

PID Principles of care

Framework for the diagnosis and
treatment of PIDs

Jose Drabwell, IPOPI President

Why did the team decide to do this?

- World-wide immunological community needs to ensure early diagnosis & treatments for all PID patients
- Relevant healthcare policies are needed everywhere
- Many patients are not diagnosed as PID is not thought of despite easy diagnosis by two simple blood tests
- Access to treatment varies widely between regions and countries within the same continent

This document sets out comprehensive principles for PID care world-wide, to assist PID communities in persuading healthcare agencies to improve services by setting standards

The Haemophilia community were very successful in widening services throughout the world

Preparation & Development phases



A worldwide multi-disciplinary team of specialists + the Editorial Board

H. Chapel, H. B. Gaspar, T. Español, F. A. Bonilla,

J. Prevot, L. Solis, J. Drabwell for IPOPI

M. Ballow (USA)	J. Kerr (Germany)	J. Puck (USA)
L. Brown (UK)	C. Kinnon (UK)	S. Sánchez Ramon
B. T. Costa-	Y. L. Lau (Hong	(Spain)
Carvalho (Brazil)	Kong)	R. E. Schmidt
J.D. Edgar (NI)	J. Litzman (Czech	(Germany)
W. Egner (UK)	Republic)	S. Singh (India)
S. Ehl (Germany)	H. J. Longhurst	G. Spickett (UK)
M. Esser (South	(UK)	K. Sullivan (USA)
Africa)	N. Mahlaoui	A. Symes (UK)
A. Gardulf	(France)	
(Sweden)	J. S. Orange (USA)	
A. Gennery (UK);	C. Picard (France)	

How did it work?

- Each participant given a topic but a chance to comment on others too
- Consensus, if required, achieved by offering a chance to include a contrary view statement
- Editorial group reviewed each round – 6 rounds
- All participants saw second & penultimate drafts
- 12+ months to complete
- Role of IPOPI to add extra comments if needed
- Tried to make applicable to all countries whatever their PID plans/services
- Implementation up to each country- cannot set a standard for everyone

What are the 6 Principles?

1. The role for specialized centres
2. The importance of registries
3. The need for international collaborations
4. The role of patient groups
5. Management and treatment options for PIDs
6. Managing PID diagnosis and care in all countries

Principle 1: The role for specialized centres



- To establish **professional networks** to be recognised by national healthcare providers whether governmental or insurance companies
- To **answer queries** from individual physicians with limited personal experience
- To assist in establishing **national registries** as useful tools for **Health policy makers** and providers to encourage **dedicated funding for facilities**
- Often based on University Hospitals as part of research but funds for services are essential
- Promote **awareness** of PIDs in medical/nursing community

Criteria for national specialist PID centres for adults/children are listed in the document – maybe more than 1 per country

Consensus document on PIDs 1994

to increase diagnosis rates in UK due to increased awareness

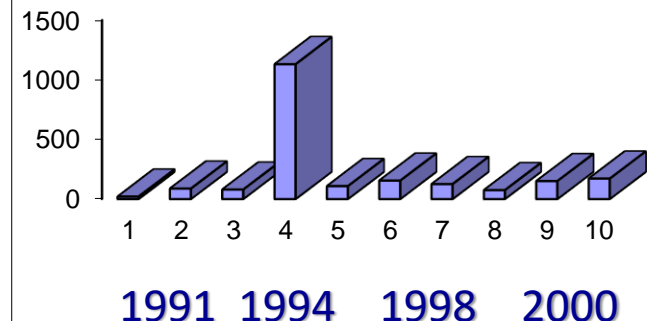
Stakeholders include representatives from

Clinical Immunology
Respiratory medicine
Rheumatology
Haematology
Paediatrics
General medicine
Infectious diseases
General practice
Patient organisation

(Chapel HM BMJ. 1994 308:581-5)

Then published widely in
specialty-related journals and presented
to Royal College of Physicians
& specialty groups for professional
endorsement as well as DoH

**Increases in registered
patients each year in decade
1991- 2000**



Principle 2: The importance of registries

- Data catches **attention of governments/healthcare policy makers**
- Enables **costs to be calculated** more accurately
- **Comparisons** with other specialty groups e.g. HIV
- Enable **publications**

PID publications from SEAN in last 15 years -Information from Pubmed....

	TOTAL	
	PID	HIV
Thailand	4	47
Singapore	2	13
Malaysia	2	14
Indonesia	0	6
Vietnam	0	18
Myanmar	0	7
	8	105

Principle 3: The need for international collaborations for scientific research & training



Molecular Diagnosis of Severe Combined Immunodeficiency—Identification of *IL2RG*, *JAK3*, *IL7R*, *DCLRE1C*, *RAG1*, and *RAG2* Mutations in a Cohort of Chinese and Southeast Asian Children

Pamela P. W. Lee • Koon-Wing Chan • Tong-Xin Chen • Li-Ping Jiang •
Xiao-Chuan Wang • Hua-Song Zeng • Xiang-Yuan Chen • Woei-Kang Liew •
Jing Chen • Kit-Man Chu • Lee-Lee Chan • Lynette Shek • Anselm C. W. Lee •
Hsin-Hui Yu • Qiang Li • Chen-Guang Xu • Geraldine Sultan-Ugdoracion •
Zarina Abdul Latiff • Amir Hamzah Abdul Latiff • Orathai Jirapongsananuruk •
Marco H. K. Ho • Tsz-Leung Lee • Xi-Qiang Yang • Yu-Lung Lau

From 1991 to 2009, nine patients with SCID were diagnosed in Hong Kong and seven received hematopoietic stem cell transplantation (HSCT) in our unit. Since 2001, we received blood samples of 33 patients for molecular confirmation of SCID from 14 hospitals in mainland China, Taiwan, Singapore, Malaysia, Thailand, and the Philippines. Based on research collaboration, mutation detection

Rapid progress with increased facilities

Principle 4: The role of patient groups

- To explain, with patient stories, why is it important for PIDs to be **recognised** by healthcare providers?
- PID diagnosis has a **direct impact on patients' quality of life, prognosis and survival**, as well as their families, and society in general.
- Early diagnosis is critical; **diagnostic delay** not only damages the patient but **is wasteful of health care resources**. Prompt PID diagnosis results in lower healthcare costs.
- Treatment for PIDs can be **safe and effective**.

Principle 4: The role of patient groups

- Patient organisations are increasingly **key stakeholders in political** and healthcare decision-making processes.
- Effective national patient organisations provide **advice, education and support to patients** and families and their healthcare providers.
- Patient groups are active in collecting clinical data and **participating in the management of registries**, which help to guide decisions affecting their health.

Principle 5: Diagnosis, management and treatment options for PIDs



A. Criteria for fast and reliable PID diagnosis:

1. Early recognition of clinical manifestations suggestive before serious complications compromise the patient's health
2. High-profile medical awareness of PIDs and information campaigns for referral
3. Consensus on basic screening tests, available to all primary health care & hospital doctors (i.e., CBC plus differential; serum Ig levels)
4. Immediate access to a PID specialist for confirmation of diagnosis and speedy treatment
5. Standardization of immunological diagnostic protocols (immunophenotypes, protein analyses, in vivo and in vitro functional tests) and validation of clinical & laboratory biomarkers
6. Access to genetic counseling for the patient's family after diagnosis

Principle 5: Diagnosis, management and treatment options for PIDs



B. Current challenges to Ig therapy

1. Finances to ensure availability of several Ig products to all age groups in every country, as per WHO Essential Medicines Lists
2. Early diagnosis to prevent infection-related complications
3. Selection of optimal dosage for each patient, with regular medical follow-up
4. Expert treatment centres, with **dedicated nursing staff**, to avoid side effects due to incorrect infusion techniques
5. Training for self-infusion by suitable patients at home, with regular follow-up to ensure ongoing standards
6. PID patients are **prioritized** for Ig products in times of restriction
7. Improvement of outcomes for complex patients by finding additional therapies for disease-related complications

Raise awareness that **Immunoglobulin is on both WHO Essential Medicines Lists**

- WHO Essential Medicines Lists for adults & WHO Essential Medicines Lists for children – BOTH list therapeutic immunoglobulins due thanks to IPOPI & IUIS PID committee



- Increased availability in Europe to cover almost all countries with IVIg in 2011
- SCIg not as widely available (yet)
- Human Stem Cell Transplantation for PIDs – not enough centres

Principle 5: Diagnosis, management and treatment options for PIDs



C. Current challenges to haematopoietic stem cell transplantation

1. Identifying candidates before they sustain significant damage from infection, particularly for children or adults diagnosed late
2. Recruiting appropriate donors, since a “match” between donor and patient is essential for a good outcome
3. Improving the outcomes for the sickest patients with complex PIDs depends on determining the involvement of other tissues or organs

Principle 6: Managing PID diagnosis and care in all countries

Who can help?

- Patient organisations
- Specialists in related medical disciplines
- Research laboratories to train & support a network of smaller local laboratories for basic tests
- International collaboration between established and less experienced centres (e.g. Hong Kong)
- Consideration of integration of funding with other community healthcare workers for resources e.g malaria, HIV, tuberculosis or other locally prevalent diseases
- IUIS PID committee

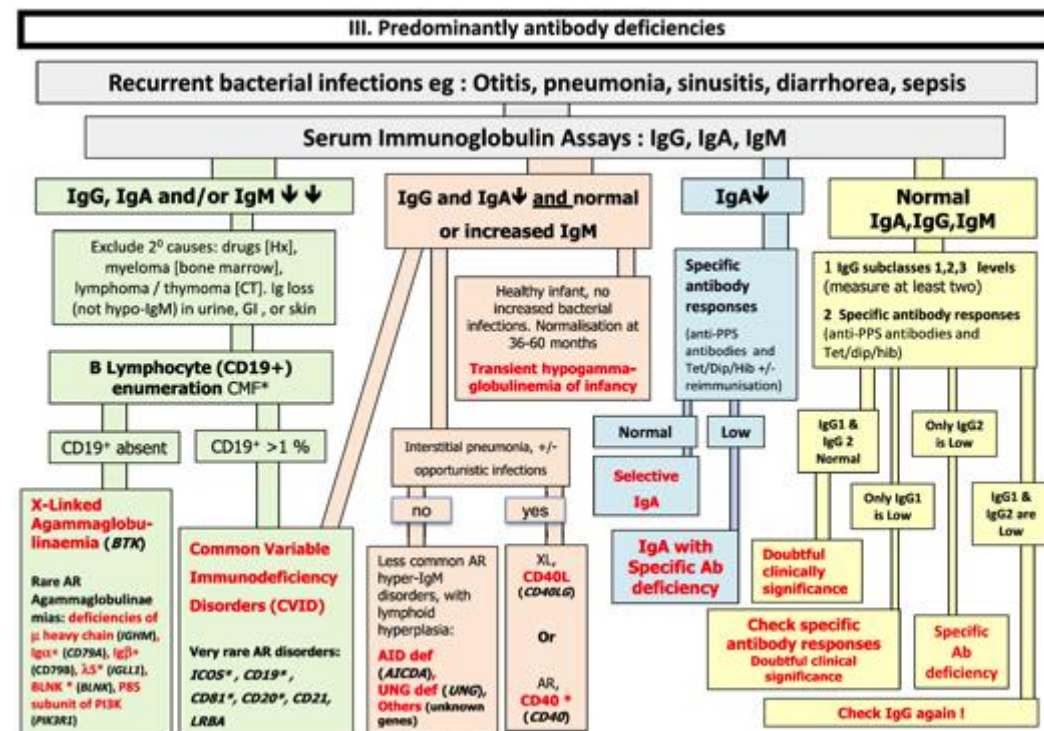
International Union of Immunological Societies

PID Expert committee



- Classification of PIDs *IUIS Expert Committee for PID. Front Immunol. 2011*
- Contribution to WHO ICD codes for PIDs Version 11 in 2018 to enable reimbursement
- Physician friendly chart for diagnosis of PIDs *Bousfiha et al J Clin Imm. 2013*

- WHO Essential Medicines
- Education for young physicians at ESID, APPID, CIS, LASID & other summer schools



Summary



National healthcare policy makers to take strong and decisive action to ensure that PID patients are:

- diagnosed as early as possible
- have appropriate access to safe, efficient, life-saving treatments
- Are managed in centres with optimum care

This involves:

- specialised centres, national registries, transnational co-operation, patient organisations, appropriate facilities for all therapies, recognition of WHO Essential Medicines List for replacement immunoglobulin therapy

What might help implementation?

For each country to consider

- Consensus Document for bringing together stakeholders and awareness
- Particular Standards for each therapy
- Dedicated facilities for diagnosing complex PIDs and their therapies: costs vs geography vs training
- Specialist treatment centres to spread good practice and train nurses
- Education