

1-2 DECEMBER 2015

WORKSHOP ON *Improving access* TO PLASMA AND PLASMA PRODUCTS IN THE *Southern African* REGION

Meeting clinical needs for Immunodeficient patients in Africa

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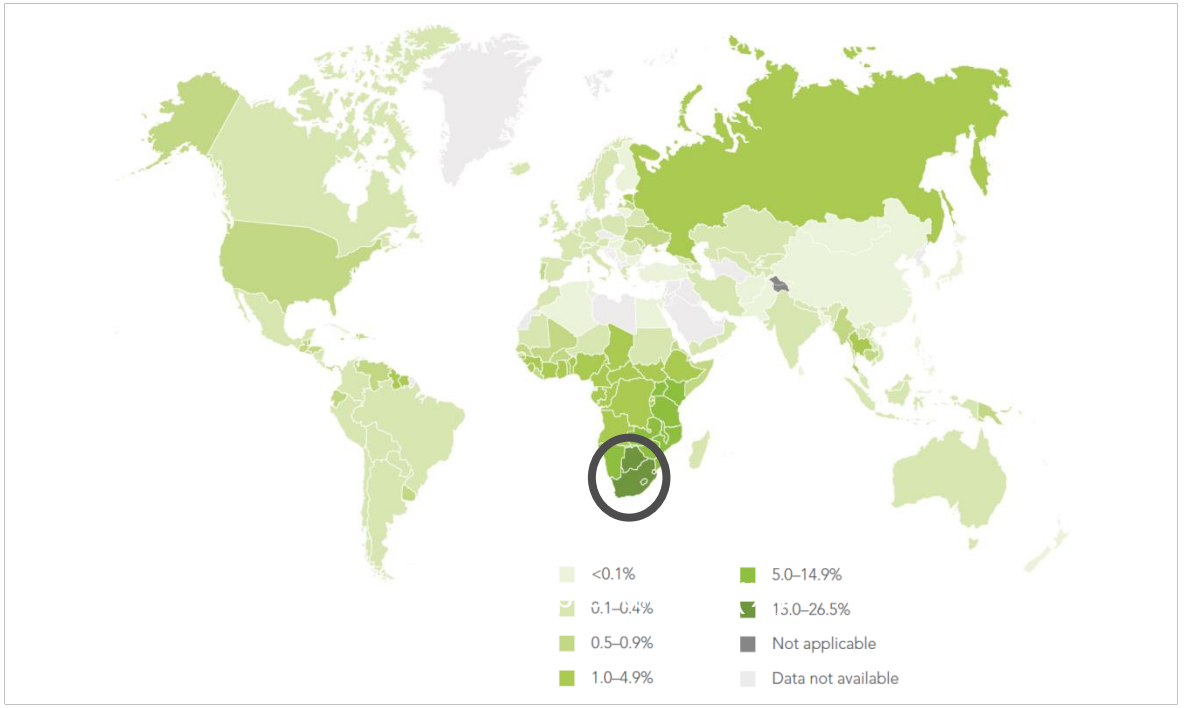
WORLD AIDS DAY

HIV & AIDS – Global view

Key facts globally;

- Only 51% people know their HIV status
- 34 million deaths globally
- 14.9 million people on ARVs (only 40% of those infected)
- 3.2 million children living with HIV
- 650 children (< 15 years)are infected with HIV every day

Globally: 36,9 million people infected with HIV



Sub-Saharan Africa: 25,8 million HIV-infected persons

Source : UN AIDS (2014) http://www.unaids.org/en/regionscountries/countries/

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But - Who and Where are the **Primary/Genetic Immunodeficient Patients (PID)** in Africa ?

Patients suffering from :

- **Severe**
- **Persistent**
- **Unusual**
- **Recurrent** Infections of genetic origin
- **Autoimmune/autoinflammatory** presentations

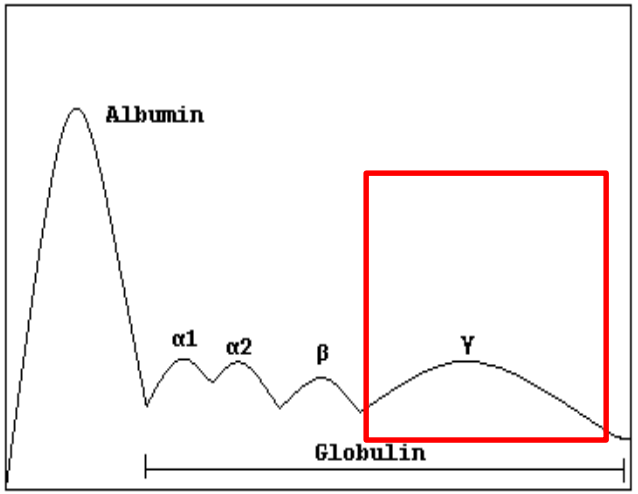
- **120 000 minimum expected** (1/10000)
- Bousfiha et al : estimates in Africa to **>900,000**

Bousfiha AA, Jeddane L, Ailal F, et al. Primary immunodeficiency diseases worldwide: more common than generally thought. J Clin Immunol 2012; doi 10.1007/s10875-012-9751-7.

Early Days of PID

- Bruton, O. C. 1952. Agammaglobulinemia. Pediatrics 9:722-728.
- Description of Immune Deficit and Treatment





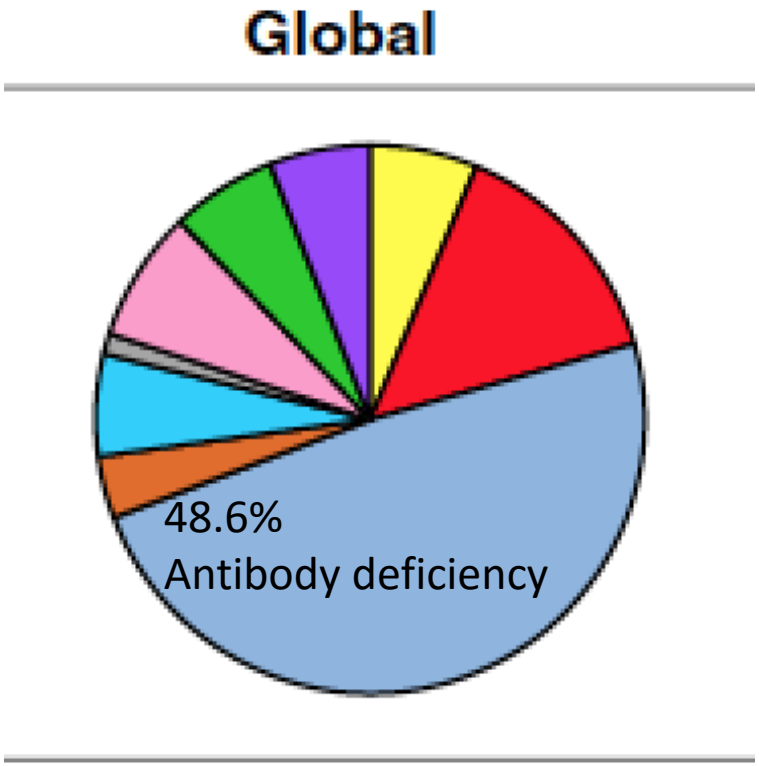
Bruton provided a relatively crude preparation of immunoglobulin via the subcutaneous route. He documented restoration of serum immunoglobulin levels and described a clinical benefit for the patient

IUIS 9 PID Groups (2014)

- 1) Combined ID
- 2) Defined Syndromes with ID
- 3) **Pred Antibody ID 50%**
- 4) Immune Dysregulation ID
- 5) Phagocyte ID
- 6) Innate Immunity ID
- 7) Autoinflammatory disorders ID
- 8) Complement ID
- 9) Phenocopies

Antibody deficiency burden

- Globally account for close to half of all PIDs
- Likely largest group of unidentified PIDs in Africa
- Could be as high as 400 000 patients!
- Secondary antibody deficiency far more common and increasing (Medications)



Modell V et al *Immunol Res* 2014
Bousfiha AA et al J *Clin Immunol* 2012

Profile of African PID Patients



>300 disease entities, >200 identified genes due to major advances of next generation and exome sequencing.

Still considered **Rare Diseases**…..

Vast differences across Africa, determined by :

- **consanguinity** and individual hereditary patterns,
- **prevalent infectious diseases**

Geographical Perspective for PID Care

True Size OF AFRICA





African countries with PID Registries



- Algeria
- Egypt
- Morocco
- Tunisia
- South Africa

More Data : African A Projects – 1 Day PID Workshops



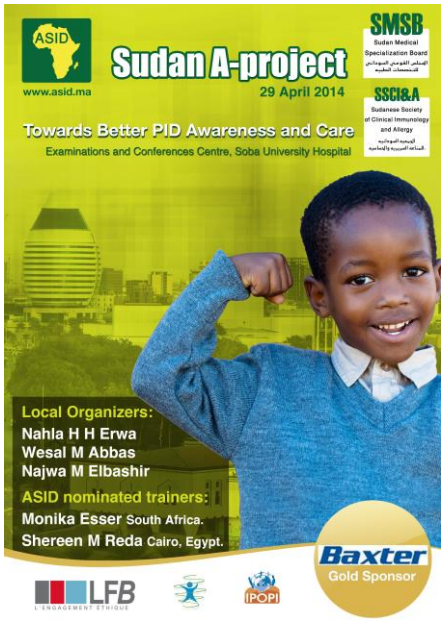
- **Benin**
- Cameroon
- Ethiopia
- **Gabon**
- Mauritania
- (Morocco)
- **Sudan**
- **Senegal**
- Uganda
- **Zambia**

(Data contributions in bold)

ASID and A Projects

The main objectives of the African Society for Immunodeficiencies (ASID)are :

to improve PID awareness and care in Africa.

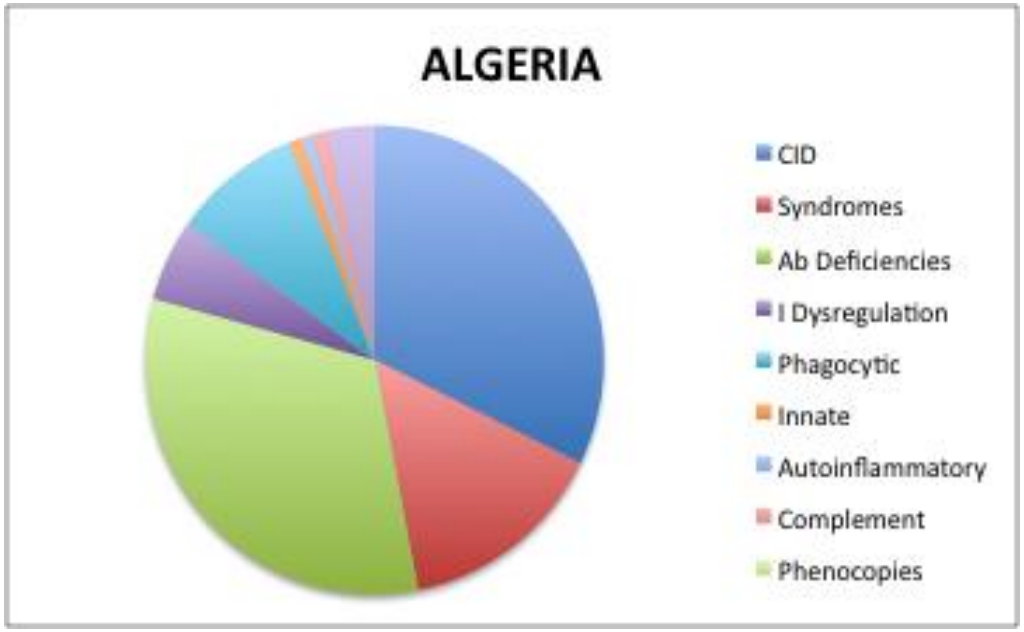




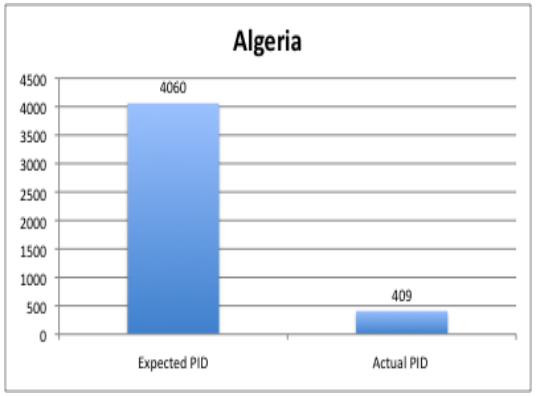
ASID

ALGERIA



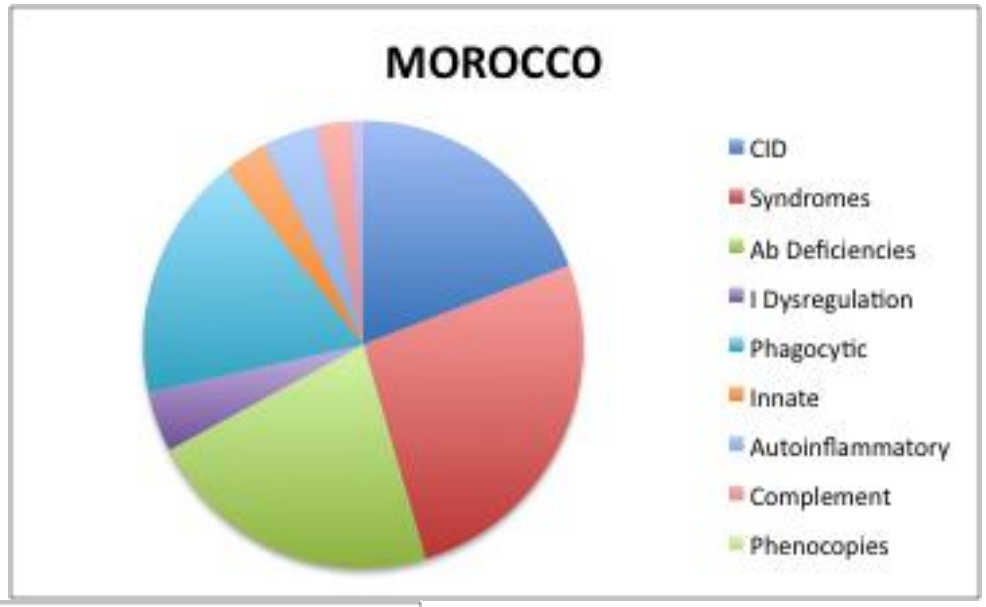


40 million pop

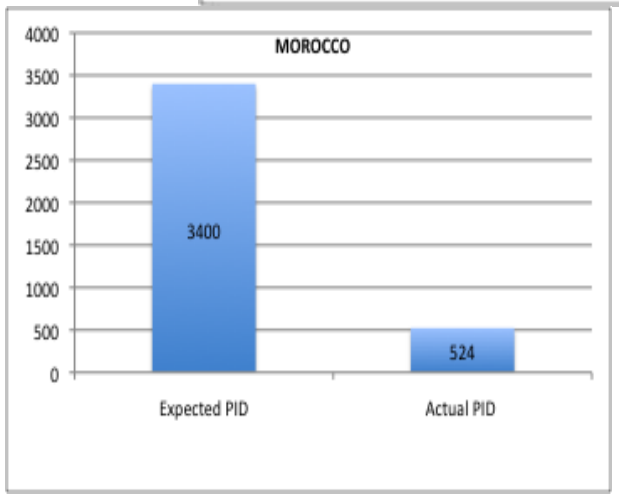


MOROCCO



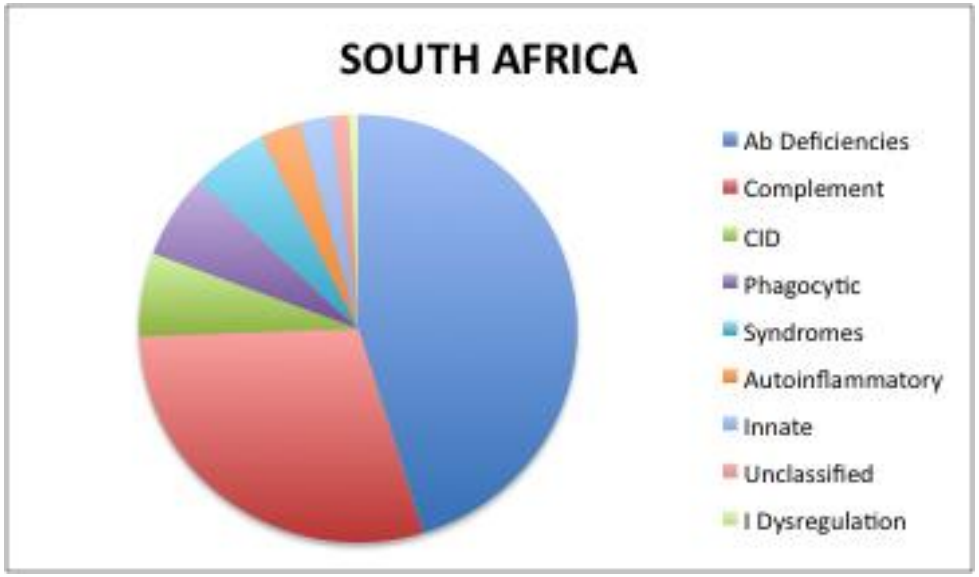


34 million pop

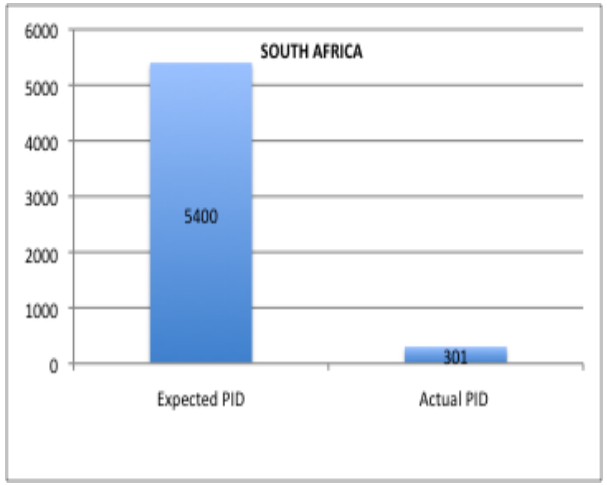


South Africa





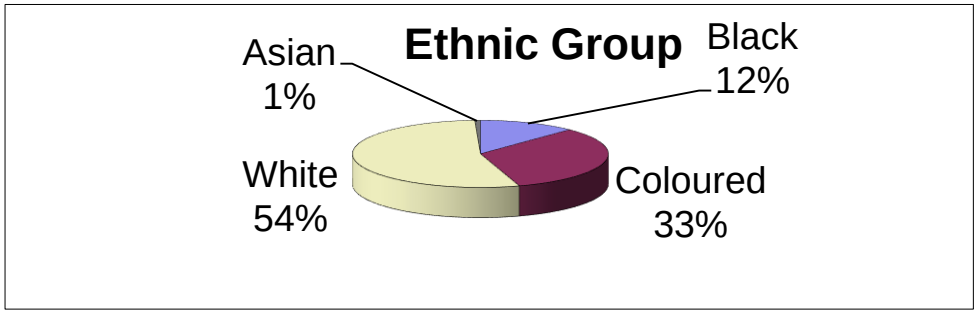
54 million pop



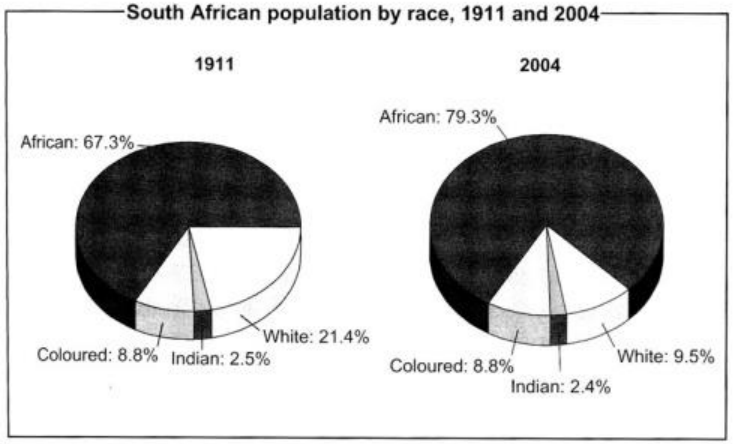
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South African Registry 2015

SA PID Registry
SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY
E-mail: rina@sun.ac.za



Severe underreporting for black population
12% (80% of population)
majority served by state health care

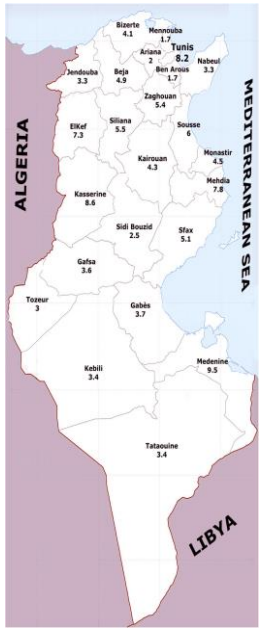


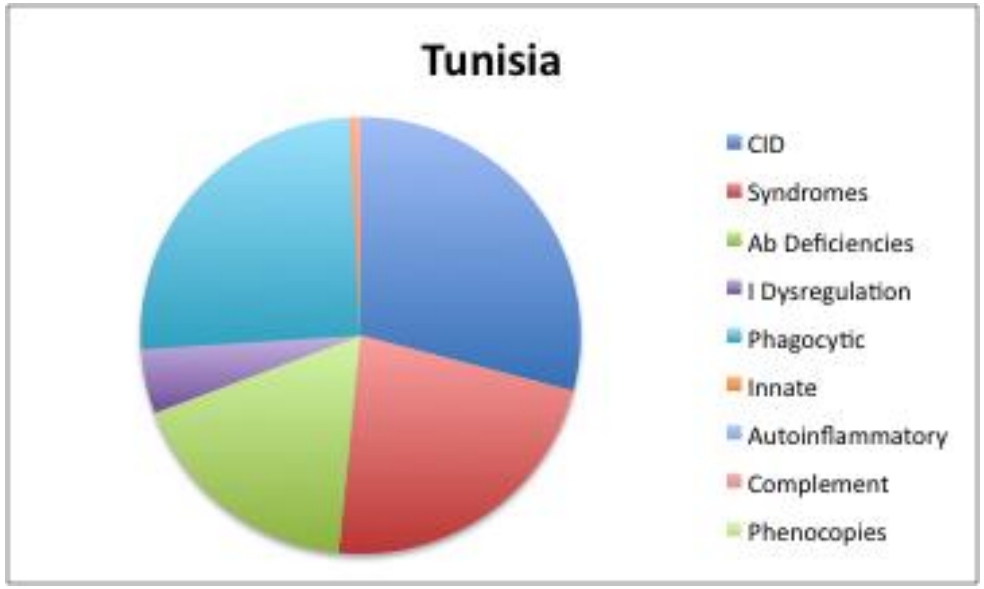
Individually relevant warning signs for PID

- history of PID, with the need for IVI antibiotics to clear infections
- >2 cases of pneumonia in 1 year
- BCG dissemination in an HIV-negative infant
- Staphylococcal liver abscess in childhood.
- Recurrent meningococcal infection

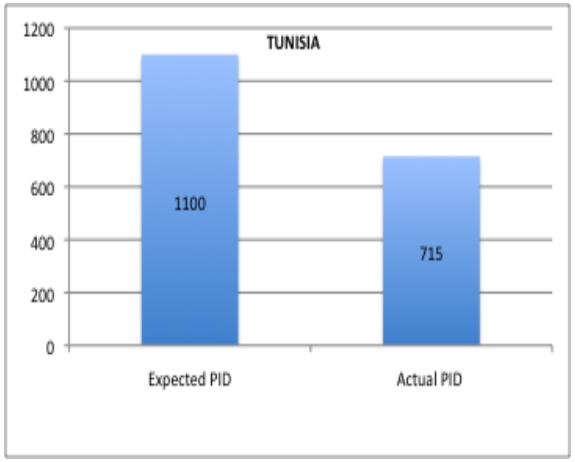


TUNISIA – Best reporting 715/1100



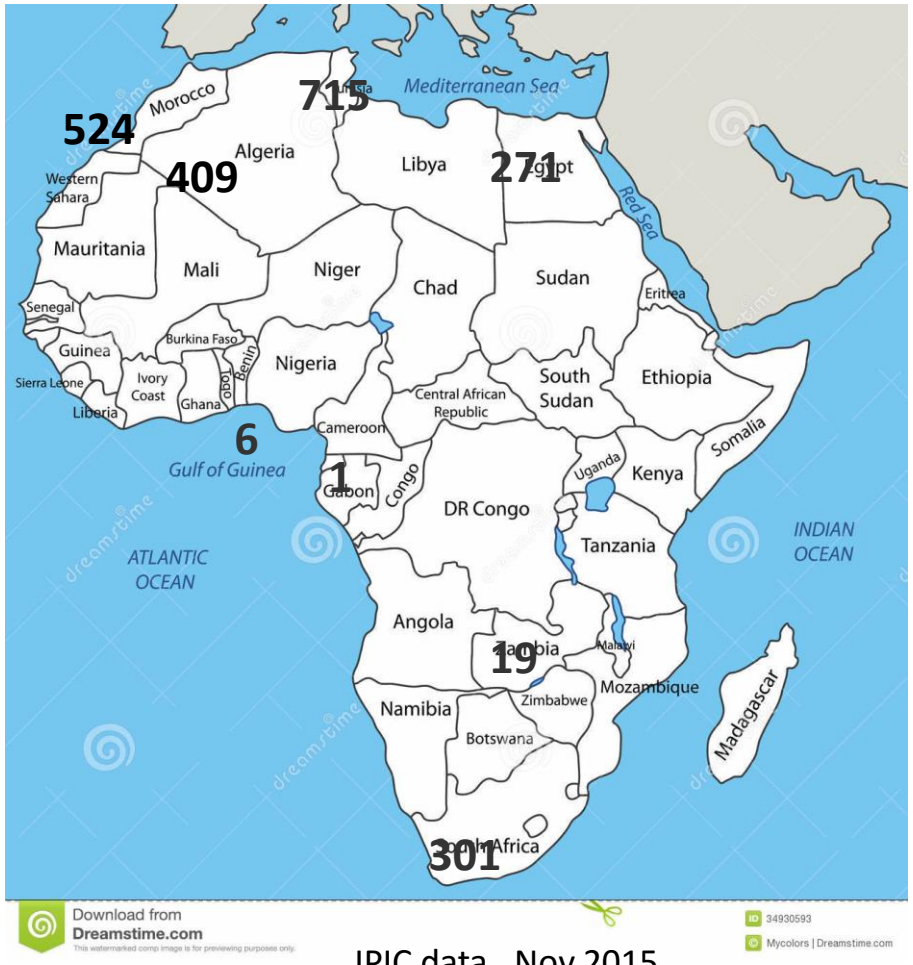


11 million pop



2291 Patients reported – 2% (ASID Data 2015)

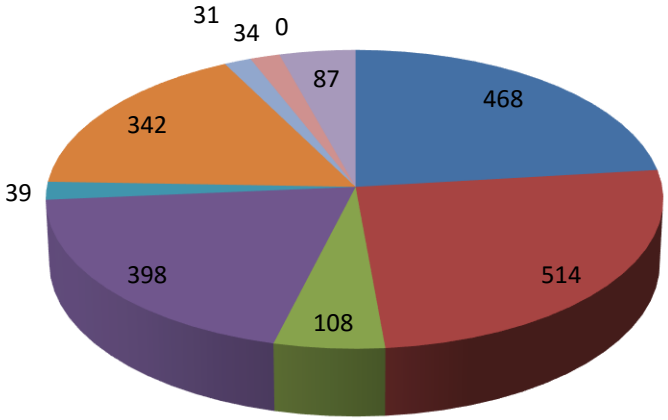
Population : 1.2 Billion



IPIC data , Nov 2015

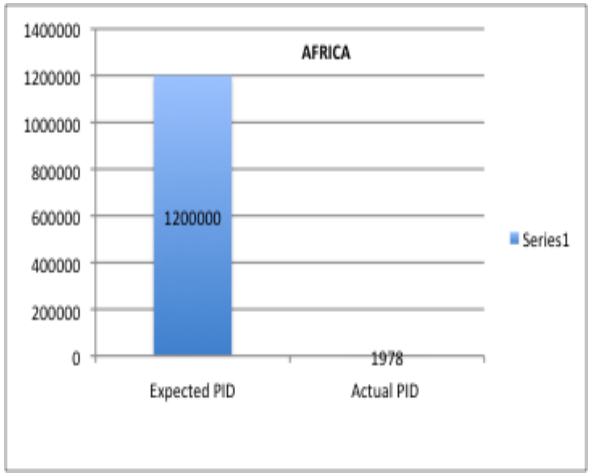
ASID 2015 – 2021 PID cases

AFRICA



- CID
- Ab Deficiencies
- Complement
- Syndromes
- Unclassified
- Phagocytic
- Innate
- Autoinflammatory
- Phenocopies
- I Dysregulation

1.2 billion



Generic Challenges to meet health needs in Africa

GDP per capita in 2014 : South Africa 6086 USD (48% of global)
Malawi **225** USD
Quatar 97,518 USD

42% of people in sub-Saharan Africa, lack access to clean water

31% of rural dwellers in developing countries have access to proper sanitation



how many get to a PID diagnosis ?

African Challenges to meet PID Care

Worldwide challenges :

access to healthcare, newborn screening, targeted treatment including transplantation & gene therapy, long term follow up and adolescent transitioning.

African challenges :

- **political instability**,
- **poverty : GDP $3400 pp to achieve SCID survival**
- **economic growth distribution**
- **inequality of access** to resources
- **Lack of organisational structure for care** and patient access to dedicated specialists and comprehensive treatment
- **Lack of training & research**

Specific key challenges for PID needs in SA

ASID Congress 2013 (IPOPI session)

- Need for **local guidelines for diagnosis and treatment** of primary Immunodeficiencies
- Need for PID to be placed on the **Chronic Disease List (CDL)** to be a defined prescribed Minimum Benefit (PMB) condition
- Need to have immunoglobulin therapy added to the **Essential Drugs list (EDL)** in South Africa
- Need to improve **access to SCIG** – the African solution for PAD treatment
- Public and private healthcare sectors both have challenges - ranging from poor administration, treatment delays, lack of coverage, limited available treatments and poor infrastructures

Physician perspective



Diagnosis & management of acquired immunodeficiency and (PID) major advances achieved in the past decade

Challenges and opportunities for the PID community in Africa significantly influenced by the needs of prevalent conditions such as **Malaria, TB and HIV**

Mis-allocation of resources, lack of accountability, lack of training and the need for greater awareness are main challenges facing the PID community rather than the lack of resources.

Developments achievable through concerted efforts and collaborations organized by the African Society for Immunodeficiencies (ASID) working hand in with other stakeholders

Key priorities and recommendations identified for the African region

the need for **clinical and diagnostic guidelines** in the region

the importance of increasing medical **awareness**

the benefits of **working with other active regional patient and advocacy groups**

the need for **more patients support**

the need for **more data** on prevalence and epidemiology,

the need for **more research** and data on impact of misdiagnosis vs diagnosis for PID patients

the importance of having an **integrated approach** to screening and diagnosis

the need for **awareness campaigns** targeting both primary care and tertiary care levels in hospitals

the importance of **tackling the lack of diagnosis** capacity in many African countries,

the need for **advocacy campaigns** targeting the health authorities for better strengthen stakeholder collaboration in the specific region, share experiences between countries, identify key regional priorities and promote PID patient organizations development in Africa.

coverage of **PID treatment**

the importance of creating **PID networks** for doctors and patients

Ig related issues/concerns in Africa

Similarity for Adult and Paediatric patient:



- PID - Same indications but specific diagnostic problems (eg THI)
- Safety
- Accessibility- huge cost issues in Africa/shortages/rising cost
- Differences in efficacy/IgA content of products
- Treatment should be started at a dose of 400 to 600 mg/kg per 4 weeks for IVIG or 100 to 150 mg/kg per week for SCIG in most patients.



Differences :

- Competing for requirements of adult neurological Ig indications in developing world (and lack of awareness of PID indications)
- Titers against specific pathogens prominent in childhood, including those that more frequently affect patients with PAD (such as Streptococcus pneumonia and Haemophilus influenzae subtype B are presently not regulated).

Known Ig replacement uses in Primary humoral/combined immunodeficiencies

including, but not limited to:

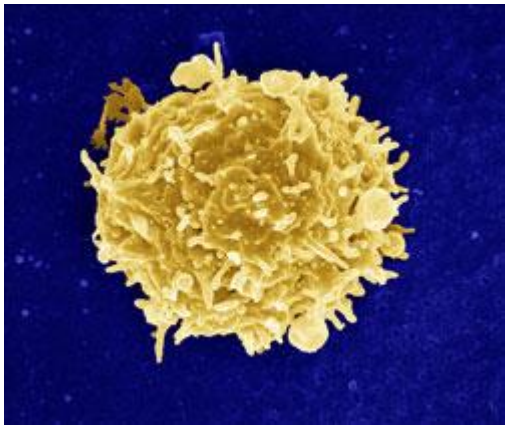
- Congenital agammaglobulinemia (X-linked agammaglobulinemia),
- Hypogammaglobulinemia,
- Common variable immunodeficiency (CVID),
- X-linked immunodeficiency,
- Severe combined immunodeficiency (e.g., X-SCID, jak3, ZAP70, ADA, PNP, RAG defects, Ataxia Telangiectasia, DiGeorge syndrome),
- Wiskott-Aldrich syndrome (IVIG has been shown to increase platelet counts and prevent infections in those patients.)
- Hyper IgM Syndrome

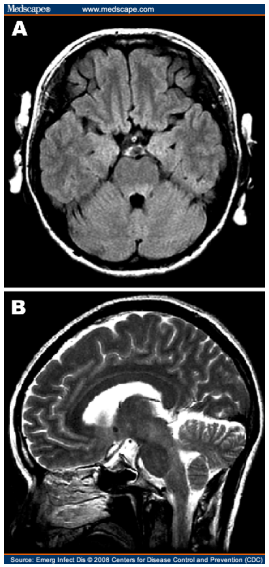
- When **ANY** of the following criteria are met:
- 1) Agammaglobulinemia: a) Total IgG < 200 mg/dL, or b) Infants with BTK gene and/or absence of B lymphocytes); **OR**
- 2) Persistent hypogammaglobulinemia : a) Total IgG < 700 mg/dL, AND b) Recurrent bacterial infections; AND c) Lack of response to protein or polysaccharide antigens (inability to make IgG antibody against EITHER diphtheria and tetanus toxoids, OR pneumococcal polysaccharide vaccine, OR both)

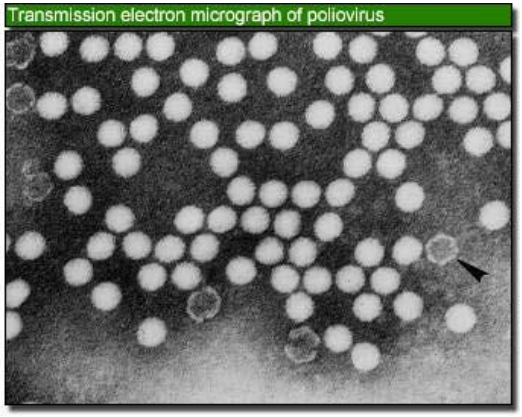
- **NOTE:** Hypogammaglobulinemia associated with cancer must meet criteria above.

Consequences of lack of IG

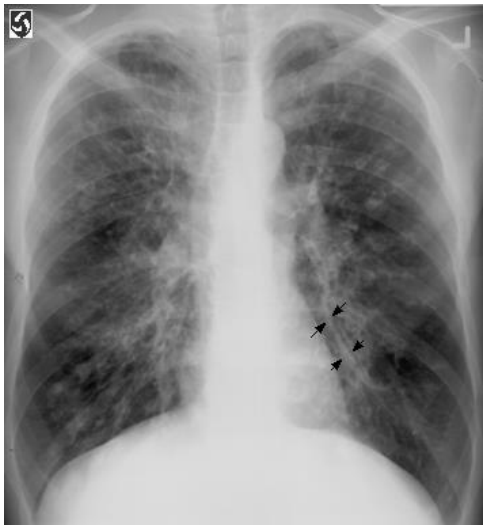
Polio virus complication







Bronchiectasis complication





Patient support group funding of Ig in Africa

- PID Patient support group Hajar's (Morocco) first ten years of existence were focused on providing support to patients and their families

- Hajar expanded on lobbying and advocacy/awareness and fundraising to finance projects on research, training, education and financial support to patients.

- Among the key objectives of the association is the support of plasma donation – family donation , the creation of a BMT centre and universal access to care for all patients in Morocco as currently still **55% of treatments for patients are covered directly by Hajar**

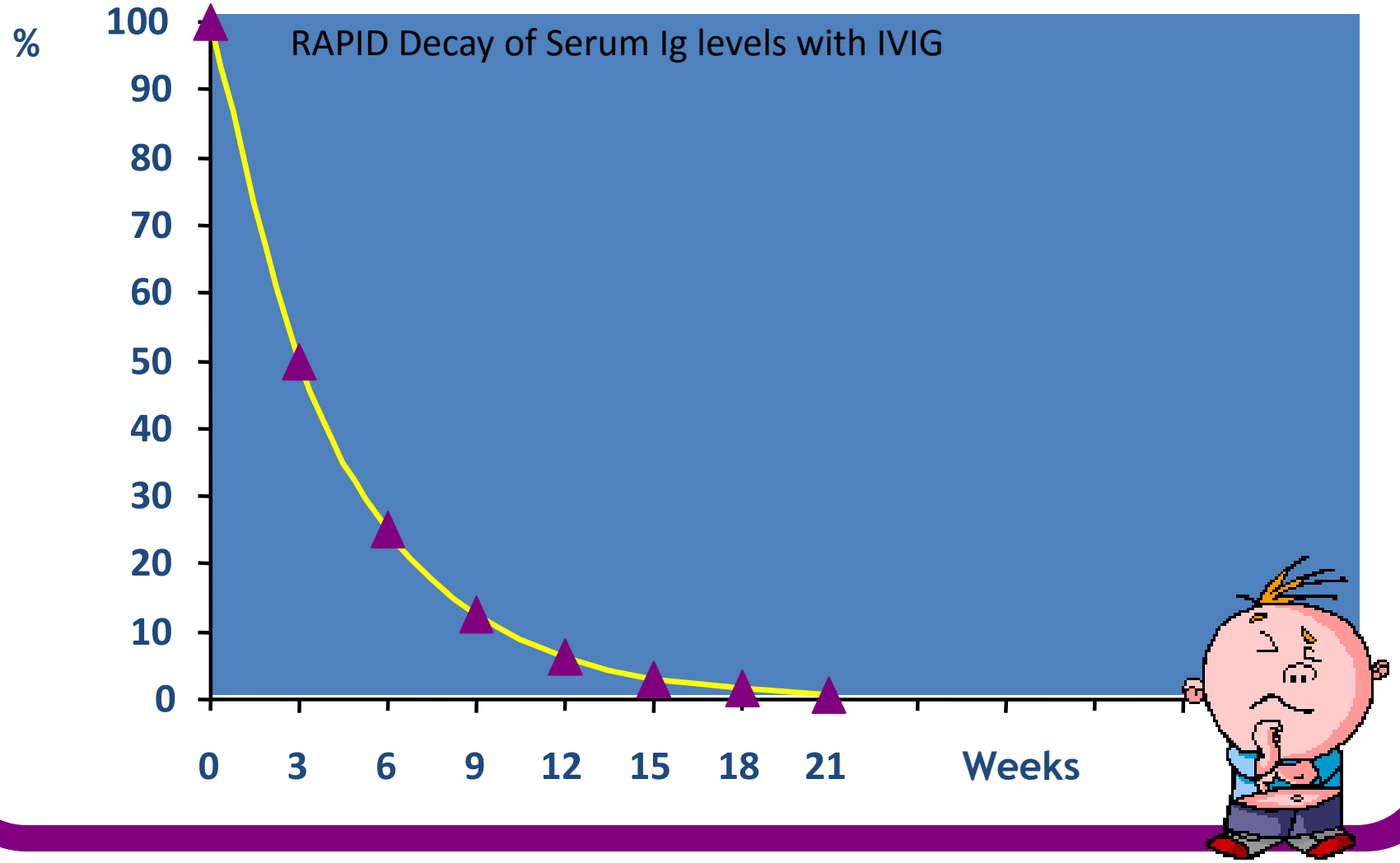
Subcutaneous Immunoglobulin treatment

- SCIG - an alternative method of administration in both children and adults
- Standard practice in Sweden and Norway
- Advantages :

  - Decreased systemic adverse events
  - Increased patient autonomy
  - No requirement for venous access
  - But still many issues in SA – especially *nursing support*

THE ANSWER FOR AFRICA ?

Half - life of IVIG



Health related QOL studies in children on SCIg showed

(European/Brazil & North American trial)

- Improved school & social functioning
- Improved overall health
- Child now as healthy as other children
- Child has better resistance to infections
- Parents have higher expectations for their child's future health
- More personal time for parents
- Fewer interruptions to family life
- Fewer concerns about well being
- Freedom to travel
- (both studies showed 100% of children preferred SCIG)



SCIG

Addressing the Issues to meet clinical needs of African PID patients



Doctors-Nurses -Patients

- **IPOPI** Awareness and Advocacy Patient Toolkits, the Awareness Campaign National Workshop Programme, the Advocacy and Media Training Regional Workshop programme as well as other IPOPI NMO support programmes such as the World Primary Immunodeficiencies Week (WPIW) support programme.
- **Stakeholder collaboration** and other international patient organisations eg **Jeffrey Modell Foundation** and the **PIA a**s a key component to successful awareness and advocacy campaigns
- **Finding opportunities for PID in the resources of epidemics**

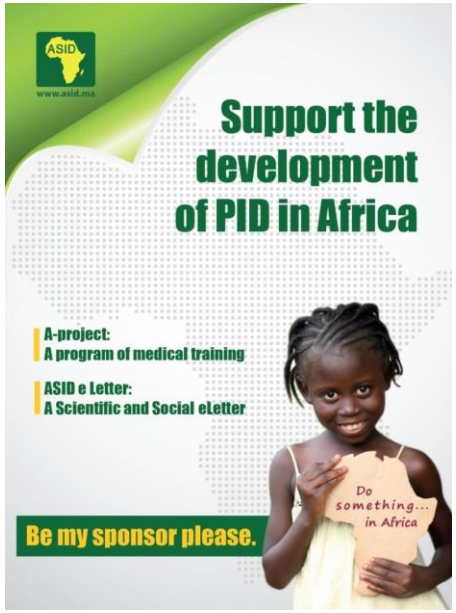
The PID Call for A.F.R.I.C.A

ASID II Congress Hammameth 2012

- **A** ppropriate awareness
- **F** oster Education of Health Professionals
- **R** esearch and data collection
- **I** dentify through early diagnosis
- **C** omprehensive and appropriate treatment

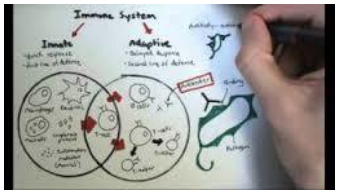
for **A** frica

and **A** Projects





Need for Immunology as a discipline



- Immunology - a rapidly expanding branch of the biomedical sciences fundamentally concerned with all aspects of the immune system.
- relevant in multiple other clinical and pathology disciplines, where the immunological test repertoire has a major impact in patient treatment and care.
- diagnosis of infectious diseases, primary immunodeficiency disease, allergollogy, autoimmune diseases, tissue immunology (transplantation) and serology testing
- in most African countries, Immunology is not a medical speciality :

  establishment of such will ensure an interdisciplinary approach including technical, scientific and clinical experts in immunology

REGISTRIES FOR PID



- FOR OUTLINING DISEASE SPECTRUM
- FOR PLANNING OF SERVICES
- FOR ADVANCING CLINICAL CARE OF INDIVIDUALS
- FOR MONITORING AND EVALUATION
- FOR REQUIRED NUMBERS AND TIMESPAN FOR RESEARCH
- ADDED BENEFIT AND MAIN GOAL :
  - INCREASED AWARENESS
  - IMPROVED CARE

Specific Aims for improving African PID Care

DIAGNOSTIC

- A project – clinical (also biological workshops)
- Syndromic diagnosis – eg Hyper IgE Syndrome
- Simple Lab Screens : pathogens eg BCG dissemination



ACCESS TO CARE

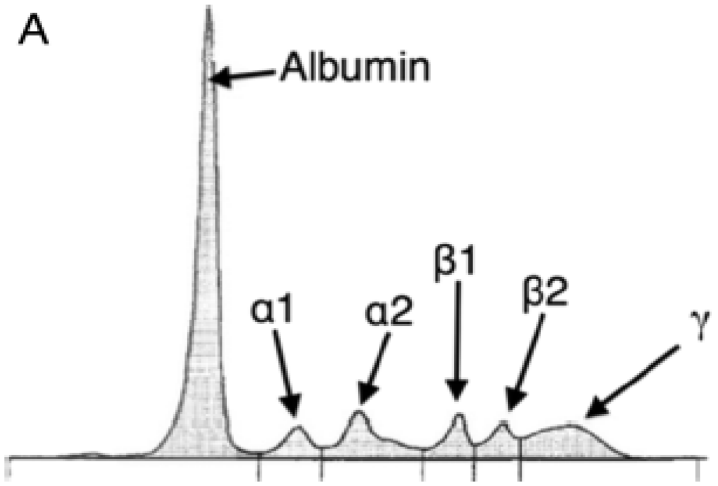
- Rare Diseases Link http://rarediseases.co.za/rare-disease-day-2014/#sthash.0w3lEWsG.dpuf
- Champions for treatment access eg Hajjar (Morocco)
- Plasma Fractionation in Africa – eg NBI, contract fractionation – North Africa
- Patient Organization establishment eg IPOPI, PiNSA, JMF
- VIP Industry collaborations with special recognition to : NBI, CSL Behring, Octapharma,

Simple Laboratory Screen for Ig deficiency
Calculated Globulin (CG)

Also known as the serum globulin gap

Calculated globulin (CG) = total serum protein (TP) – serum albumin (Alb)

(measured in g/l)



- Currently already in use in certain labs for detection of high levels associated with haematological malignancies e.g. multiple myeloma
- Performed routinely as part of LFTs in many large and small laboratories

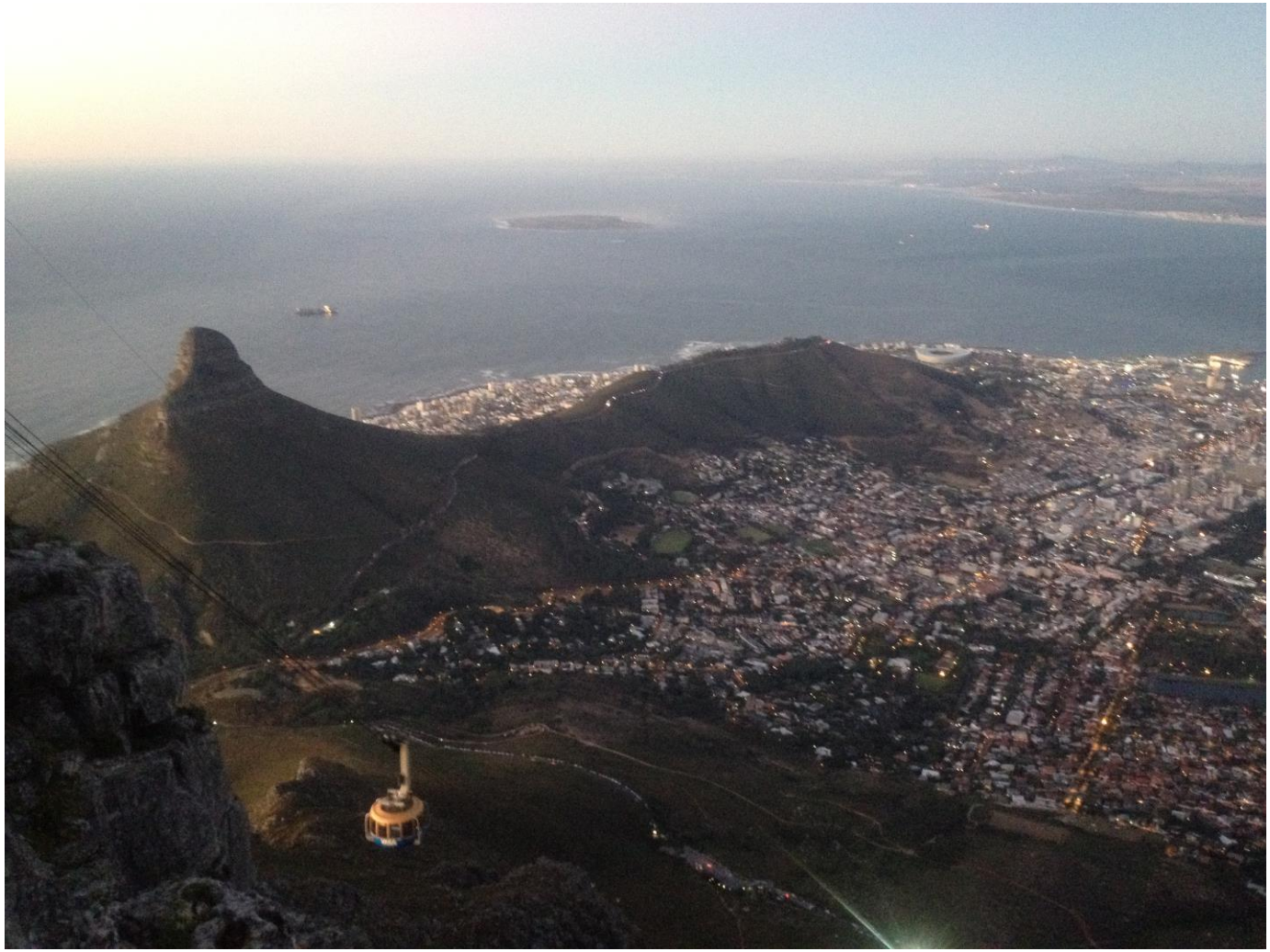
CONCLUSION

- **Different populations in Africa** : North – South, and possibly other :

  Different disease spectrum (early onset CID/later onset Ab deficiency)

  Different presentations, family history very important
- **DIAGNOSES** CAN BE ACHIEVED EVEN WITHOUT ADVANCED DIAGNOSTIC ! (SCID, SYNDROMES)
- **Registry** efforts must be part of A Projects and (biological) technical workshops as a start of finding diagnoses and reporting must become part of good clinical practice .With data - patient advocacy can be improved for access to diagnostic and appropriate treatment.
- **Public Health resources** must be accessed for inclusion in programs/education
- **Collaboration** with other African societies eg ASID, FAIS, Rare Diseases Foundation SA, International Alliance for Patient Organisations (IAPO) and the Patient Health Alliance of Non-Governmental Organisations (PHANGO) and Industry

ASID ESID



THANK YOU