



PID is Primary Immunodeficiency

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SYMPTOMS INCLUDE

Family history of PID
MONTHS ON ANTIBIOTICS

Recurrent Infections:

- Ear
- Respiratory
- Sinus
- Deep seated

H **A&E**

Pneumonias

Deep skin abscesses
Persistent thrush
Antibiotics (IV)

Failure to thrive

CASE REVIEW: EXECUTIVE SUMMARY



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Is there a delay in the diagnosis of Primary Immunodeficiency (PID)?

Abstract of Case Review Results (The "Is it PID?" Advisory Group)

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Aims:

To investigate the current diagnostic delay in PID and its impact on morbidity and quality of life.

Methods:

A case review study conducted by 20 UK Immunology departments as part of the "Is it PID?" Campaign analysed the route to diagnosis of 62 newly diagnosed PID patients in 2008 (adults and children). The results were also compared with those of a patient survey undertaken recently with UK PIA members.

Results:

The mean age at diagnosis was 32 years, the commonest diagnoses were common variable immunodeficiency (CVID, 56%), specific antibody deficiency (10%), X-linked agammaglobulinaemia (8%) and hereditary angioedema (8%). Commonest preceding symptoms were upper (79%) and lower (40%) respiratory infections and diarrhoea (13%). 34% of patients suffered other serious infections. 27% of patients waited ≥ 7 years before diagnosis, median for CVID 4 years. The majority of patients (85%) had seen ≥ 1 specialist before seeing an immunologist, most frequently a respiratory physician, and 35% had seen ≥ 2 specialists. More than 50% had ≥ 1 hospital admission before diagnosis.

Conclusions:

- Both surveys demonstrate a reduction in time to diagnosis of PID compared to previous studies.
- However, late diagnosis remains a significant problem; 66% had infections, 30% respiratory complications and 43% anxiety/stress and depression. Following diagnosis and treatment, 40% had an improvement in anxiety/stress and depression.
- This is the first report to compare clinicians and patients' perspectives at national level.
- The authors accept that potential ascertainment bias cannot totally be excluded.



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Case Review Results **Executive Summary**

20 hospitals completed a review of three of their PID patients diagnosed in the last 12 months, using the patient record.

Hospitals taking part in the case review:

- Aberdeen Royal Infirmary
- St. George's Hospital, London
- City Hospital, Birmingham
- Leicester Royal Infirmary
- Addenbrooke's Hospital
- Manchester Royal Infirmary
- Ninewell hospital, Dundee
- Newcastle General Hospital
- Birmingham Heartlands
- Derriford Hospital, Plymouth
- Oxford Radcliffe Hospitals
- Papworth Hospital, NHS Trust
- Nottingham University Hospital
- Royal Brompton Hospital, London
- Alder Hey Children's Hospital
- Birmingham Heartlands
- The Royal Hospitals, Belfast
- Barts and the London NHS Trust
- Northern General Hospital
- Leeds Teaching Hospitals (St. James University Hospital)
- University College Cork



Those taking part in the case review were asked to give their numbers of PID and HAE patients and the total number across these hospitals was 2023. The proportion of each condition was given as:

■ Common variable immunodeficiency (CVID)	37%
■ Hereditary angioedema (HAE)	21%
■ Other	12%
■ Specific antibody deficiency	11%
■ X-linked agammaglobulinaemia (XLA)	5%
■ IgG subclass deficiency	4%
■ Other unspecified antibody deficiency	4%
■ IgA deficiency	3%
■ Type I cytokine defect	2%
■ Hyper IgE syndrome	2%
■ Combined immunodeficiency (CID)	2%
■ Severe combined immunodeficiency (SCID)	1%
■ X-linked lymphoproliferative disease (XLP)	1%
■ Wiskott-Aldrich syndrome (WAS)	1%
■ Chronic granulomatous disease (CGD)	1%
■ Neutrophil defect	1%



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Section 1 – Case review patient’s demographics: 56 patients

- 1. Gender:** 61% male, 39% female
- 2. Age range:** 19 mths – 82 yrs
Average age 32.3 yrs
- 3. Age at diagnosis:** (range) 6 mths–82 yrs
Average age at diagnosis = 32.7 yrs
Average length of time with diagnosis = 1.5 yrs
- 4. Occupation** Student (6), Retired (6), Accountant, Actor, Building conservationist, English Language Editor, Factory Worker, Finance Manager, Upholsterer, Geologist, Housewife, Hygienist, Information Advisor - call centre, IT Specialist, Joiner, Office worker, Fireman, Physiotherapy assistant, Plumber / decorator, Production Officer, Research Scientist, Decorator, Sales Manager, Sales Representative, Taxi Driver.
- 5. Racial group:**
- 77% - White Other
 - 15% - White Irish
 - 5% - Asian or Asian British
 - 2% - Mixed
 - 2% - Black or Black British
 - 0% - Chinese
 - 0% - Other
- 6. Diagnosis:**
- 56% - Common variable immunodeficiency (CVID)
 - 10% - Specific antibody deficiency
 - 8% - X-linked agammaglobulinaemia (XLA)
 - 8% - Hereditary angioedema (HAE)
 - 3% - Hyper IgE syndrome
 - 3% - Chronic granulomatous disease (CGD)
 - 2% - Combined immunodeficiency (CID)
 - 2% - IgA deficiency
 - 2% - Type I cytokine defect
 - 2% - Wiskott-Aldrich syndrome (WAS)
 - 13% - Other: DNA 4 Ligase Deficiency, Absent Btk protein expression, proven Btk gene mutation C7T point mutation at coding nucleotide 877, Hypogamma related to congenital rubella, Good’s Syndrome x 2, Complement deficiency, ITP/Coeliac, IgG Lambola puraprotein with immunosuppression.





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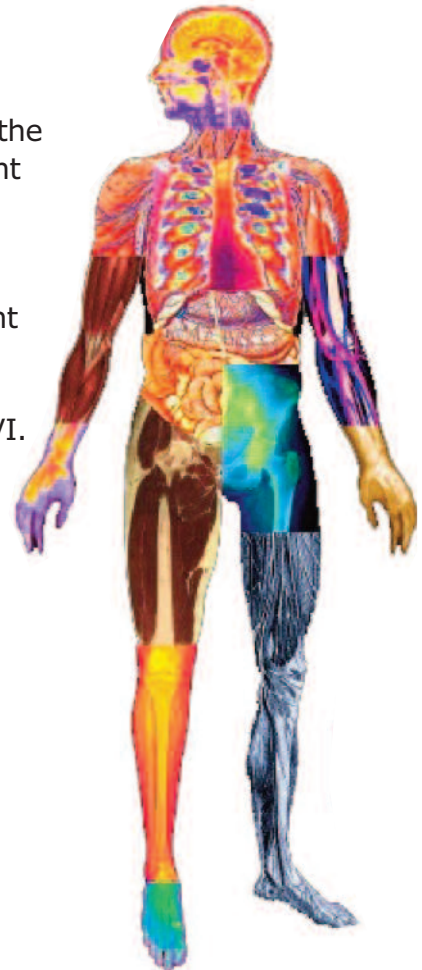
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Section 2 – The route to diagnosis and treatment

7. Patient's preceding symptoms:

- 79% - Chest infections/pneumonias
- 40% - Upper respiratory tract infections
- 38% - Other (the review asked the respondent to specify, the following were reported): septic arthritis of the knee, frequent exacerbations of asthma, recurrent ear infections x 6, microcephaly, umbilical infection, swellings with and without trauma, skin rashes, coeliac disease x 2, previous IgA deficiency, recurrent swellings and abdominal pains, recurrent prostatitis, chronic cough, asthma and reflux, neutropenia, thrombocytopenia, preseptal cellulitis, lymphadenitis, shingles, conjunctivitis, sinusitis, iron deficiency anaemia, CVI.
- 13% - Diarrhoea
- 11% Autoimmune phenomena – celiac disease, idiopathic inflammatory bowel disease, autoimmune haemolytic anaemia, abdominal pain, throat swelling, ITP
- 9% - Fungal infections: aspergillosis, tinea cruris, tinea unguium, candida, skin infections
- 8% - Eye infection
- 8% - Abscesses/boils
- 6% - Sepsis (blood poisoning)
- 6% - Failure to thrive (paediatrics)
- 6% - Urinary infection



8. Time elapsed from onset of symptoms to diagnosis:

- 10% - Under six months
- 11% - 6-12 months
- 23% - 2 years
- 13% - 3 years
- 3% - 4 years
- 8% - 5 years
- 3% - 6 years
- 2% - 7 years
- 27% - 7+ years

Commonest preceding symptoms were upper (79%) and lower (40%) respiratory infections and diarrhoea (13%). 34% of patients suffered other serious infections. 27% of patients waited ≥ 7 years before diagnosis, median for CVID 4 years. The majority of patients (85%) had seen ≥ 1 specialist before an immunologist, most frequently a respiratory physician, and 35% had seen ≥ 2 specialists. More than 50% had ≥ 1 hospital admission before diagnosis.



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12. Before PID was diagnosed what other diagnoses were made?

■ Bronchiectasis	11 patients
■ URTI	4 patients
■ ITP	3 patients
■ Asthma	3 patients
■ Chronic middle ear infections	3 patients
■ Splenomegaly	3 patients
■ UTI	2 patients
■ Allergic asthma	2 patients
■ IgA deficiency	2 patients
■ Coeliac disease	2 patients
■ Maltoma	2 patients
■ Chronic sinusitis	1 patient
■ Keratoconjunctivitis	1 patient
■ Vesicoureteric reflux grade 2-3	1 patient
■ Pneumonia	1 patient
■ Autoimmune haemolytic anaemia	1 patient
■ Allergic bronchopulmonary aspergillosis	1 patient
■ Loin pain haematuria syndrome	1 patient
■ Thin basement membrane nephropathy	1 patient
■ Arthralgia	1 patient
■ Latex allergy	1 patient
■ Lupin allergy	1 patient
■ Chronic necrotising pulmonary aspergillosis	1 patient
■ GORD	1 patient
■ Cervical lymphadenitis	1 patient
■ Cervical abscess	1 patient
■ Chronic diarrhoea	1 patient
■ Poor weight gain and failure to thrive	1 patient
■ Pseudomonas infection	1 patient
■ Infections	1 patient
■ Recurrent febrile convulsions	1 patient
■ Infantile eczema	1 patient
■ Tonsilectomy, adenoids removed, grommets	1 patient
■ Murmurs – leaky valve	1 patient
■ Primary biliary cirrhosis	1 patient
■ Immune thrombocytopaenia	1 patient
■ Widespread lymphadenopathy	1 patient
■ Eczema	1 patient
■ Juvenile RA	1 patient
■ Sinusitis	1 patient
■ Prostatitis	1 patient
■ LIP	1 patient
■ AIHA	1 patient
■ Congenital rubella	1 patient
■ Deafness	1 patient
■ Chronic cough	1 patient
■ Thrombocytopaenia	1 patient
■ Thymoma	1 patient
■ Irritable bowel syndrome	1 patient
■ Fallots tetralogy	1 patient



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13. Please list all major and specialised investigations the patient underwent prior to the diagnosis of PID including those required for the diagnosis:

- 66% Radiography
- 11% BMA
- 29% Molecular blood
- 32% Other

14. Time elapsed from diagnosis to initiation of therapy:

- 32% No delay (watch and wait)
- 42% 1 month
- 8% 2 months
- 2% 3 months
- 6% 4 months
- 2% 5 months
- 3% 6 months
- 0% 6-12 months
- 2% 12-18 months
- 0% 18-24 months
- 5% over 2 years



15. Does the patient have any concurrent diseases related to PID or any complications?

- 34% Bronchiectasis
- 32% Other*
- 24% None
- 10% Autoimmune cytopenias
- 6% Granulomatous disease
- 3% Liver disease – incl abscesses on treatment, primary biliary cirrhosis
- 2% Hyposplenism/splenectomy

*Other includes – recurrent sinusitis and infective conjunctivitis, idiopathic inflammation of the bowel, asthma, latex and lupin allergy, hayfever, oral allergy syndrome, EBV localised lymphoma post BMT, chronic lung disease, generalised lymphadenopathy, splenomegaly, coeliac, empyema (lobectomy), sinusitis, prostatitis, mild splenomegaly, LIP, GILID, anaemia, hypothyroidism, enteropathy, chronic suppurative otitis media, concurrent pulmonary fibrosis.

16. Patient's treatment:

- 57% IVIg in hospital
- 34% Antibiotics (oral)
- 18% SCIg at home
- 10% Antibiotics (Intravenous)
- 6% SCIg in hospital
- 3% Bone Marrow Transplant
- 2% Surgery
- 0% IVIg at home
- 0% Gene Therapy
- 0% Fresh Frozen Plasma
- 0% No treatment





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Section 3 – The impact of diagnosis

17. In your opinion did diagnosis and treatment improve the patient's health?

■ 95% Yes, 0% No*

*5% of the sample did not answer

18. Number of in-patient stays following diagnosis:

■ 0 days	- 33%
■ 1 day	- 5%
■ 2 days	- 3%
■ 3-5 days	- 0%
■ 6 days	- 1%
■ 7-10+ days	- 0%



19. What has been the impact of diagnostic delay, if any, on the patient's health?

■ 66%	- Repeated infections
■ 40%	- Anxiety/stress
■ 29%	- Lung damage
■ 11%	- None
■ 10%	- Other: parental anxiety, severe infection and failure to thrive, cough, ITP, significant reduction in activity
■ 6%	- Frequent swellings (HAE)
■ 3%	- Depression
■ 3%	- Constant pain
■ 0%	- Death
■ 0%	- Permanent disability

20. Since diagnosis and treatment has there been an improvement in any of the following?

■ 71%	- Repeated infections
■ 3%	- Lung damage
■ 3%	- Depression
■ 37%	- Anxiety/stress
■ 3%	- Constant pain
■ 5%	- Frequent swellings (HAE)
■ 8%	- None
■ 0%	- Death
■ 0%	- Permanent disability
■ 27%	- Other parental anxiety x 2, general health and wellbeing, reduction of exacerbations in asthma, lethargy x 2, now realises that there is a specific treatment, failure to thrive, a lot more energy x 2, improvement in ITP, too early to tell x 5.