

**ASID-IPOPI African PID Patients Meeting**  
**IRESSEF, Diamniado, DAKAR**  
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# PID treatment possibilities in developing countries

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**CEREDIH:** The French National Reference Center for PID

& **SCETIDE:** Stem Cell Transplantation for PID in Europe Registry

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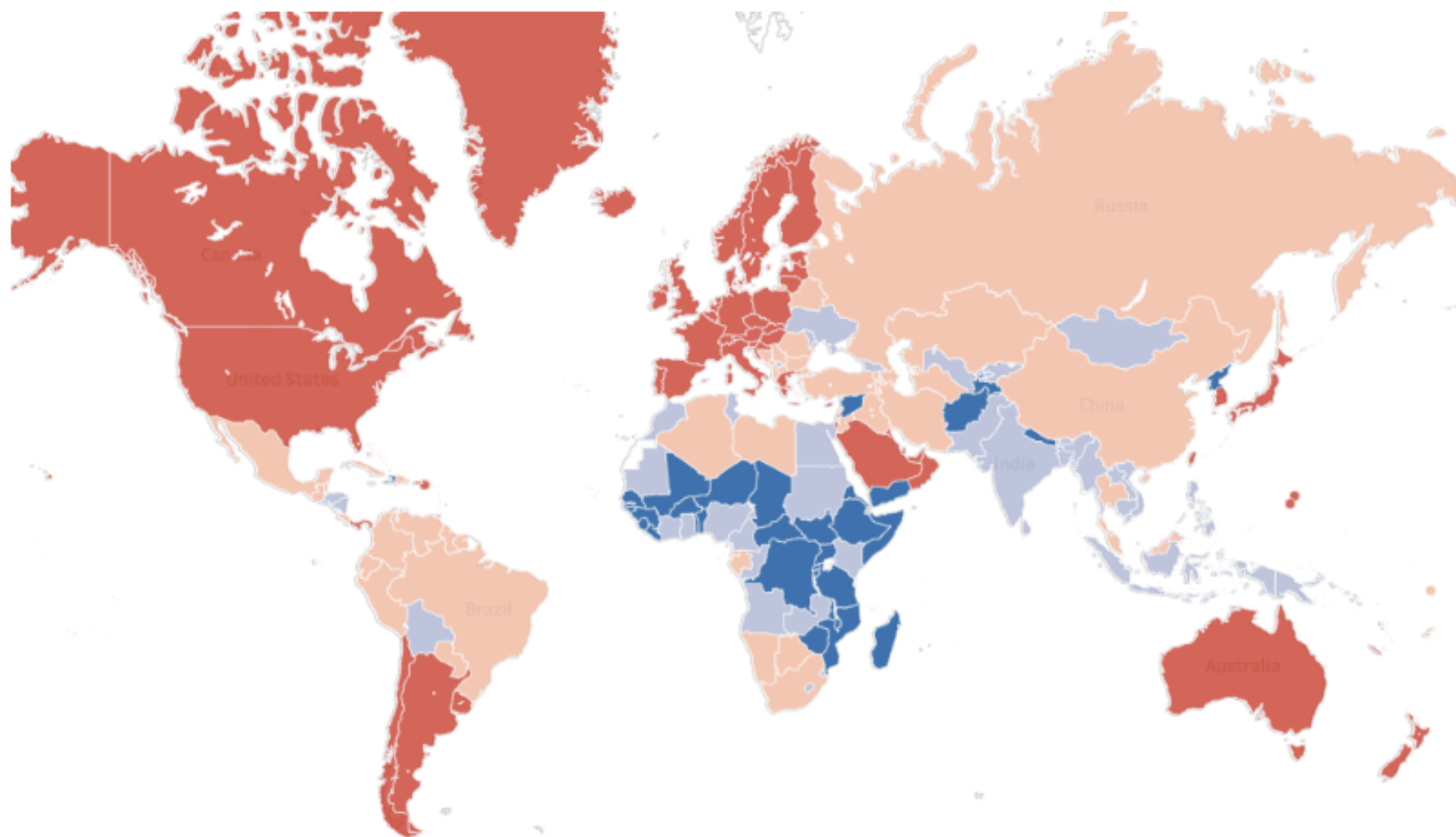
Website: [www.ceredih.fr](http://www.ceredih.fr)



ASID-IPOPI African PID Patients Meeting



The World by income - 2017



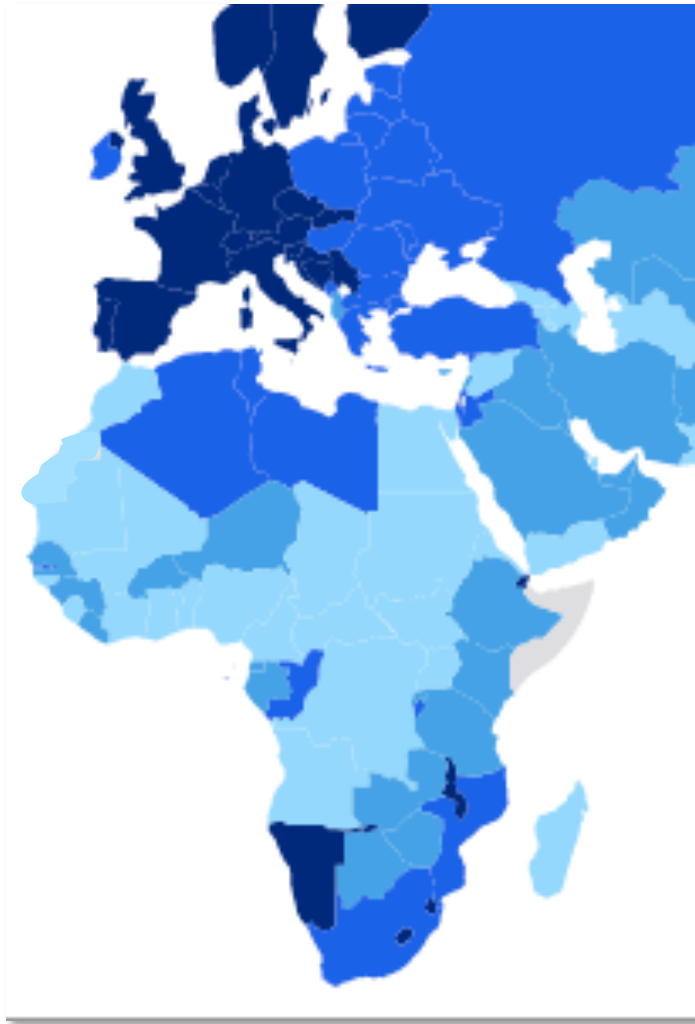
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Income Group

- |                          |                          |    |
|--------------------------|--------------------------|----|
| Low income (L)           | Upper middle income (UM) | NA |
| Lower middle income (LM) | High income (H)          |    |

# Public health expenditure (% of GDP)

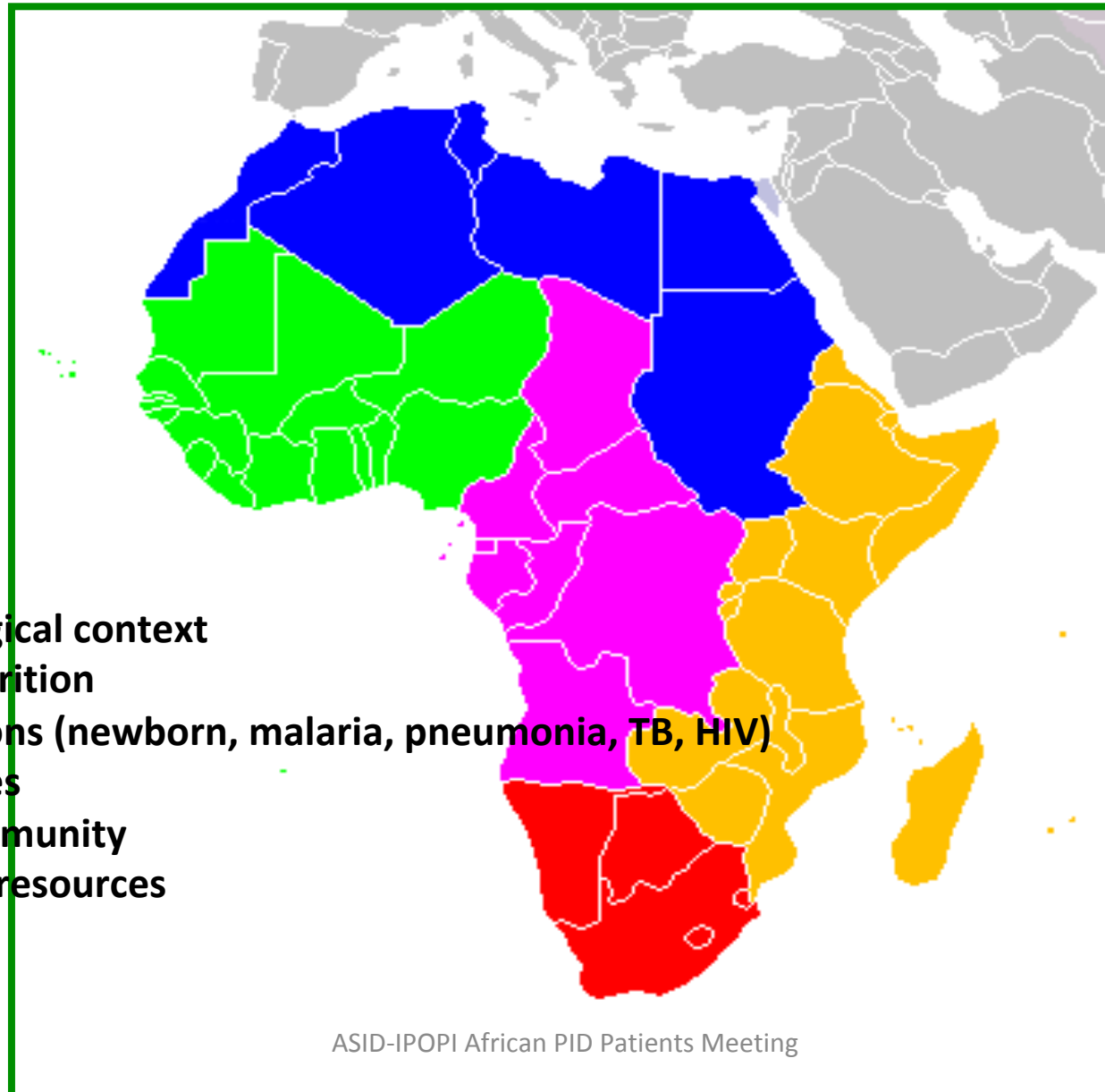


- World's second largest and second most densely populated continent
- 1.2 billion people as of 2016  
= about 16% of the world's human population
- The world's youngest amongst all the continents: median age in 2012 was 19.7 (30.4 worldwide)
- Very diverse situations regarding Health

# Look for underlying PID

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- **Epidemiological context**
  - **Malnutrition**
  - **Infections (newborn, malaria, pneumonia, TB, HIV)**
  - **Allergies**
  - **Autoimmunity**
- **Economical resources**



# PID situation in Africa on short

## Strengths:

- Committed physicians and patients representatives
- Leading countries (South Africa, Tunisia, Morocco, ...) 18 countries have treatment centres
- Fair amount of available data

## Weaknesses:

- Low diagnosis rate
- Lack of education among patients
- Lack of awareness among physicians
- Lack of registries
- Little interest/awareness among decision makers, payers and funders
- Competition between diseases

## Opportunities:

- Example from other rare diseases (haemophilia)
- Examples from other continents
- Multi-stakeholders collaboration
- Growing economy

## Threats:

- Financial and socio-economical issues
- Poor healthcare infrastructure
- Access to healthcare in remote areas
- High consanguinity rate in some regions

# Primary Immunodeficiency



Courtoisie du Pr C. Picard (Necker), adapté de Boisson *et al.*, 2015

# General considerations

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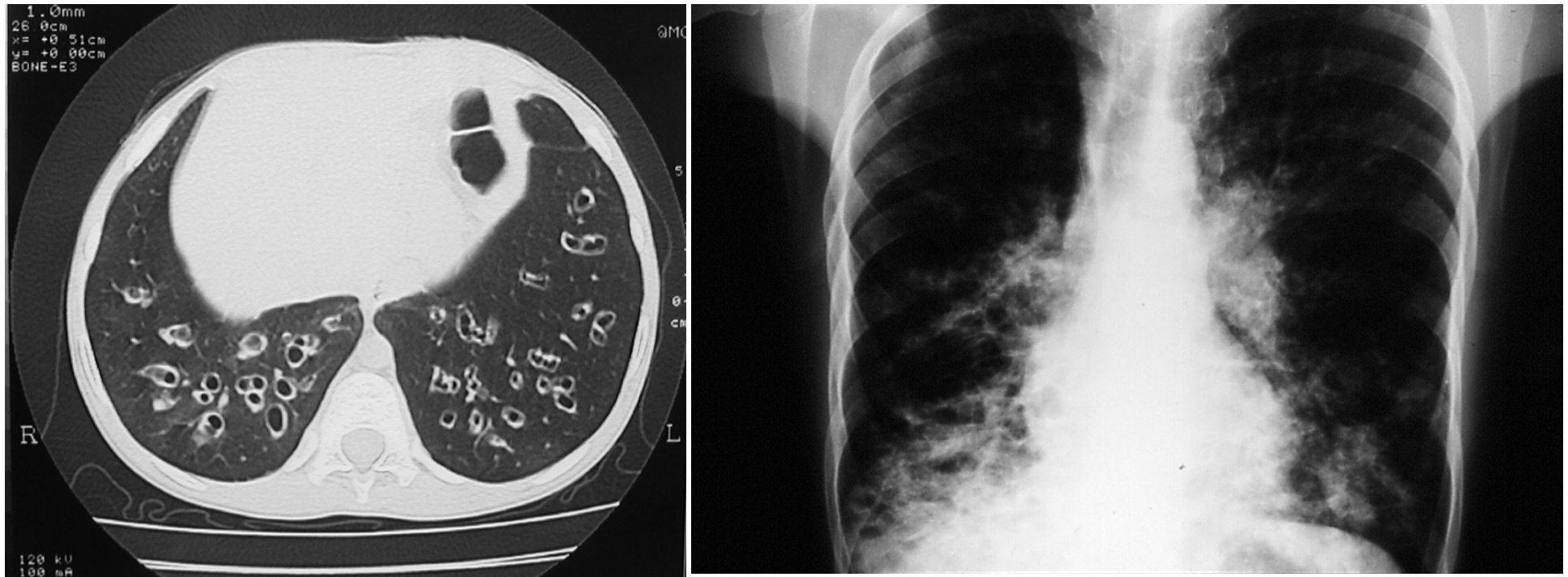
- Appropriate Diagnosis: **Early & Accurate**>Better Prog.
- **Early recognition**
  - Improve early diagnosis (education of doctors, nurses,...).
  - Diagnostic delay is associated with poorer outcome and long-term sequelae
- **Accurate evaluation**
  - Thorough assessment of Immune functions (1st-2nd intention)
  - Thorough assessment of complications (infections, neoplasia...)
  - Avoid redundant exams (lab/radio/...)
  - Genetic diagnosis when available
  - Familial screening-Genetic counseling (Prenatal or Preimplantary diagnosis)
- **Quick referral to appropriate specialists**
- **Multidisciplinary management**
- **Foster adherence & autonomy of patients**
- **Patients' needs (traveling, moving, holidays,...)**



# Lung Complications

## Severe Bronchiectasies (Diagnostic delay)

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- CF-like lung disease in a young adult with a B cell deficiency





- Dose: dependent on clinical status +++ .
- Trough IgG plasma levels: 7+ g/L. Adapted to each patient++
- Assessment of microbial carriage:
  - sputum, stool, blood – IF, PCR, Culture
- Chest/Sinus Xray/CT-Scan
- In some patients, add regular prophylactic antibiotics, Physiotherapy (bronchiectasias), Nebulizations...
- Doctor-Nurse-Patient shared decision making**

# Management of infections

- Please collect biological samples (e.g. sputum, blood and urine cultures) wherever possible and if clinically indicated.
- Always treat aggressively with wide-range anti-infectious agents (I.v.) until documentation
- Steroids in CGD+++ (IS >>> infectious risk+++)
- Granulocyte Transfusions (CGD, LAD, SCN)
- Surgery (diagnosis, therapy – experimented team)
  - Splenectomy >>> infectious risk
- Nebulizations of bronchitis exacerbation (antibiotics)
- Primary/Secondary Drug prophylaxis:
  - cotrimoxazole, acyclovir, antifungal drugs,
  - immunoglobulin replacement therapy,
  - cytokines (G-CSF,  $\gamma$ IFN,... )
  - > Beware of drug toxicities.

# Management of infections

- Other prophylactic approaches:
  - Hygiene measures (personal/familial)
  - Improvement of General status (nutrition,...)
  - Physiotherapy (lungs, joints,...)
  - Adapt Work station/Hobbies (gardening,...)
- Immunizations:
  - Entourage & Patient:
    - Can also lead to a vaccine disease
    - Patients with severe deficiencies should **avoid all live viral and bacterial vaccines.**

# Management of infections

- Other prophylactic approaches
  - Hygiene measures (personal/familial)
  - Improvement of General status (nutrition,...)
  - Physiotherapy (lungs, joints,...)
  - Adapt Work station/Hobbies (gardening,...)
- Immunizations: See recommendations
  - Child & Entourage/Can also lead to a vaccine disease
- Careful clinical and specific lab monitoring (Microbiology, Xray, Chemistry, Hematology...)
- ***Please note patients with aberrant immune systems do not always mount typical inflammatory responses, where concerned treat and contact specialist.***

# **Management of infections**

- **In case of severe sepsis** (severe hyperthermia, bad tolerance, with chills that may be associated or not to hemodynamic disorders), **breathing problems accompanied with fever or not**
  - **Contact immediately the emergency number for an immediate hospitalisation;**
  - **Inform the treating doctor about the PID;**
  - **Start with broad-spectrum IV antibiotic (danger of serious bacterial sepsis) and take symptomatic actions** (i.e. treatment shock, breathing problems...);
  - **Contact the indicated PID specialist doctor**

# In case of surgery

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- An antibiotic prophylaxis may be needed in case of dental or digestive surgery for certain patients
  - ask the specialist doctor;
- There is no contraindication for local or general anaesthesia, unless there is a developed bronchitis with problems in the breathing system;
- Before any action is taken, contact the indicated specialist.

# In case of pain

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- Use the **painkillers as usual** (fracture, abdominal, dental pain, headaches...). There is no contraindication for painkillers.
- For **any other recommendation specific to the PID, contact the indicated specialist doctor.**



# Auto-Immunity/Granuloma

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- Might be a hallmark of disease (ALPS, CGD...) or a complication (WAS, DGS,...)
- Immunosuppressive/modulatory drugs:
  - Steroids, 5-ASA, Azathioprine, aCD20 mAb, aTNF, IVIg, Cyclophosphamide,...
  - (...Splenectomy ☹ )
  - Might increase infectious rates: use lowest doses and shortest courses whenever possible

# Lymphoproliferation/Neoplasia

- AT, Hypogammaglobulinemia (CVID)
- Hemopathies, solid tumors
- Careful pathology examinations +++ & Nosology (WHO 2008)
- Use all available tools (immune stainings, EBV or other Ag, karyotype analysis, molecular biology,...)
- aCD20 mAb, CTL, HSCT, GT
- Use of classical chemotherapy approach
  - increase infectious rate,
  - worsen immune deficiency

# Curative Approaches

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- **Hematopoietic Stem Cell Transplantation** (first HSCT for a PID in 1968):
  - dramatical improvement of survival and long-term results
  - better understanding of mechanisms of diseases
  - better conditioning regimens
  - better HLA typing methods
  - new donor sources such as unrelated donors and cord blood units
  - use of better supportive care (especially, the care of infections in immunocompromized hosts).
- **Gene Therapy**
  - $\gamma$ C-SCID, ADA, CGD, WAS (others in the future)

- **Thymus Transplantation**: complete DGS, FOXP1 def

# Challenges

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- **PID in adults: not only CVID**
  - More adults with ‘pediatric’ PID (Late onset Bruton, CGD, HIES, XLP,...)
  - Delayed diagnosis
  - Minimal clinical manifestations/Symptoms overlooked
  - Social and professional integration
  - Psychological impact/Handicap
- **Transition:** Follow-up of pediatric PID in adulthood
  - Increased life expectancy

# Improving health outcomes

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- Evaluation of outcomes:
  - new/unexpected complications?
  - Long term follow-up to ensure best quality of care and QoL
- Improvement of treatment and care
  - By translating reliable knowledge into changes in practice
  - By increasing awareness
- Registries and outcome measures as indicators of efficacy in improving the care of patients at the population level



# Foster interactions

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- Patients organizations
  - National & Int'l
- Health Authorities:  
reducing inequalities in  
access to care
- Patients/Families &  
Doctors/Nurses  
Meetings
- Information Leaflets
- Diagnosis centers
- Reference centers
- Advocacy
- Training
- Link with HIV specialists



VERS UNE PRISE  
EN CHARGE DES **DÉFICITS**  
**IMMUNITAIRES PRIMITIFS EN AFRIQUE**