Approach to a child with recurrent infections

Dave le Roux

9 March 2012
Jeffrey Modell Foundation

- http://www.info4pi.org
Welcome to INFO4PI, the official webpage of the Jeffrey Modell Foundation and your online resource center for Primary Immunodeficiencies (PI).

INFO4PI is designed for patients and their families, physicians, researchers, government officials, pharmaceutical companies, industry, and the general public to be able to quickly and seamlessly access information on Primary Immunodeficiency diseases and to realize earliest precise diagnoses, appropriate treatments and sometimes cures of the more than 150 different PI diseases affecting more than 10,000,000 children and adults worldwide.

10 Warning Signs

If You Have 2 or More of These Warnings Signs in 1 Year, You May Have a PI

Find an Expert

Find an Expert in Our Worldwide Referral Network
Search by Physician, State or Country
Find an Expert Immunologist

South Africa

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Recurrent infections Le Roux March 2012
Primary immune deficiencies: myths

• PID’s are very very rare
  – Selective IgA 1:333
• PID’s are most likely diagnosed in early infancy
  – Most in adolescents / adults
• All children with recurrent infections should be screened for a PID
• PID’s are largely untreatable
Primary immune deficiencies

• 4 typical presentations:
  – Infections
  – Failure to thrive
  – Auto-immunity
  – Secondary aspect of another well-defined syndrome
Infections

• Increased frequency
• Increased severity
• Opportunistic / low virulence pathogens
• Multiple sites
Infections: increased frequency

• What is abnormal frequency of infections?
• What is *normal* frequency of infections?
Frequency and severity of infections in day care: Three-year follow-up

Ellen R. Wald, MD, Nancy Guerra, PNP, and Carol Byers, PNP

From the Department of Pediatrics, University of Pittsburgh School of Medicine and Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania.

This study was undertaken to compare prospectively the frequency, nature, and severity of infections in children participating in three types of child care arrangements: home care, group care (two to six children), and day care (seven or more children). Children were enrolled at birth and observed for at least 36 months. The families were telephoned every 2 weeks to record on a standardized form the type and severity of illness during the previous interval. Children remaining in their original child care group for 1, 2, or 3 years were compared with regard to the frequency and severity of illness. Each child care group had the highest number of infections in year 2. Children in day care had more respiratory infections during each year than children in home care, but the magnitude of the differences decreased in year 3. When the child care groups were compared for the proportion of children with more than six illnesses per year or more than 60 days of respiratory illness per year, significant differences observed in years 1 and 2 for day care children compared with home care children were no longer significant in year 3. We conclude that there is a trend toward stabilized or decreased rates of infection, duration of illness, and risk of hospitalization for children from the second through the third year for 3 years. (J Pediatr 1991;118:509-14)
• Frequency and severity of infections in day care
• 244 term infants born in a single maternity unit in Pennsylvania in 1985/1986
• Mostly white, upper middle class, mostly small families (2/3 families had no other children)
• Followed for 3 years, daily health calendar, 2 weekly phone call by study nurse
• Home care – children from a single family, in a home
• Group care – group of 2-6 children, at least 1 non-family member, 20 hours/week, in a home
• Day care – at least 7 children, 20 hours/week, non-residential
• Year 1:
  Home care: 4.2 infections/year
  Group care: 6.5
  Day care: 7.0
• All groups: most frequent infections in year 2, slightly fewer in year 3

_Wald J Ped 1991_  
Recurrent infections Le Roux March 2012
• Percent of children having at least 6 infections in year 2:
  Home care: 50%
  Group care: 82%
  Day care: 75%

_Wald J Ped 1991_
• How does this apply outside of Allegheny County in 1985?

• In South Africa 2012:
  – Larger families, more biomass exposure, cigarette smoke, air pollution
  – Probably more infections in our context!
What is normal?

• E Richard Stiehme:
  • Average child: 4-8 RTI / year
    – Can be 10-12 (siblings, smokers, day care)
  • Mean duration symptoms: viral URTI 8 days
    – Can be >14 days
  • Normal child can be symptomatic for 24 weeks

• “it is difficult to assign a precise frequency of infections that defines increased susceptibility...”

• “rather than defining an arbitrary number...that is too many, the nature and pattern of those infections provide a more reliable guide to identify the child who deserves further evaluation”

(Lederman in Leung)
Infections: increased frequency

• What is abnormal frequency of infections?
  – More than 1 episode of pneumonia per decade
  – Increasing frequency of otitis media in children older than 2 years
  – Persistent otitis media despite tympanostomy tubes (grommets)
  – Persistent sinusitis despite medical / surgical treatment

  (Lederman in Leung)
Causes of recurrent infections

• “Normal” – no cause found: 50%
• Atopy / allergy – 30%
• Chronic disease – 10%
  – CF, GOR, cardiac, aspiration
• Immune deficiency – 10%
  – Secondary – HIV, diabetes, immunesuppression, steroids, malignancy, chemotherapy
  – Primary

Infections

• Increased frequency
• Increased severity
• Opportunistic / low virulence pathogens
• Multiple sites
Infections: increased severity

- Pneumonia with empyema
- Bacterial meningitis, arthritis, osteomyelitis
- Septicaemia
- Mastoiditis
Infections

- Increased frequency
- Increased severity
- Opportunistic / low virulence pathogens
- Multiple sites
Infections: Opportunistic pathogens

• *Pneumocystis jirovecii*
• Mucocutaneous candidiasis
• Deep fungal infection (aspergillus, cryptococcus)
• Vaccine-acquired polio
• BCG disease after vaccination
• Toxoplasma, cryptosporidium
Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1:500 persons are affected by one of the known Primary Immunodeficiencies. If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.

1. Four or more new ear infections within 1 year.
2. Two or more serious sinus infections within 1 year.
3. Two or more months on antibiotics with little effect.
4. Two or more pneumonias within 1 year.
5. Failure of an infant to gain weight or grow normally.
6. Recurrent, deep skin or organ abscesses.
7. Persistent thrush in mouth or fungal infection on skin.
8. Need for intravenous antibiotics to clear infections.
9. Two or more deep-seated infections including septicemia.
10. A family history of PI.
Approach to primary immune deficiencies
Traditional classification
(Lederman in Leung)

• Components of the immune system
  – Cell mediated
  – Antibody
  – Phagocyte
  – Complement

• Technically correct but difficult to apply clinically
Advanced classification (Notarangelo 2010)

- Combined immune deficiencies
- T cell immune deficiency caused by thymic defects
- Antibody deficiencies
- Immunodeficiency with immune dysregulation
- Immunodeficiency with impaired cell-mediated cytotoxicity
- Defects of innate immunity
  - Phagocytes
  - Toll-like receptors
  - IL-12 / IFN-gamma pathway
  - Complement
- Syndromes – ataxia telangiectasia, Wiskott-Aldrich, hyper IgE syndrome, etc
Clinical presentation: European Society for Immunodeficiencies

Abstract

Efficient early identification of primary immunodeficiency disease (PID) is important for prognosis, but is not an easy task for non-immunologists. The Clinical Working Party of the European Society for Immunodeficiencies (ESID) has composed a multi-stage diagnostic protocol that is based on expert opinion, in order to increase the awareness of PID among doctors working in different fields. The protocol starts from the clinical presentation of the patient; immunological skills are not needed for its use. The multi-stage design allows cost-effective screening for PID within the large pool of potential cases in all hospitals in the early phases, while more expensive tests are reserved for definitive classification in collaboration with an immunologist at a later stage. Although many PIDs present in childhood, others may present at any age. The protocols presented here are therefore aimed at both adult physicians and paediatricians. While designed for use throughout Europe, there will be national differences which may make modification of this generic algorithm necessary.

Keywords: diagnostic protocol, immunological evaluation, primary immunodeficiency diseases (PIDs), patient-centred care.
• Recognise patterns of clinical presentation
• Table 1: Symptoms and signs that could point to potential PID
• Table 2: Different clinical presentations of PID
• 3 Protocols for investigation
• Consider all the non-PID causes of recurrent infections
Table 1. Symptoms and signs that could point to potential PID.

1. The hallmark of immunodeficiency: infections
   Recurrent (proven) bacterial infections
   Severe infections (e.g. meningitis, osteomyelitis, pneumonia)
   Infections that present atypically, are unusually severe or chronic or fail regular treatment
   Infections caused by an unexpected or opportunistic pathogen
   Severe or long-lasting warts, generalized mollusca contagiosa
   Extensive candidiasis
   Complications of vaccination (disseminated bacille Calmette–Guérin (BCG) or vaccinia infection, para-
   Abscesses of internal organs; recurrent subcutaneous abscesses
   Prolonged or recurrent diarrhoea

2. Remember the family history
   Consanguinity in the parents
   Unexplained early infant deaths
   Family history of possible immunodeficiency; familial occurrence of similar symptoms (affected males re-
   pattern of inheritance)
3. Miscellaneous signs: they could point to PID, but may not
   Abnormal hair
   Absence of immunological tissue: a/hypoplasia of thymus, absence of lymph nodes and tonsils
   Angioedema (without urticaria)
   Ataxia
   Auto-immunity
   Auto-immune disease in several family members
   Bleeding tendency, thrombocytopenia, small platelets
   Congenital cardiac anomalies
   Chronic diarrhoea (malabsorption, pancreatic insufficiency)
   Delayed separation of umbilical cord (> 4 weeks)
   Delayed shedding of primary teeth
   Dental crowding or other anomalies
   Developmental delay
   Difficult-to-treat obstructive lung disease
   Digital clubbing
   Dysmorphism
   Eczema, dermatitis (severe)
   Eosinophilia (unexplained)
   Facial abnormalities
   Failure to thrive (child) or wasting (adult)
   Giant granules in phagocytes
   Gingivostomatitis (severe), recurrent aphthae
   Graft-versus-host reaction after blood transfusion, or mother-to-child (infant)
   Hypersensitivity to sunlight
   Hypocalcaemic seizures
   Lymphadenopathy (excessive)
   Lymphocytopenia
   Malignancy (mainly lymphoma)
Table 2: clinical presentations of PID

• Recurrent ENT / airway infections
• Failure to thrive from early infancy
• Recurrent pyogenic infections
• Unusual infections / unusually severe course
• Recurrent infections with same pathogen
• Autoimmune, chronic inflammation, lympho-proliferation
• Characteristic clinical features occurring in eponymous syndromes
• Angioedema
3 Protocols for investigation

• 1 – antibody deficiency, neutropaenia, complement
• 2 – SCID / HIV / T cell disorders
• 3 – Neutropaenia, phagocyte dysfunction, complement
Case 1: Antibody deficiency

• Patient SL: 15 months
• Atopic / allergic family
• 11 documented courses of antibiotics (+3 undocumented)
• Otitis, pharyngitis, bronchiolitis
• 1 admission (acute GE with stomatitis)
• 2 older siblings, in day care, no smokers
• Fully vaccinated
<table>
<thead>
<tr>
<th>Column 1</th>
<th>Column 2</th>
<th>Column 3</th>
<th>Column 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical presentation</td>
<td>Suspected immunodeficiencies</td>
<td>Encountered pathogens</td>
<td>Special features</td>
</tr>
<tr>
<td>Recurrent ENT and airway infections</td>
<td>Selective antibody deficiencies [14], complement deficiencies [15], CVID [16] Sometimes phagocyte deficiency (mainly neutropenia) [17,18], WAS [19], HIV [13]</td>
<td>Mainly extra-cellular bacteria such as non-typable H. influenzae, pneumococcus. Sometimes: S. aureus, meningococcus, group A streptococcus, M. pneumoniae, U. urealyticum, C. jejuni, enteroviruses (Echovirus, poliovirus), giardia lamblia when gut, urinary and meningeal systems are also involved</td>
<td>Giardia infection may lead to a period of failure to thrive. Enteroviral meningoencephalitis is a severe complication in inadequately substituted agammaglobulinaemia. Unexplained bronchiectasis; recurrent bronchitis in a non-smoker</td>
</tr>
<tr>
<td>Column 5</td>
<td>Column 6</td>
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<tr>
<td><strong>Diagnostic protocol</strong></td>
<td><strong>Non-immunological differential diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go to Protocol 1</td>
<td>Frequent: normal frequency of infection in infants (day-care, passive smoking), bronchial hyperreactivity, allergy, asthma, adenoidal hypertrophy, iron deficiency anaemia, gastro-oesophageal reflux.</td>
<td></td>
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</tr>
<tr>
<td>Most patients do not have PID. Even if they do, it is seldom life-threatening in the short term.</td>
<td>Infrequent: cystic fibrosis, inhaled foreign body, congenital anomaly, BPD; intestinal or renal protein loss. Rare: ciliary dyskinesia, α1-anti-trypsin deficiency</td>
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<tr>
<td>Exclude more frequent non-immunological problems first, except in case of a positive family history</td>
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</tbody>
</table>
# Protocol 1

## Step 1

### Perform

Rule out severe antibody deficiency and neutropenia.

<table>
<thead>
<tr>
<th>Perform</th>
<th>Next step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood count and differential (platelet volume, absolute lymphocyte count, neutrophil and eosinophil counts), IgG, IgA, and IgM</td>
<td>Neutropenia: go to Protocol 3, step 2. Agammaglobulinaemia: go to step 3. Decreased level of at least one isotype: go to step 2. IgA deficiency: go to step 2. Normal results: in case of recurrent meningococcal infection go to step 2b; in case of recurrent ENT and airway infection wait for 3–6 months to see if clinical condition resolves; if problems persist: go to step 2 (a+b)</td>
</tr>
</tbody>
</table>

Recurrent infections Le Roux March 2012
• FBC/diff – N
• IgG, IgM – N
• Low IgA
<table>
<thead>
<tr>
<th>Step 2a</th>
<th>Antibody deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perform</strong></td>
<td>If not secondary to drugs, lymphoid malignancy, immunoglobulin loss (urine, faeces); booster responses (tetanus; unconjugated pneumococcal vaccine if &gt; 2–3 years of age; a rise in titre appropriate for age to above a defined level should be considered a positive response). Consider IgG-subclasses and M-proteins</td>
</tr>
<tr>
<td><strong>Next step</strong></td>
<td>Go to step 3.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2b</th>
<th>Complement deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perform</strong></td>
<td>CH&lt;sub&gt;50&lt;/sub&gt; and AP&lt;sub&gt;50&lt;/sub&gt;. Consider MBL. In case of angioedema: C1-inhibitor (level), C4 during attack</td>
</tr>
<tr>
<td><strong>Next step</strong></td>
<td>Go to step 3</td>
</tr>
</tbody>
</table>

Shaded boxes – “Collaboration with an immunologist is highly recommended for this step”
• IgG subclasses – N
• Lymphocyte subsets – N
• Vaccine antibody levels:
  – Pertussis, tetanus, diphtheria, pneumococcus – N
  – Low *Haemophilus influenzae* B
• Revaccinate (Pentaxim)
• Amoxil prophylaxis
• Repeat antibody levels in 4 weeks
<table>
<thead>
<tr>
<th>Step 3</th>
<th>Continue with</th>
<th>Possible diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agammaglobulinaemia</strong> <em>step 1</em></td>
<td>Lymphocyte subpopulations (Table 3), consider lymphocyte proliferation tests (Table 3), genetic determination of defect if possible</td>
<td>X-linked or autosomal recessive form of congenital agammaglobulinaemia</td>
</tr>
<tr>
<td>Normal results in step 2a</td>
<td>Wait and see. If problems persist repeat total IgG, IgA, IgM, and IgG-subclasses after 1–2 years (6 months if &lt; 1 year of age), and booster responses after 3–5 years. Consider Protocol 3. Consider lymphocyte subpopulations (Table 3)</td>
<td>No immunodeficiency, isolated IgA deficiency, developing CVID. TLR-signalling deficiency (IRAK4) (not associated with antibody deficiency)</td>
</tr>
<tr>
<td>Abnormal results in step 2a:</td>
<td>Consider lymphocyte subpopulations (Table 3), genetic determination of defect if possible. Consider lymphocyte proliferation tests (Table 3), chromosomal analysis, CD40, CD40L after stimulation, α-fetoprotein</td>
<td><strong>Polysaccharide antibody deficiency, THI, CVID</strong></td>
</tr>
<tr>
<td>IgA and/or IgG2 deficiency Abnormal booster responses Hypogammaglobulinaemia</td>
<td></td>
<td>thymoma, XLP, HIGM syndrome, WHIM, ICF syndrome, AT, Nijmegen breakage syndrome, Bloom syndrome, WAS</td>
</tr>
<tr>
<td>After step 2b</td>
<td>In case of abnormal CH50 or AP50: determination of separate complement components (C1q,C2,C4,C5-C9). ANA. In case of angioedema: C1-inhibitor function (if level is normal)</td>
<td>Inherited complement deficiency, complement consumption (SLE). Hereditary angioedema</td>
</tr>
</tbody>
</table>
Specific antibody deficiency

- Patient CM
- Recurrent LFTI / otitis
- Low B cells
- Persistently low *S. pneumoniae* antibody levels
- Never responded to re-vaccination
- Age 8 years: bronchiectasis
- IVIG replacement therapy
- Also low IgG subclass 4 deficiency: probably incidental
Recurrent infection

- Patient KS: 5 year old boy
- Well until 16 months old
- 3 courses of TB treatment
- Now severe, persistent left lower lobar consolidation
- 4 males relatives on mother’s side died in infancy
Fig. 1. Pedigree of the family showing the affected patient (■) and carrier female (mother), genetically normal male (father) and male deaths in the maternal family. (Cyrillic Pedigree Editor Version 2.0.1.0)
Recurrent infections with the same type of pathogen

Dependent on type of pathogen


Normally no other recurrent infectious problems
Normally no other recurrent infectious problems

Dependent on (type of) pathogen, go to:

Intracellular bacteria (e.g. salmonella, mycobacteria):
Protocol 2,
Step 3. Meningococci:
Protocol 1. Candida:
Protocols 2 and 3.
Encapsulated bacteria:
Protocol 1; perform splenic ultrasound in case of sepsis.
Viruses: Protocol 2. Many have no PID, but the recurrent infections may be life-threatening. Screening is therefore warranted

Increased exposure, coincidence
Inadequate treatment of first infection
Anatomical defect (e.g. fistula)
## Protocol 2

<table>
<thead>
<tr>
<th>Step 1</th>
<th><strong>Don’t hesitate to rule out SCID and AIDS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perform</strong></td>
<td>Blood count and differential (platelet volume, absolute lymphocyte count, neutrophil and eosinophil counts), IgG, IgA, and IgM, lymphocyte subpopulations (Table 3), tests for HIV</td>
</tr>
<tr>
<td><strong>Next step</strong></td>
<td>HIV-positive: treat accordingly. Agammaglobulinaemia, lymphocytopenia: go to step 2. Normal results, but no improvement, no other diagnosis: go to step 2. The possibility of SCID is an emergency! Early SCT can save lives</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td>Identify the different forms of (severe) combined immunodeficiency</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **Perform** | Lymphocyte proliferation tests (Table 3)  
Consider lymphocyte subpopulations using a more extended protocol than the one mentioned in Table 3, CD40(L), STAT1, IκBα. If no agammaglobulinaemia: IgG-subclasses, booster responses, M-proteins |
| **Next step** | Abnormal results: go to step 4. Normal results: go to Protocol 3 |
### Protocol 3

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Identify neutropenia</th>
<th>Possible diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perform</strong></td>
<td>Blood count and differential (absolute neutrophil count, microscopic evaluation); perform repeatedly in case of cyclic pattern of fever and infections (no evidence-based guidelines exist; 3×/week for 3–6 weeks is advocated in several reviews)</td>
<td>Cyclic neutropenia, Chediak–Higashi syndrome (giant granules), specific granule deficiency (bilobed nuclei), asplenia (Howell–Jolly bodies)</td>
</tr>
</tbody>
</table>

| Next step | Neutropenia: go to step 2. Normal results: determine IgG, IgA, and IgM, CH~50~; go to step 3. Neutrophilia: go to step 3 |

### Step 2

<table>
<thead>
<tr>
<th>Isolated neutropenia</th>
<th>Identify the cause of the neutropenia</th>
<th>Possible diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider secondary causes. Drug use, autoantibodies, ANA, C3/C4, RF, ANCA, Coombs, IgG, IgA and IgM. If normal: analysis of bone marrow (morphology, chromosomes, culture), mobilization tests (G-CSF, prednisone), pancreatic function tests. Consider metabolic disorder and appropriate tests</td>
<td>Drug-induced neutropenia, isolated autoimmune neutropenia, systemic autoimmune disease complicated by neutropenia, agammaglobulinaemia, certain metabolic disorders (e.g. Pearson syndrome), Shwachman–Diamond syndrome, Kostmann syndrome</td>
<td></td>
</tr>
</tbody>
</table>

<p>| Pancytopenia | Analysis of bone marrow (morphology, chromosomes, immunophenotyping) | Haematological malignancy, aplastic anaemia |</p>
<table>
<thead>
<tr>
<th>Step 3</th>
<th>Identify defects in phagocyte function</th>
<th>Possible diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform</td>
<td>Phagocyte function tests (Table 4). Serum IgE. Consider hair evaluation, consider CD11/18 and sLeX expression (flowcytometry, in case of neutrophilia)</td>
<td>CGD, hyper-IgE syndrome, Griscelli syndrome, G6PD deficiency, MPO deficiency, LAD, SGD</td>
</tr>
</tbody>
</table>
A novel CYBB mutation with the first genetically confirmed case of chronic granulomatous disease in South Africa

R Naidoo, N Jordaan, K W Chan, D M le Roux, S Pienaar,
J Nuttall, Y L Lau, B S Eley

A case of a child with chronic granulomatous disease (CGD) presenting with recurrent mycobacterial infections and invasive Aspergillus fumigatus disease is described. Genetic analysis confirmed X-linked CGD with a novel mutation in exon 10 of the CYBB gene – the first South African report of genetically confirmed CGD.

Chronic granulomatous disease

• Abnormal neutrophil killing
• Neutrophil burst test
  – Replaced the previous “nitro blue tetrazolium”
  – Measures neutrophil chemotaxis, phagocytosis, free radical production
  – If abnormal neutrophil burst: measure each component separately (but technically tricky)
• Needs to be arranged with lab at TBH: takes 6 hours, fresh specimen – must get there early morning

Recurrent infections Le Roux March 2012
• Persistent lobar consolidation: lung biopsy Aspergillosis
• Needed IV amphotericin B for 2 months
• Vertebral involvement – multi level thoracic spine with cord compression
• Posterior decompression and fusion
• Will complete 2 years of oral voriconazole in August 2012
• Then will start life-long itraconazole prophylaxis
• Lung lesion and spinal cord compression completely resolved
• December 2012: “Pain over surgical site after doing too many cartwheels on the beach or somersaults on the trampoline”
• Will remove rods end 2012 / early 2013!
Primary Immunodeficiencies: A 27-Year Review at a Tertiary Paediatric Hospital in Cape Town, South Africa

Reené Naidoo · Lisa Ungerer · Margaret Cooper · Sandra Pienaar · Brian S. Eley

Received: 18 June 2010 / Accepted: 8 September 2010 / Published online: 22 September 2010 © Springer Science+Business Media, LLC 2010

Abstract
Introduction The epidemiology of primary immunodeficiencies (PID) is not well documented in Africa. The objective of this study was to describe the spectrum of PID at a tertiary paediatric centre in South Africa.
Methods A retrospective study was conducted on 168 patients diagnosed with PID from 1983 to 2009.

PID at Red Cross

Recurrent infections Le Roux March 2012
Advances over the last 27 years include significant improvement in the mean age of diagnosis; however, declining numbers of diagnoses may suggest that a number of patients are still not being recognized as having PID.
Conclusion

• We should be diagnosing more PID’s!
• Recurrent infections are common, but primary immune deficiencies are not
• Rational approach to investigation
• Please call me if there are any patients you are concerned about
MEMORANDUM: IMMUNOLOGY SERVICE

This memorandum is to inform staff about the Clinical Immunology Service at Red Cross War Memorial Children’s Hospital.

Clinical Responsibilities

Prof Brian Eley is responsible for the overall service. Day-to-day consultations are performed by the duty ID senior registrar-consultant team who may be contacted via the telephone exchange.

Outpatient Clinic

The clinic takes place every Monday morning between 08h00 and 12h00 in S27, Medical Outpatients Department. New patients must be discussed with the duty ID senior registrar before bookings are arranged.

Inpatient referrals

Please arrange inpatient consultations with the duty ID senior registrar or consultant.

Immunology Investigations

Immune function tests are expensive, e.g. a standard lymphocyte subset panel currently costs R876.95, and IgG subclasses R618.24. To avoid unnecessary or inappropriate testing, all requests for immune investigations (including repeat investigations) should be discussed with the duty ID senior registrar/consultant. Thereafter, relevant tests may be arranged with the Chemical Pathology Laboratory (extension 5225). Blood specimens should ideally be sent to the laboratory before 09h30. The specimens are transported to the Immunology laboratory at Tygerberg Hospital where the tests are performed. Results are obtainable from the Chemical Pathology laboratory, Red Cross War Memorial Hospital.
Recurrent infections Le Roux March 2012

The clinic takes place every Monday morning between 09h00 and 12h00 in the Medical Outpatients Department. New patients must be discussed with the duty ID senior registrar before bookings are arranged.

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<table>
<thead>
<tr>
<th>Test name</th>
<th>Specimen requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoglobulin concentrations</td>
<td>2-3 ml clotted tube</td>
</tr>
<tr>
<td>I\textsubscript{G}G subclass concentrations</td>
<td>2-3 ml clotted tube</td>
</tr>
<tr>
<td>Specific I\textsubscript{G}G subclasses</td>
<td>2-3 ml clotted blood</td>
</tr>
<tr>
<td>Lymphocyte subset analysis</td>
<td>2-3 ml EDTA blood</td>
</tr>
<tr>
<td>Oxidative burst test</td>
<td>2-3 ml heparinised blood</td>
</tr>
<tr>
<td>CH50 (Total haemolytic complement)</td>
<td>2-3 ml clotted blood on Ice</td>
</tr>
<tr>
<td>Lymphocyte proliferative tests</td>
<td>2-3 ml EDTA blood</td>
</tr>
<tr>
<td>Leucocyte adhesion markers</td>
<td>2-3 ml EDTA blood</td>
</tr>
</tbody>
</table>