Optimal follow-up and monitoring of patients receiving immunoglobulin replacement

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17 September 2017

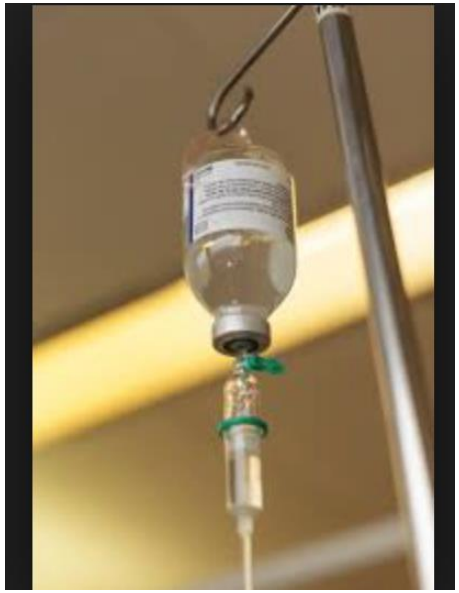
PIDDSA primary immune deficiency deseases south africa

ESID

ASID

Overview

- Goals of IRT`
- Baseline
- Individualized monitoring
- Longterm surveillance
- Adverse reactions
- Transitioning/empowerment
- Issues specific to SA



Introduction

- Replacement immune globulin (Ig) therapy has become the standard of care in patients with primary and secondary antibody defects.
- Benefit of Ig replacement documented
- Increasing number of patients on this therapy, and **diversity of physicians** in **various specialities** who care for them.
- Requires practical guidelines for the use of Ig

Patients with PIDs should be managed in regional specialist PID centers

(Primary Immune Deficiencies - Principles of Care. H Chapel)

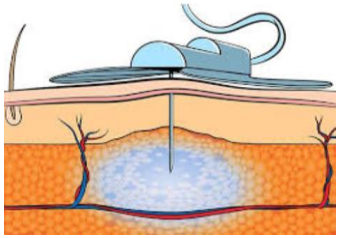
- To enable equitable geographical access to medical and nursing expertise in these diseases.

- Formal links should exist between these regional immunology centers, with recognized referral pathways for treatments.

- National centers in different countries will vary depending on geography, available resources and expertise but all should reach internationally agreed standards of care, as in other rare diseases .
- Registries an essential part of patient care

GOALS of IRT

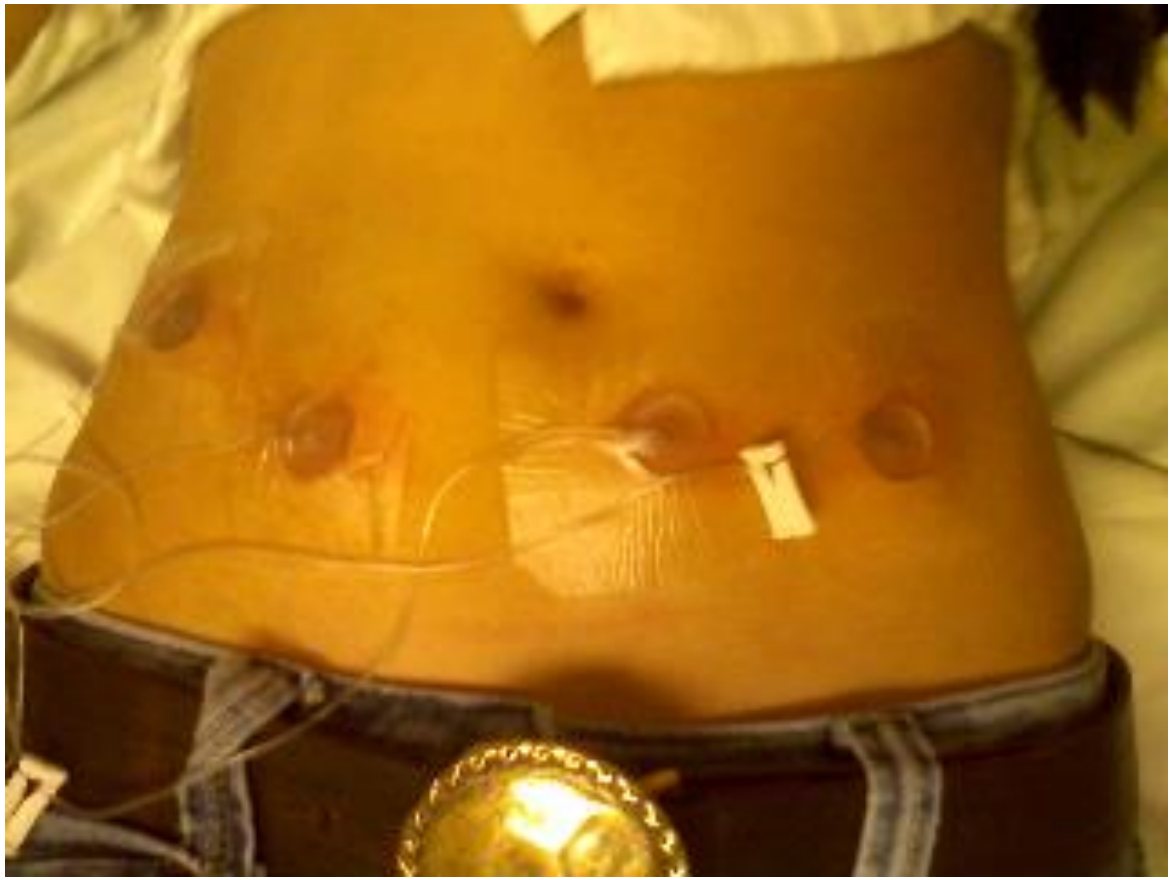
- The immediate goal for patients with PIDD :
  1) treatment of current infections
  2) prevention of future infections



- Tailor therapy of IVIG and SCIG products, both considered safe and effective
  But each method distinguished by
  characteristic pharmacokinetic and adverse reaction profiles

- Working through the early stages of treatment :
  establishing continued follow-up
  defining patient expectations

Subcutaneous Infusion



Expections : Ig replacement is not a “Cure for All”

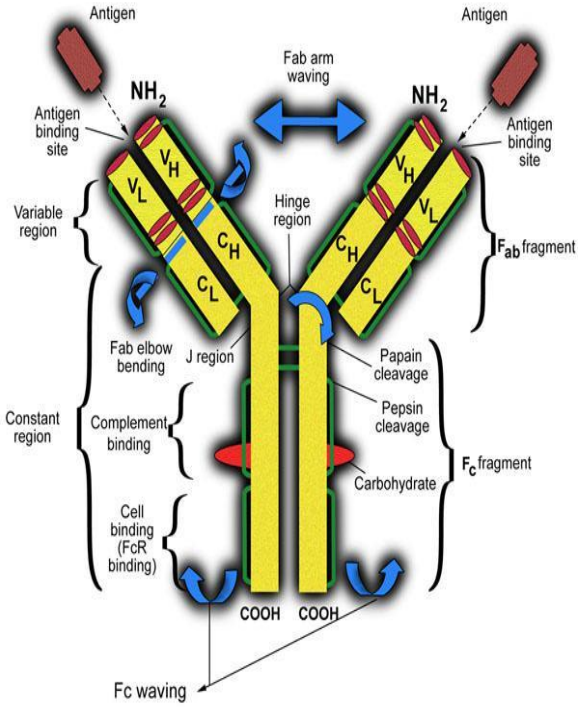
Most primary immune defects are accompanied by loss of immunoglobulin (Ig) or antibody defects.

Hence :

Bacterial infections are much less common in Ig-treated subjects.

However IgA related infections remain

And continued evidence of **inflammatory complications and autoimmunity, viral infections**



Where (if) there is a choice….

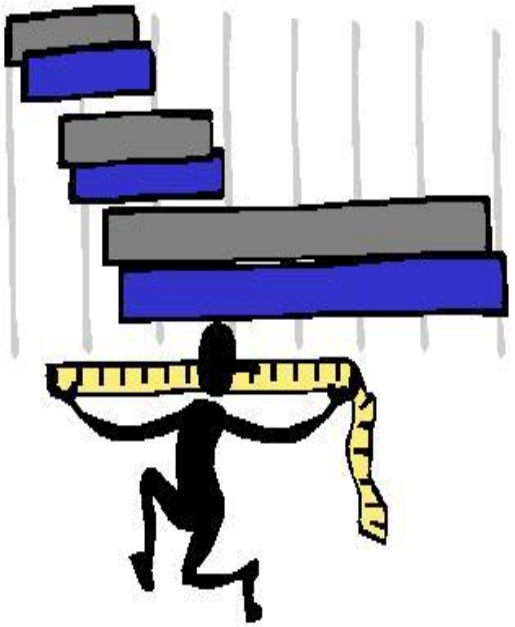
- Most patients will tolerate the first product. However, 10-15% of patients “have to” change product due to side effects.

- This, together with potential supply tensions, ideally calls for a wide range of products being made available to patients, to ensure that they can have access to the most adequate Ig.

- Availability of broad range of products optimises treatment for PID patients and reduces hidden costs. In addition, a wider choice means a greater quality of life for patients

Baseline - before monitoring/assessing Rx response

- Thorough clinical assessment review indications
- Growth assessment
- Infection patterns and frequency
- Comorbidities
- Functional lab : Igs , natural antibodies ,vaccine responses
- Enrol onto registry



Individualized Monitoring

- Logbook/passport
- Dosage and lot number of product
- Epinephrine, emergency meds and resusc trolley nearby –(anaphylaxis extremely rare)
- All side effects during infusion recorded
- Full follow up evaluation : -
  - 3-4 monthly during first year of IRT and
  - 6-12 monthly subsequently (more in Children)
- Growth and development

- Treatment review

  1) for efficacy – trough/steady state Se IgG
  2) for tolerability
  3) for safety – FBC & diff, ALT ,urine (renal function)

- Change of product : limited product or poor tolerability

- **Saved serum samples** – retrospective review of viral infection aquisition
- (Infections during IRT – rely on PCR not Ab measurement)

Ig level Monitoring

- IVIG administered every 3 to 4 weeks Ig - high peak then decrease to a trough before the next infusion.
- Trough periods much less pronounced with weekly or biweekly administration of SCIG more uniform, steady-state IgG level. Trough SeIgG level corresponds directly proportional to the Ig dose
- Total IgG sufficient, not subclasses !

- **Monitoring clinical health is more important.**

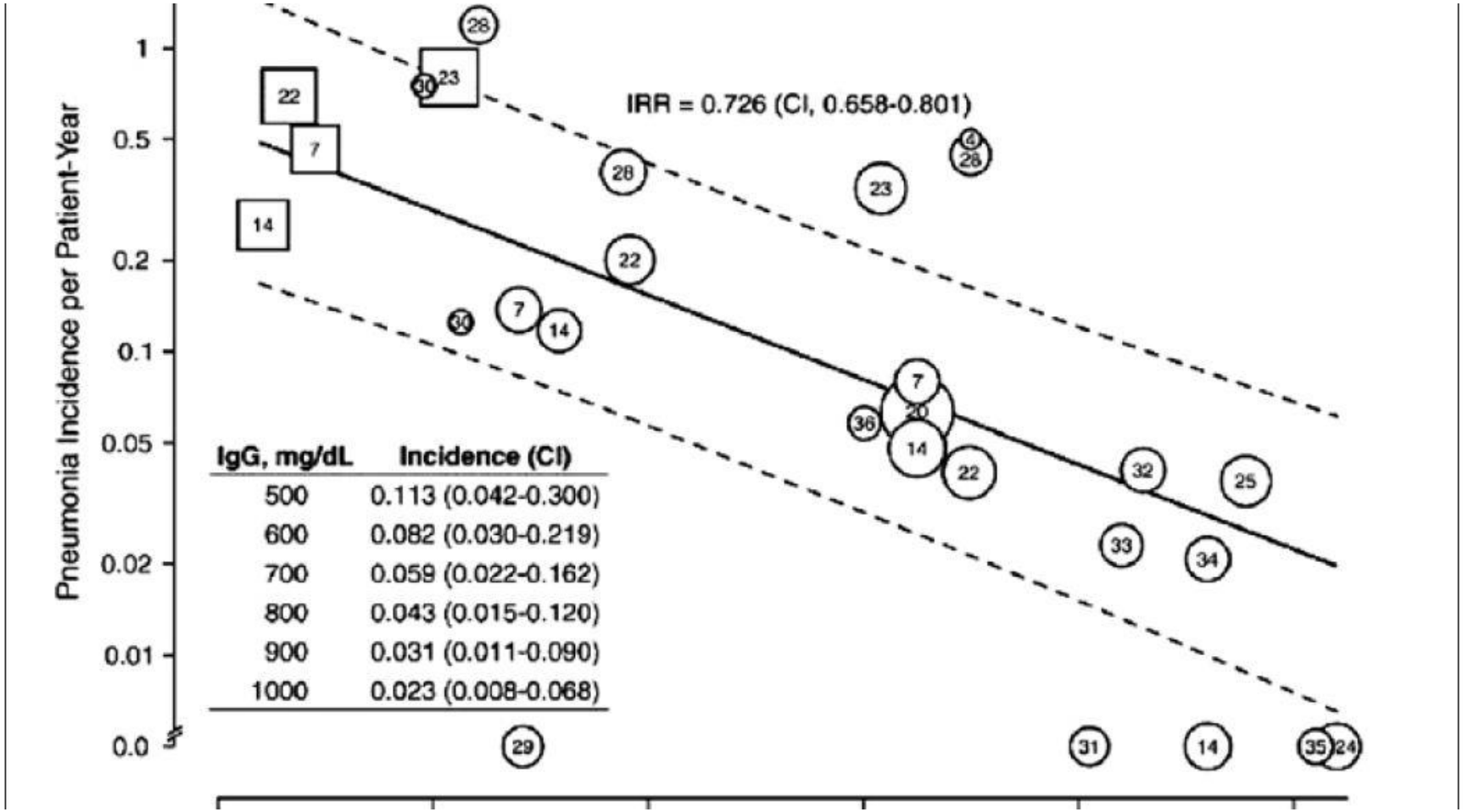
Bioavailability-Equilibrium-1/2 life

“Polyvalent human normal immunoglobulin is **immediately and completely bioavailable in the patient's circulation** after intravenous administration.

It is distributed relatively rapidly between plasma and extravascular fluid, and after approximately **3 - 5 days equilibrium is reached between the intra- and extravascular** compartments.

Polyvalent human normal immunoglobulin has **a half-life of about 19 - 27 days in normal individuals. This half-life may vary from patient to patient** and is also dependent on the patient's diagnosis”

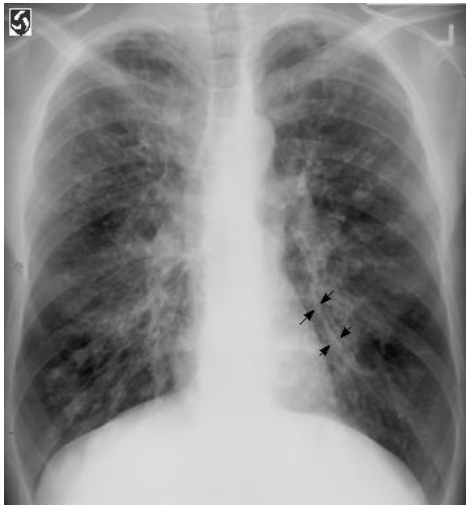
Ideal Trough ?
Trough IgG(mg/dL) and Pneumonia
(Orange JS et al)



Monitoring patients over time

- Minimum : 6–12/12 physical examination, blood counts and chemistry screening tests and IgG trough levels.

- Other monitoring : spirometry, with lung disease : monoxide diffusion capacity and chest computed tomography scans.



- Prevalence of bronchiectasis in CVID and XLA increases with age

PRIMARY IMMUNODEFICIENCY PATIENT ANNUAL RISK ASSESSMENT

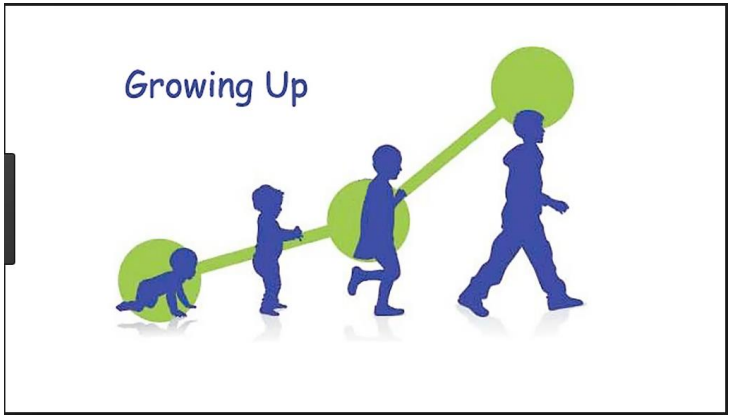
King's College Hospital NHS
NHS Foundation Trust

Name:
Date of birth:
Hospital number:
Assessed by:
Diagnosis:
Current evidence for diagnosis in this patient:
Current treatment:
Potential benefits of treatment:
Potential risks of treatment:
What type of evidence supports the use of the treatment?
What peer review has been used to assess the treatment?
Are changes to diagnosis or treatment indicated?
Have yearly investigations been done?
Eg: serum save, Hepatitis serology, Lymphocyte subsets.
Lung function test

The risk assessment had been discussed with the patient: Yes /No
Signed:
Date:

Special attention/monitoring of Ig doses

- growing children
- in case of weight loss or gain
- pregnancy and
- for subjects in whom more rapid consumption of Ig is likely, including febrile patients or those with gastrointestinal or lung disease



Still having infections..

- SeIg steady state measurement : 3/12
- Reasons for declining efficacy :

  1) emerging new comorbidities

  2) persistent infection

  3) IgG loss – gut/kidney

  4) poor compliance

IVIG Adverse reactions

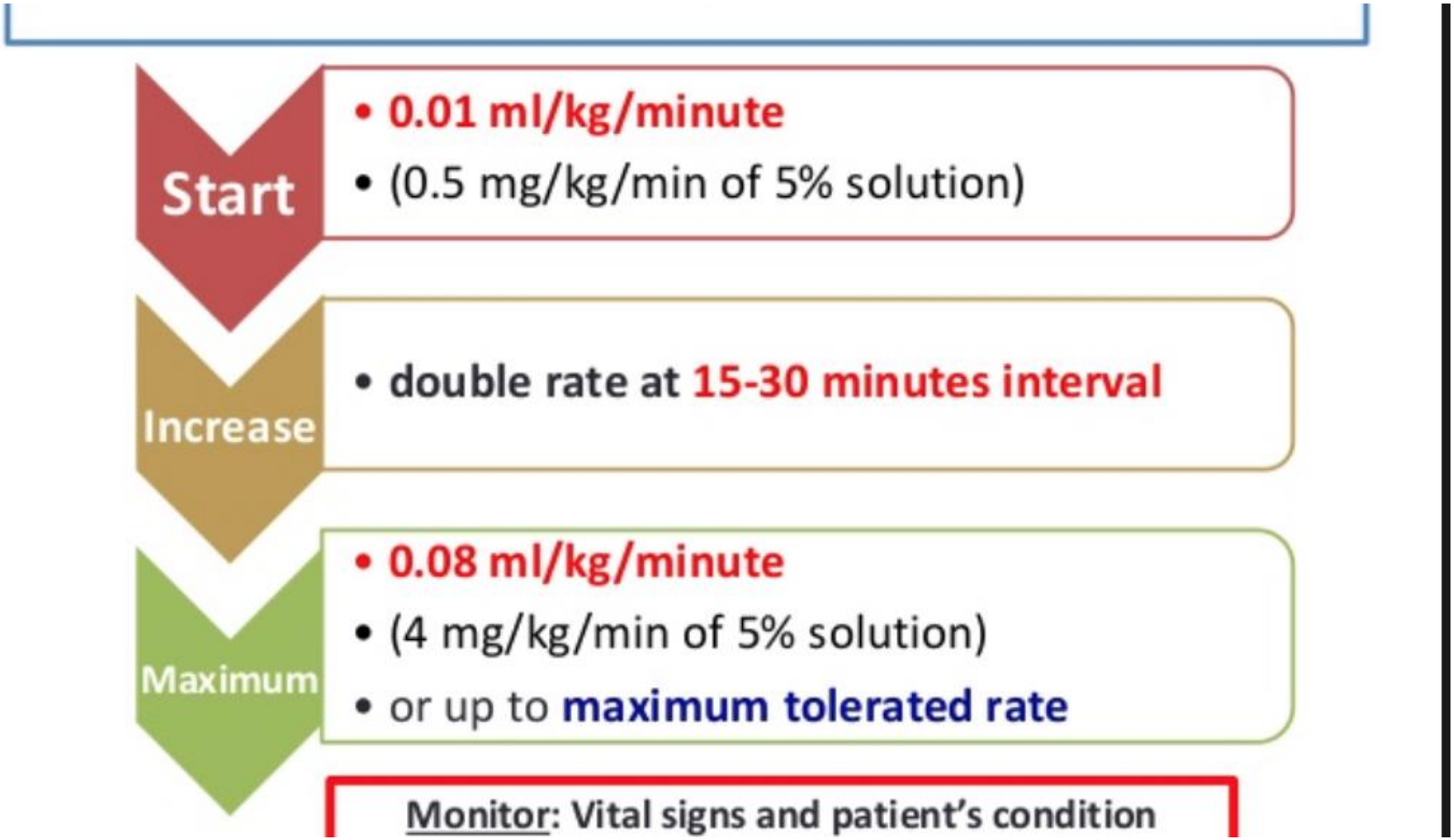
- Around 30% - systemic AEs during or within 72 hours of Ig infusion
- Mostly benign

- Nearly all result of components in the Ig product, rapid infusion rate, patient risk factors or combinations.

- Mild adverse reactions : headache, fever, muscle ache , usually mitigated by adjusting the rate of infusion, insuring adequate hydration, and/or administering acetaminophen or corticosteroid premedication.

Recommended IVIG Infusion rate

Berger M. Immunol Allergy Clin N Am 2008;28:413-437



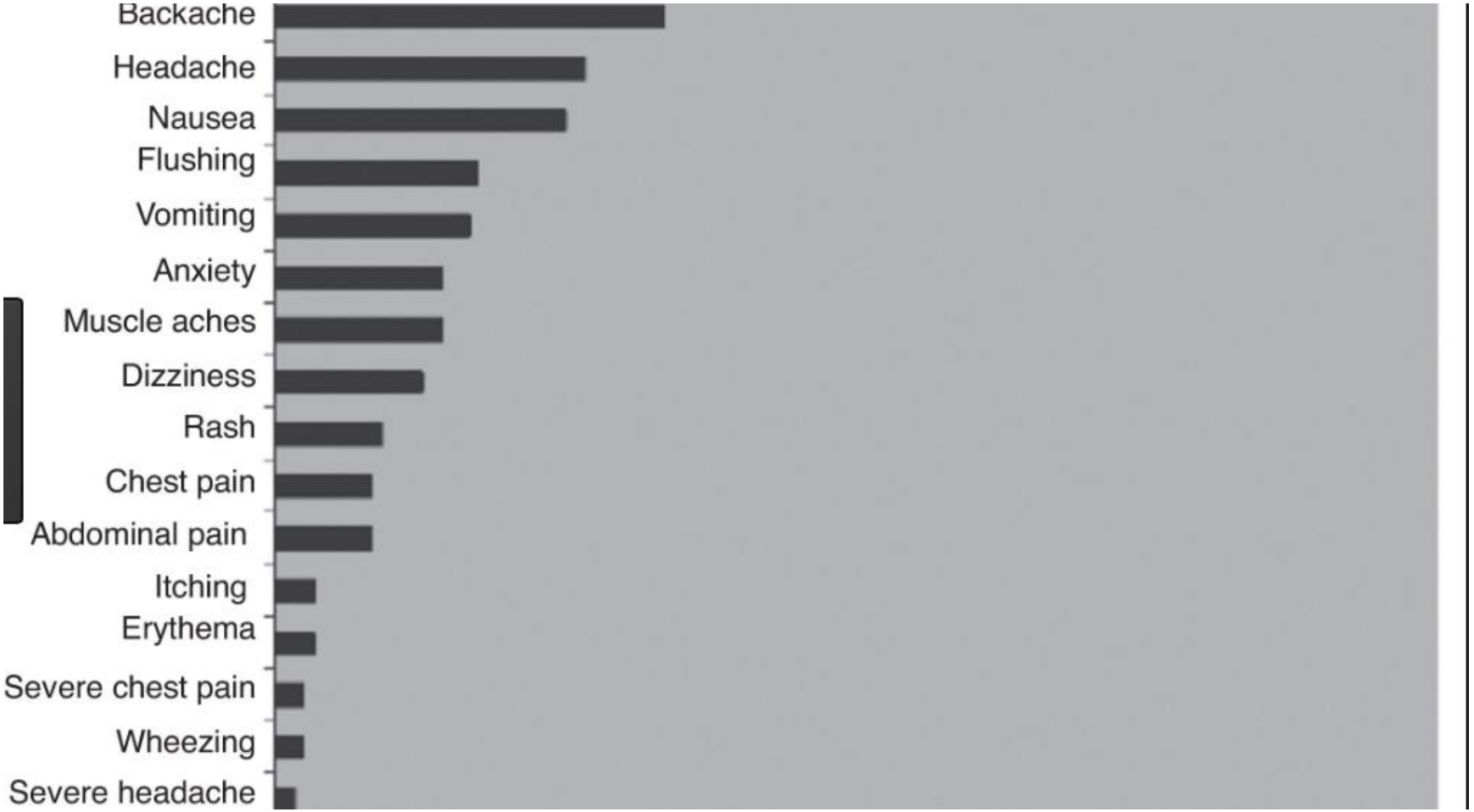
- Adverse reactions typically diminish in intensity with repeated administrations, particularly with SCIG.

- Rare adverse events : acute kidney failure, stroke, thrombotic events, anaphylactic reactions, hemolysis, and aseptic meningitis.

- Patients with risk factors predisposing them to these complications should be monitored closely during and after treatment.

- SCIG may be considered for patients who have systemic adverse reactions with IVIG, as adverse reactions following SCIG therapy are mostly confined to mild, transient, local infusion site reactions.

Adverse Reactions



Transitioning

- The nightmare for paediatricians !

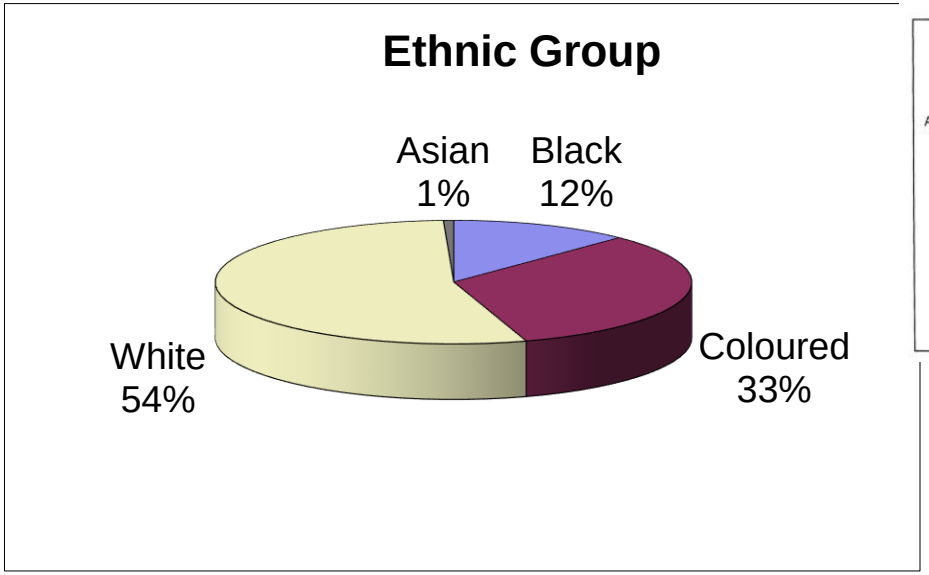
Transition from adolescence to adulthood is characterized by changes of many kinds: physical, social, psychological, educational, and domestic **AND A CHRONIC DISEASE**

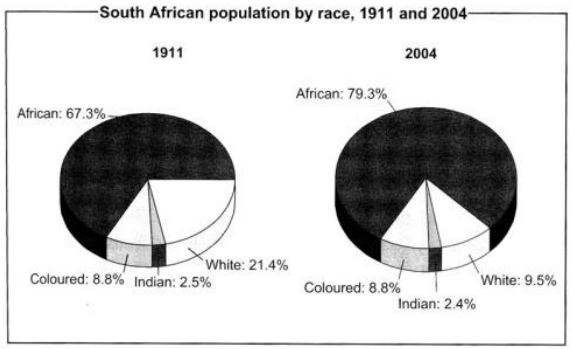
- Need to identify “adult” service/colleague.
- Transitioning PLAN
- Coach and empower the parent/patient
- Ensure connection with patient support

South Africa
The role of the Primary Care Practitioner in “long distance relationships”

- Successful treatment depends on effective “care team” and the continued collaboration of that team.
- Patients will continue to experience the same medical issues and challenges as those without PIDD.
- PCP addresses the majority of the patient’s medical needs and serves as nexus of the patient’s care.
- Communication with all of the specialists involved in the care of an individual with PIDD is key to successful patient outcomes.
- VIP access to local or international society support eg PiNSA, IPOPI,PIA

Bridging the GAP: Diagnosis and Access to Treatment





SA PID Registry
SOUTH AFRICAN PRIMARY IMMUNODEFICIENCY REGISTRY

The Future

Choice of Products

Quality of life assessments

Reduce Burden of Disease and Treatment

Thank you

References

- Key aspects for successful immunoglobulin therapy of primary immunodeficiencies. C Cunningham-Rundles. Clinical and Experimental Immunology. 2011
- Primary Immune Deficiencies-Principles of Care. H Chapel et al . Frontiers in Immunology. 2014