hakimah Ismail*
1000 - 1030	**TEA BREAK**
1030 - 1115	**Immunoglobulin Replacement Therapy in PID: Past, Present and Future** *Prof Martin van Hagen*
1115 - 1200	**Bone Marrow Transplantation for SCID and Non-SCID Cases** *Dr Nizar Mahlaoui*
1200 - 1240	**PID Molecular Testing in South East Asia** *Dr Narissara Suratannon*
1240 - 1415	**LUNCH AND PRAYER**
1415 - 1500	**PID Investigations and Latest Tests Available in Malaysia and its Dilemma** *Dr Adiratna Mat Ripen*
1500 - 1530	**TEA BREAK**
1530 - 1600	**Malaysian Experience in BMT for PID** *Dr Mohamed Najib Mohamed Unni*
1600 - 1630	**Interesting PID Cases 2** *Dr Intan Juliana Abd Hamid*
1630 - 1700	**Closing Remarks** *Dr Amir Hamzah Abdul Latiff*

SCIENTIFIC SESSIONS ABSTRACTS

The abstracts contained within are printed as received. The organising committee of MSAI has not edited the abstracts in any way.

CLINICAL DIAGNOSIS OF PATIENTS WITH PID

Prof Surjit Singh
Head, Department of Pediatrics and Chief, Allergy Immunology Unit, Advanced Pediatrics Centre
Post Graduate Institute of Medical Education and Research (PGIMER)
Chandigarh, India

This talk will involve several case discussions and would be very clinically oriented and based on real life patients that we have seen and managed over the years.

WHEN TO SUSPECT PRIMARY IMMUNEDEFICIENCIES IN ADULTS

Dr Leong Chee Loon
General Physician and Infectious Diseases Consultant
Infectious Disease Unit, Medical Department
Hospital Kuala Lumpur
Kuala Lumpur, Malaysia

We do see patients coming for recurrent infection as Infectious Diseases Clinician.

It is important for us to be aware when to suspect immunodeficiency in adult patients. When to suspect Primary immunodeficiency in adult patients is challenging.

Whenever we see patients with recurrent opportunistic infection, immediately we would screen for HIV Infection. If patient has been screened for HIV infection and found to be non-HIV infected patients, we will look for underlying Diabetes, SLE or malignancy. We seldom look hard for underlying Primary Immunodeficiency other then screening for all immunoglobulin A to E.

It is important to know when to screen for Primary Immunodeficiency in adults as some of our patients may not manifest clinical features during childhood.

We need to know what investigations that are available and what are the algorithms we should follow for patients suspected to have Primary Immunodeficiency.

PRIMARY IMMUNODEFICIENCIES (PID) OVER 4 DECADES IN MALAYSIA: A PRE 2020 AWAKENING

Prof Dr Lokman Mohd Noh
Honorary Consultant Paediatrician (Immunology)
Departments of Paediatrics
Women Children Hospital (WCH) Kuala Lumpur
Kuala Lumpur, Malaysia

Not many knew that a paediatric immunologist from Malaysia (YH Thong) was amongst the earliest to publish a report on PID in 1977 (Wiskott-Aldrich syndrome) and in 1979 (selective IgA deficiency) from the developing countries; the earliest was from South Africa by Professor David Beatty, University of Cape Town (chronic granulomatous disease) in 1975. The next wave of PID report in Malaysia began in 1986 with the return of the author from training in University of California at Palo Alto at a time when HIV/AIDS was raging in the US, especially California.

PID in 1986 being an extremely rare disease was easily overtaken by HIV infection, a secondary immunodeficiency, to receive National attention for a programme to curb spread of HIV. HIV-AIDS was also a rare immune deficiency then.

It was a struggle to ensure that PID patients receive similar adequate clinical care, when awareness was lacking, resources limited, facilities rudimentary, and the expertise was only available in Universiti Kebangsaan Malaysia (UKM) unit, General Hospital Kuala Lumpur.

Nonetheless, the PID service improved albeit slowly over the four decades and with addition of immunologically trained paediatric specialist, beginning in 2007, other clinical centres were set up at UKM, Universiti Sains Malaysia (USM), Universiti Putra Malaysia (UPM) and Women Children Hospital (WCH) Kuala Lumpur. The need to move to other institutions outside the federal capital, building the specialty along the way revealed that PID is more widespread than once thought of.

With the formation of MyPIN (Malaysian Primary Immunodeficiency Network) and with funding from USM's Advanced Medical & Dental Institute, Kepala Batas, Penang, plans were set to strengthen the service, upgrade facilities for both clinical care and laboratory diagnostics and to create a subspecialty programme for Clinical Immunology. In addition for advocacy, a patient group, Malaysian Patient Organisation for Primary Immunodeficiencies (MyPOPI), an affiliation of the International Patient Organisation for Primary Immunodeficiencies (IPOPI), had its early beginning at UKM Medical Centre (UKMMC) Kuala Lumpur. In the absence of a central registry, MyPIN registry was set where patients seen at the immunology clinics in participating hospitals could have the salient data recorded separately to ensure statistics on prevalence, diagnosis, treatment, and progress of PID would be available to help benchmark status of PID service and research of the country.

The record shows of the increase of new PID yearly especially with the addition of the immunologically trained physician specialists to MyPIN team beginning in 2007. The patients diagnosed as PID increased 4-7 times in the decade after (2007-2016). Specific therapy including immunoglobulin replacement therapy (IRT) via IV infusion for antibody deficiency was made available in 1986 at General Hospital Kuala Lumpur. Infusion of immunoglobulin via subcutaneous route (IGSC) was introduced in 2015 at UKMMC Kuala Lumpur, the earliest in South East Asia (SEA). With availability of bone marrow transplant (BMT) in Institute of Paediatrics, Hospital Kuala Lumpur and at Department of Paediatrics, University Malaya Medical Centre, Kuala Lumpier, the mortality for severe combined immunodeficiency (SCID) by 2017 was reduced from 100% to 90%. In good centres overseas, the survival is more than 90% as most BMT is done early by 3.5 months of age.

After four decades of PID existing in Malaysia the progress to attain better PID care although improving, still lag behind a few countries in SEA. Ideally, the role of organising for improvement of PID care falls on the clinical immunologists. Credentialing of clinical immunologist is still on hold, when most of the five clinical immunologists trained in reputed centres abroad had been servicing PID patients for almost a decade or more in Malaysia. Creating a subspecialty programme for a standalone Paediatric Immunology remains fallow. Providing clinical immunologist for adult patient is even more critical as more PID children move in transition to adults beside the existing PID adults diagnosed late in life. There are no clinical immunologist for adult PID in the public hospitals in Malaysia.

Year 2020 should be the turning point for better cares to the PID patients in Malaysia.

INTERESTING PID CASES - FROM COMMON TO UNCOMMON

Dr Mohd Azri bin Zainal Abidin
Paediatrician and Clinical Lecturer
Department of Paediatrics
Faculty of Medicine and Health Sciences, UPM
Serdang, Malaysia

Primary Immunodeficiency diseases (PID) is a heterogenous group of disorders in which part of the body's immune system is missing or dysfunctional. Antibody, phagocytic disorders, T and/or B-cell defects and complement deficiencies are common primary immunodeficiencies. I will describe 3 cases that encompass the common to uncommon disorders in PID namely X-linked agammaglobulinemia, chronic granulomatous disease and activated PI3K delta syndrome (APDS).

OUR JOURNEY WITH PRIMARY IMMUNODEFICIENCY DISORDERS AT CHANDIGARH, NORTH INDIA: TRIALS, TRIBULATIONS AND SOME SUCCESS

Prof Surjit Singh
Head, Department of Pediatrics and Chief, Allergy Immunology Unit, Advanced Pediatrics Centre
Post Graduate Institute of Medical Education and Research (PGIMER)
Chandigarh, India

Primary immunodeficiency disorders (PIDs) are a group of genetic defects characterized by abnormalities in one or more components of the immune system. Whilst there have been several advances in diagnosis, management, and research in the field of PIDs, these continue to remain underdiagnosed, especially in less affluent countries. This is largely because of lack of awareness about these conditions both among the laity and medical professionals. Despite several limitations and challenges, India has advanced significantly in the field of PIDs in the last few years.

Although there are no nationwide data on prevalence of PIDs in India, based on statistical projections it is estimated that the number of patients with PID is likely to be more than one million. The Foundation for Primary Immunodeficiency Diseases (FPID) [co-founded by Dr. Sudhir Gupta and Dr. Abha Gupta in the USA] is spearheading efforts at establishing PID centers in India and is currently supporting activities at 7 institutions in the country, including our own.

Very few developing countries have a dedicated society for PID - India is one of them. The Indian Society for Primary immune Deficiency (ISPID) was registered in March 2011. The inception of ISPID has led to significant progress in the spread of awareness and setting up of more advanced diagnostic facilities for PIDs in our country. There has also been a quantum jump in the number and quality of publications on PIDs from India in the last 8 years. Publications prior to 2011 were mostly case reports and clinical reviews; however, the more recent ones are based on a plethora of molecular and genetic details.

India is also fortunate in having two patient care societies that have been working actively to improve the quality of life of individuals with PIDs in our country. The Indian Patients Society for Primary Immunodeficiency (IPSPI) was set up in 2005 and the Primary Immunodeficiency Patients Welfare Society (PIDPWS) in 2012.

The spectrum of PIDs seen at PGIMER, Chandigarh is no different from that in a developed country. Most common PIDs diagnosed at our centre include X-linked agammaglobulinemia (n=65), severe combined immunodeficiency (n=84), chronic granulomatous disease (n=69), Wiskott Aldrich syndrome (n=45), and common variable immunodeficiency (n=42).

The outlook for patients with PIDs in India now appears to be much brighter than was the case a decade earlier. There has been an exponential increase in awareness of these disorders both amongst physicians and specialists. Availability of more refined diagnostic facilities (including candidate gene sequencing) and setting up of facilities for prenatal diagnosis for common PIDs have been important milestones in our journey.

Considering the importance of immunological disorders in the pediatric curriculum, our institute set up the first post-doctoral 3 years training programme (DM) in Pediatric Clinical Immunology and Rheumatology in January 2014. We have already trained 7 Fellows and 10 more are undergoing training at this time. This is the first, and till date the only, such training programme on the subject in India. Fellows who have completed their training with us have gone on to set up similar centres in other parts of the country.

The year 2015 remains a landmark in history of PID in India. The Indian Council Medical Research (ICMR) helped set up the Centre for Advanced Research (CAR) for PIDs in India at PGIMER, Chandigarh through a federal grant. The second such ICMR CAR in PID has recently been set up at the NIIH, Mumbai. The major objectives for these CARs are training of physicians / scientists, development and standardization of diagnostic facilities, establishment of nomograms, and creation of state-of-art facilities for diagnosis and management of PIDs. Till now we have conducted 9 Introductory Courses on Basics of PIDs for pediatricians under the aegis of ICMR. With the establishment of a Next generation Sequencing (NGS) platform in our laboratory in June 2018, there has been a big leap in genetic diagnosis of PIDs. This has resulted in diagnosis of several unique genetic defects in our patients with PIDs.

Cost of intravenous immunoglobulin (IVIg) therapy is a major constraint in the management of children with PIDs in India, as also in other developing countries. However, with recent policy changes initiated by the federal and state governments there has been a significant improvement in the provision and supply of this product to patients with PIDs. Several state governments are now providing IVIg *gratis* to all patients with hypogammaglobulinemia and other PIDs as well. We are also making steady progress towards creation of dedicated facilities for hematopoietic stem cell transplantation for patients with cellular immune defects in India. However, there are severe logistic, financial and resource constraints.

Managing PIDs in the context of a developing country is not easy but India has shown the will to take up this formidable challenge.

"LA SUITE-NECKER": AN INNOVATIVE TRANSITION CARE PROGRAM FOR TEENAGERS AND YOUNG ADULTS WITH RARE OR CHRONIC DISEASES

Dr Nizar Mahlaoui
CEREDIH (French National Reference Centre for PID)
Paediatric Immunology and Haematology Department
Necker-Enfants Malades University Hospital
Paris, France

A rare (or "orphan") disease is a chronic inherited disease affecting less than 1/2000 inhabitant. There are more than 8,000 rare disease and overall, it is estimated that there are 4 million patient in France (amongst 30 millions in Europe). Often times, these diseases are complex and need high level of multidisciplinary medical management.

Necker-Enfants maladies hospital is a highly specialized hospital; especially in rare diseases since more than 4000 patients aged 13-25 years accounting for 4000 rare diseases are seen every year in one of the 40 national reference centers located at Necker Hospital.

Life expectancy has improved over decades. Thus, transfer to adult care of adolescents and young adults with rare or chronic diseases treated in our hospital has become a major topic since a few years.

In fact, it is a challenge for patients and their family but also for the medical team.

Along with the patients themselves, patients associations, the Necker healthcare community (doctors including surgeons and psychiatrists, nurses, psychologists, social workers and board of Directors) and adult hospitals in Paris (12 million inhabitants), a large program to tackle issues related with Transition Care (2015-2020) was designed with the following aims:

1. Building stronger partnerships between Necker and close adult hospitals where patients are taken care upon transfer.
2. Improve the transitional care from Necker's end.
3. Address unmet needs for the cohort of adolescents and young adults followed at Necker Hospital, within a newly designed and built space, called "La Suite-Necker", along with the dedicated website and mobile app. The goals are:
   - Take care of themselves
   - Work on their self-esteem
   - Prepare their future
   - Plan their life with the disease
   - Learn how become an independent adult

This space is open to any AYA followed at Necker for a chronic disease. Their parents are welcome upon the first time and should let their child alone for any of the one-on-one appointment, should it be medical (gynecology-andrology) or non-medical (body image, socio-aesthetics, adapted physical exercise, relaxation, shiatsu, yoga); or any of the group activities (patient therapeutic education programs or dedicated workshops) usually with a qualified reception, health prevention and promotion for an easier transfer from pediatric department to an adult department.

Introduction to the space itself and these resources is made by the coordinator of this space (social worker with a training in adolescent care). Resources can also be offered to inpatients if need be.

La Suite-Necker is the first project of its kind, hence experimental and has welcome more than 200 patients since Oct 2016.

Many pediatric hospitals in France have showed interest in our project and are about to design a project in relation to their needs.

In July 2018, the Georges-Pompidou European Hospital (Paris) opened the Marina Picasso Space for young adults transitioning from a pediatric hospital (mostly from Necker Hospital) with many more collaborative projects to come.

INFECTIOUS AND NON-INFECTIOUS MANIFESTATION OF PRIMARY IMMUNODEFICIENCIES IN CHILDREN

Dr Jeeyaseelan P Nachiappan
Head & Paediatric Infectious Disease Consultant
Department of Paediatrics
Hospital Raja Permaisuri Bainun
Ipoh, Malaysia

Primary immunodeficiencies are a group of disorders that result from a defect in immune system. There are a wide spectrum of presentation depending on the severity of the defect in the innate and adaptive component. These defects have a genetic / hereditary basis. The primary presentation is an increase risk for infection. The defect also affects the other functions of the immune system - prevention of autoimmunity, host microbial interactions / symbiosis and cancer surveillance. Therefore, it is not surprising that children with primary immunodeficiency have an increased association with autoimmunity, autoinflammatory conditions, allergy, and haematological malignancies. It is important to recognise these associations as these may be the presenting feature rather than infections.

RECURRENT RESPIRATORY ILLNESS AND PRIMARY IMMUNODEFICIENCY

Dr Dayang Zuraini Sahadan
Paediatric Respiratory Physician
Hospital Serdang
Selangor, Malaysia

Primary Immunodeficiency patients share a significant susceptibility to recurrent respiratory diseases that represent a relevant cause of morbidity and mortality. The recurrent respiratory symptoms and complications of PIDs can affect primarily either *upper airways* (e.g. sinusitis and otitis media) or *lower respiratory tract* [e.g. pneumonia, bronchiectasis, and interstitial lung diseases (ILDs)]. The complications from lower respiratory tract are usually considered to be more important and also more specific for PID and they determinate patients' prognosis.

The recurrent respiratory illness of PID can be divided into infectious and non-infectious. Respiratory infection in PIDs can be distinguished with severe, persistent, recurrent symptoms and caused by unusual organisms. PIDs predispose to severe and recurrent pulmonary infections which can result in chronic lung disease including bronchiectasis.

Non-infections respiratory illness of PID can be the results of recurrent pulmonary infections or are the consequences of the PID itself. The recurrent pyogenic bacterial pulmonary infections lead to the air-trapping, bronchial wall thickening, atelectasis development, and bronchiectasis. However, the development of lung disease in PID may not be solely the result of recurrent bacterial infection or a consequence of bronchiectasis. Recent characterization of monogenic immune dysregulation disorders and more extensive study of common variable immunodeficiency has demonstrated that interstitial lung disease (ILD) in PIDs can result from generalized immune dysregulation and frequently occurs in the absence of pneumonia history or bronchiectasis. This distinction between bronchiectasis and ILD has important consequences in the evaluation and management of lung disease in PIDs.

Final development of chronic respiratory changes is the consequence of inter-play among different factors and mechanisms. Regular examinations by the appropriate tests should reveal the respiratory pathologies in early stages and should be used also for the monitoring of already existing abnormalities.

VACCINATION AND PID

Assoc Prof Dr Intan Hakimah Ismail
Consultant Paediatrician
Clinical Immunologist and Allergist
Head of Department and Clinical Immunology Unit
Department of Paediatrics
Faculty of Medicine and Health Sciences, Universiti Putra Malaysia
Selangor, Malaysia

Vaccines are developed to prevent or modulate the course of infectious and non-infectious diseases. Many diseases that used to be epidemic can now be prevented. Despite their proven efficacy in the population at large, vaccines can be problematic for patients with primary immunodeficiency diseases (PID). For example, vaccine-associated diseases in which viable vaccine organisms causing diseases in immunodeficient hosts causing catastrophe especially in PID patients.

On the other hand, some types of PID could interfere with the body's ability to make antibodies in response to vaccination. Taken together, there are uncertainty regarding which vaccines can be given to patients with PID. There are also concern for immunodeficient patients acquiring infections from healthy individuals who have not been immunised.

Vaccination of a large proportion of healthy population will not only prevent disease in the vaccinated individuals, but also lead to herd immunity. Herd immunity would protect immunocompromised people such as PID patients who cannot be vaccinated because of their weak immune system or vaccines might cause them diseases.

Vaccines are classified as live versus inactivated or killed vaccines. Categorisation of a patient's immunodeficiency is helpful in the assessment of the risk-benefit ratio for vaccination. In general, inactivated or killed vaccines are safe in immunocompromised patients and should be given per the routine schedule. Some PID patients are unlikely to have any benefit such as those with severe antibody deficiency or combined immunodeficiency and patients receiving immunoglobulin replacement therapy. While incomplete protection through killed/inactivated vaccines is likely, vaccination studies still demonstrated a protective effect especially in reducing complications, treatment costs and even mortality to vaccine-preventable infections. Even a partial protective effect clearly outweighs the minimal or nearly non-existent risk associated with the use of an inactivated, toxoid or recombinant vaccine.

For the reason of contracting vaccine-derived diseases, which can be lethal and cause severe or disseminated disease, live vaccines such as oral polio vaccine (OPV) and Bacillus Calmette-Guerin (BCG) vaccinations are contraindicated in all immuno-compromised populations. Other live vaccines such as measles, mumps and rubella (MMR), varicella zoster, rotavirus and live attenuated influenza vaccines are contraindicated in PID patients with severe antibody and combined immune impairment.

Apart from the prevention of diseases as an important component of care for patients with PID, vaccination with inactivated vaccines also served as part of assessment of the immune response before the decision regarding initiation of immunoglobulin treatment is made. For patients who do not respond to diagnostic vaccination as characterised by poor antibody responses towards certain vaccines, immunoglobulin replacement is the mainstay of therapy.

In conclusion, awareness of the importance of vaccination for PID patients among primary physicians and specialists who are taking care of those immunocompromised patients is essential to ensure safe and appropriate advice are given.

IMMUNOGLOBULIN REPLACEMENT THERAPY IN PID: PAST, PRESENT AND FUTURE

Prof Martin van Hagen
Head, Clinical Immunology Unit
Department of Internal Medicine
Erasmus Medical Center
Rotterdam, The Netherlands

Human normal class G immunoglobulin (IgG) therapies (IG) are used to treat various medical conditions ranging from prevention of life-threatening infections to the treatment of immune mediated inflammatory processes. The World Health Organization (WHO) labeled normal human IG as an Essential Medicine.

IG replacement therapy (IG-RT) is the standard of care treatment for patients with a compromised antibody response which results in recurrent infections. Bruton was the first in the early fifties who treated a young boy who suffered from recurrent pneumococcal sepsis with IG. The frequency of the recurrent infections declined dramatically. Genetic analysis, decennia later, revealed a defective signal molecule in B cell precursors. This defect results in an impaired B cell differentiation and is nowadays known as Bruton's tyrosine kinase, resulting in agammaglobulinaemia. Common variable immune deficiency (CVID) however is an immunodysregulation disease and is the most prevalent and diverse PID of unknown origin. Individuals affected with this condition represent the most frequent of all "PID" IG users. Currently, multiple IG preparations are available for intravenous (IVIG), subcutaneous (SCIG), facilitated subcutaneous (fSCIG), and intramuscular (IMIG) administration. The choice of IG administration is made by the caregiver and the particular patient and depends on medical and patient's personal reasons. IG therapy is generally well tolerated however, the brand and route of administration should be adjusted to the patients characteristics. Plasma-derived polyclonal/polyvalent IG therapies belong to a distinct class of biologics that depend on the availability of appropriate donors. The world plasma availablility is relatively limited and needs exploration, particularly in developing countries. Future therapeutic strategies, including gene therapy and gene-editing in order to correct genetic variants in the B cell development may be an option but are still at a preliminary research-laboratory level.

HEMATOPOIETIC STEM CELL TRANSPLANTATION PRIMARY IMMUNE DEFICIENCY

Dr Nizar Mahlaoui
CEREDIH (French National Reference Centre for PID)
Paediatric Immunology and Haematology Department
Necker-Enfants Malades University Hospital
Paris, France

Hematopoietic stem cell transplantation (HSCT) is curative treatment for severe combined immunodeficiency (SCID) and other PIDs. First HSCT for PID was performed in 1968 in the USA for SCID in 1 patient and for WAS in another patient.

Since then, insight in the genetic basis of PID has markedly increased. In parallel, developments in HSCT supportive care as well as HLA typing technology have contributed to the quality of HSCT.

To improve knowledge on HSCT outcome and care for patients with PID, the SCETIDE registry (www.scetide.org) was created 30 years ago on behalf of the EBMT Inborn Error Working Party, aiming at assessing some disease-specific outcome parameters.

Survival in HSCT recipients transplanted more than thirty years ago is 60%.

The superior outcome in young patients and patients without active infections SCID has important implications for the scheduled introduction of newborn screening for SCID.

Outcome of HSCT for PID has significantly improved during last five decades. Better outcome in unrelated donor HSCT, younger age at HSCT and better HLA typing as well as better supportive care have contributed to this improved outcome.

PID MOLECULAR TESTING IN SOUTH EAST ASIA

Dr Narissara Suratannon
Assistant Professor, Division of Allergy and Immunology
Department of Pediatrics, Faculty of Medicine, Chulalongkorn University
Head, Pediatric Allergy & Clinical Immunology Research Unit
Faculty of Medicine, Chulalongkorn University
Bangkok, Thailand

Current genetic tests for Primary Immunodeficiency Disorders (PIDs) are costly, time-consuming, and not accessible in developing countries. South-East Asia PID network (SEAPID), International Patient Organisation for Primary Immunodeficiencies (IPOPI), and Erasmus Medical Center, the Netherlands developed a customized Single Nucleotide Variant (SNV) microarray to detect 277 PID causing variants as well as copy number variation (CNV) in for the material price of 40 Euros. Our proof of principle study demonstrated that our tool has high accuracy with diagnostic yield of the test around 51%. With an updated version of the array adding several newly identified mutations, the yield of the test can reach up to 90%.

In summary, our robust customized GSA is promising as a first-line rapid screening tool for PID at affordable costs and saving ~50% of costs. The technique is scalable to enlarge numbers of additional genes and offer new perspectives for genetic testing especially for countries which genetic testing is not available.

LAB INVESTIGATIONS AND LATEST TESTS AVAILABLE FOR PID IN MALAYSIA

Dr Adiratna Mat Ripen
Head of Primary Immunodeficiency Unit Immunologist
Allergy & Immunology Research Centre (AIRC)
Institute for Medical Research
Pahang, Malaysia

Primary immunodeficiency diseases (PID) are a group of genetically determined disorders with diverse presentations. PID comprises of more than 300 distinct disorders characterized by defects in the development of specific components of the immune system. The diverse nature and variable presentation of PID make diagnosis a challenge. Early diagnosis therefore requires a high index of suspicion in combination with a detailed clinical history, thorough physical examination, and supportive laboratory investigations. PID unit of Institute for Medical Research (IMR) has been the reference laboratory for the Primary Immunodeficiency screening in Malaysia since late 1990s. We had been providing some basic screening tests like, the lymphocyte subset enumeration, phagocytic function test and quantitative immunoglobulin tests. As we became more familiar with the flow cytometry, we had developed new tests and slowly transferred our research output to diagnostics. We began offering Bruton agammaglobulinemia tyrosine kinase (Btk) protein expression, Dihydrorhodamine (DHR) assay, Lymphocyte Transformation Assay, CD40 ligand expression and CD40 protein expression by flow cytometry. We have not been expanding the laboratory tests recently but our research team and pathology diagnostic team are looking into possibility of designing targeted panels for PID patients in Malaysia based on our recent whole exome sequencing research data.

MALAYSIAN EXPERIENCE IN BMT FOR PID

Dr Mohamed Najib Mohamed Unni
Paediatric Hemato-Oncologist
Women and Children Hospital Kuala Lumpur
Kuala Lumpur, Malaysia

Bone Marrow Transplant Unit of the Institute of Paediatrics Hospital Kuala Lumpur has recently moved to our new home in Women and Children Hospital Kuala Lumpur. We have performed over 500 transplants to date including cases of primary immunodeficiencies. We will highlight few interesting cases of primary immunodeficiencies that has been transplanted at our centre.

INTERESTING PID CASES - THE MANY FACES OF STAT3

Dr Intan Juliana Abdul Hamid
Paediatric Immunologist, Institut Perubatan & Pergigian Termaju, Universiti Sains Malaysia
Penang, Malaysia

Autosomal Dominant Hyper IgE Syndrome (HIES) is caused by mutations in the signal transducer and activator of transcription 3 (STAT3). Patients usually presented with recurrent sinopulmonary infections, chronic eczematous dermatitis, high serum IgE levels and eosinophilia. I will describe 2 cases of STAT3 autosomal dominant HIES under my care. These cases highlight the phenotypic's variability of STAT3 mutation disorders in Malaysian cohort. Thus, highlighting the needs for increased awareness among the primary healthcare in picking up and early referral to Paediatric Immunologist.