# Elective Report

Panagiotis Kamperidis

**Objectives set by the School:**

**a) What are the prevalent immunodeficiency conditions seen at The Royal London? How do they compare to the rest of the UK?**

**b) How is clinical care of primary immunodeficiency patients managed in The Royal London and how does it compare with the rest of the UK?**

The Immunology department at the Royal London provides a full consultant-led service for the diagnosis and monitoring of patients with immunodeficiencies, autoimmune diseases and allergic conditions. The staff provide a 24-hour advice service for clinical and laboratory enquiries. If required, patients may be referred where specialised inpatient, outpatient, day-care and home therapy immunology services are available. The department is particularly well-equipped with a flow cytometry suite in order to diagnose and monitor immunodeficiency disorders. The Immunology laboratory is also a referral centre for routine and specialist tests including those for systemic lupus erythematosus (SLE) and hereditary angioedema investigations. The adult primary immunodeficiency disease (PID) service offers a weekly outpatient clinic, outpatient infusions as well as inpatient facilities. The service is led by three consultants, while SpRs provide additional medical input. Additionally, there is a monthly paediatric outpatient clinic, three-monthly rheumatology clinic and weekly allergy clinics at the London Chest. It is among the five biggest centres in the country treating immunodeficiency, as seen in the UKPID Registry[1] (Table 1).

PIDs, seen at the Royal London, are a heterogeneous group of disorders of immune regulation and function and distinct disease phenotypes exist, ranging from the potentially benign IgA deficiency to potentially catastrophic diagnoses such as severe combined immunodeficiency (SCID). They are characterised by increased susceptibility to infection, and through dysregulation of immunity, may also predispose to malignancy and autoimmune disease. Humoral (antibody) immunodeficiencies, in particular Common Variable Immunodeficiency (CVID), are the most frequently encountered PID requiring treatment (Figure 1). Treatment for such antibody deficiencies involves regular, lifelong immunoglobulin replacement therapy[2-5].

In particular, antibody deficiencies are defined by a loss of immunoglobulins or failure of immunoglobulin function, resulting in increased susceptibility to infection, and are

sub-classified into primary and secondary. In primary deficiencies inherited or sporadic genetic mutation(s), in some cases with unknown environmental cofactors, are suspected with no other known cause. Secondary antibody deficiency occurs as a consequence of other diseases or medications. Antibody deficiencies are associated with infections, immune dysfunction, end organ damage and significant morbidity and mortality. Immunoglobulin replacement for primary antibody deficiency is known to reduce infections, morbidity and mortality. A small number of studies have demonstrated that immunoglobulin replacement therapy is also effective in reducing severe infections in those with secondary antibody deficiency[6-12]. Table 2 shows the latest results of patients with primary or secondary antibody immunodeficiency receiving immunoglobulin therapy at the Royal London. It can be seen that the preferred place of administration for patients at this hospital is at home, which is in keep with the home-led patient-centred care approach at this hospital, in contrast to other sites in the country.

CVID is the most prevalent primary antibody deficiency requiring medical attention, and is characterised by decreased antibody production, recurrent sinopulmonary and gastrointestinal infections and an increased risk of immune dysregulation, manifesting as autoimmune cytopenias, granulomatous disease, and inflammatory bowel disease[13]. It is the most prevalent antibody PID, which is also the case in the Royal London (Table 3).

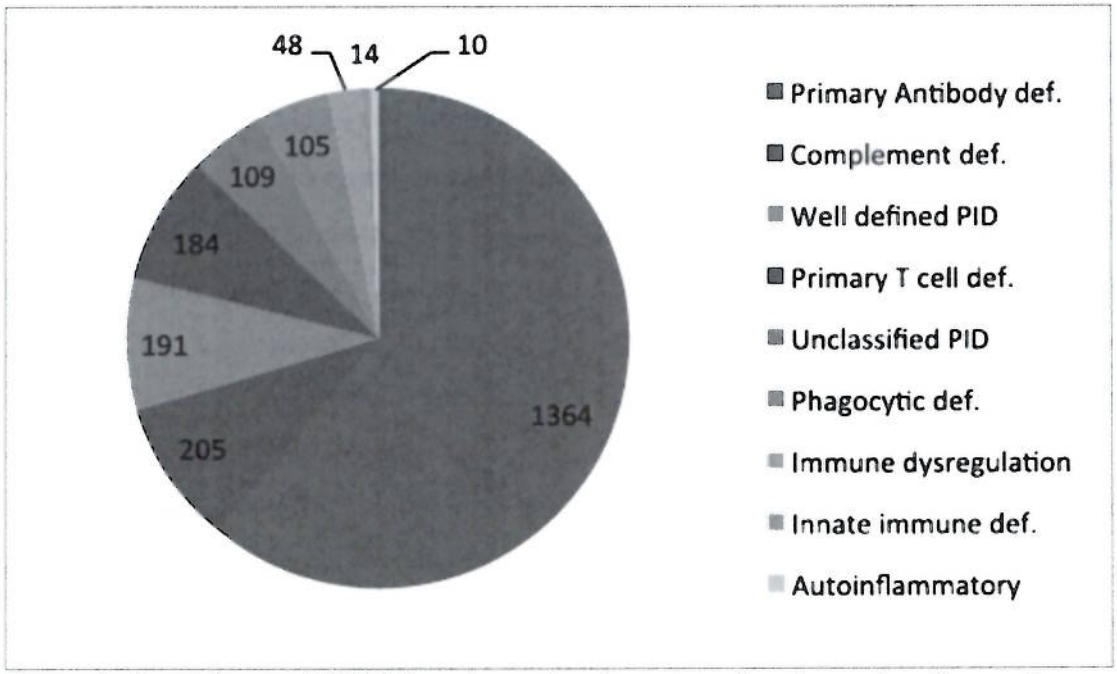


**Figure 1**. Breakdown of UKPID registered patients into the nine major diagnostic categories[1]. Antibody deficiency is the prevalent PID

| Centre | No. of patients registered | Centre | No. of patients registered |
|---|---|---|---|
| Royal Free Hospital, UCL London | 456 | Salford Royal NHS Foundation Trust | 59 |
| Great North Children's Hospital, Newcastle | 263 | Sheffield Teaching Hospitals NHS Foundation Trust | 53 |
| Great Ormond Street Hospital and Institute of Child Health, London | 248 | Epsom and St Helier University Hospitals Trust | 23 |
| Central Manchester University Hospitals | 201 | Hull and East Yorkshire Hospitals NHS Trust | 21 |
| Barts and the London NHS Trust | 151 | Royal Victoria Infirmary, Newcastle | 18 |
| Birmingham Heartlands Hospital | 98 | Royal Liverpool and Broadgreen University Hospitals | 14 |
| Addenbrooke's Hospital, Cambridge | 94 | Alder Hey Children's Hospital Liverpool | 14 |
| The Royal Hospitals, Belfast | 82 | Ninewells Hospital Dundee | 12 |
| Papworth NHS Foundation Trust, Cambridge | 79 | Queen's Medical Centre, Nottingham Queen's Medical Centre, Nottingham | 10 |
| Derriford Hospital, Plymouth | 76 | St George's Hospital, London | 9 |
| Leeds Teaching Hospitals NHS Trust | 74 | Aberdeen Royal Infirmary | 9 |
| John Radcliffe Hospital, Oxford | 73 | Birmingham City Hospital | 9 |
| University Hospital of Wales, Cardiff | 71 | Scottish National Blood Transfusion Service, Edinburgh | 7 |

**Table 1**. Participating centres in the UKPID registry (adapted from Edgar et al[1]). The Royal London is the fifth biggest centre countrywide

| Immunodeficiency Type | | PRIMARY | SECONDARY |
|---|---|---|---|
| Median number of years on Ig-replacement (range) | | 3 (<1-28) | 1 (<1-9) |
| Route of administration | | | |
| | IV | 60 (47.6%) | 13 (33.3%) |
| | SC | 66 (52.4%) | 26 (66.6%) |
| Place of administration | | | |
| | Home | 80 (63.5%) | 25 (64.1%) |
| | Barts Health | 26 (20.6%) | 9 (23.1%) |
| | Other local hospital | 20 (15.9%) | 5 (12.8%) |

**Table 2**.Latest compiled data of patients receiving immunoglobulin therapy at the Royal London Hospital. Home based therapy is the preferred place of administration

| | PRIMARY | PROBABLE PRIMARY | SECONDARY | PROBABLE SECONDARY | UNKNOWN |
|---|---|---|---|---|---|
| TOTAL | 113 | 13 | 26 | 13 | 2 |
| CVID | 79 (69.9%) | 8 (61.5%) | - | - | - |
| CVID | 63 | - | - | - | - |
| Inflammatory CVID | 16 | - | - | - | - |
| Probable CVID | - | 8 | - | - | - |
| Hypogammaglobulinaemia | 5 (4.4%) | 3 (23.1%) | 21 (80.8%) | 9 (69.2%) | 2 (100%) |
| Specific or subclass deficiency | 10 (8.9%) | 2 (15.4%) | 4 (15.4%) | 4 (30.8%) | - |
| Agammaglobulinaemia | 12 (10.6%) | - | - | - | - |
| Other | 7 (6.2%) | - | 1 (3.8%) | - | - |

**Table 3**. Latest compiled data of the immunodeficiency patient cohort at the Royal London receiving immunoglobulin-replacement treatment. CVID patients are the prevalent group

**Objectives set by the student:**

**c) What is the role of MDT approach in the management of primary immunodeficiencies?**

**d) i) Expand knowledge of immunological conditions**

**ii) Develop relevant clinical skills**

**iii) Understand investigation & management options of seen conditions**

**iv) Become familiar with relevant lab results and forms**

The multidisciplinary team approach is an integral part of the management of PIDs at the Immunology department of The Royal London. Firstly, there is a departmental MDT meeting once a week, where all outpatients and inpatients are discussed comprehensively among doctors (consultants, SpRs, SHOs), nursing staff and a lab representative. Patient progress and treatment options are discussed, while updated lists of patients are kept for methodical follow-up. Secondly, there is another departmental weekly meeting, among doctors and all lab staff, where diagnostic protocols are reviewed and any problems addressed promptly. There is also important ongoing research taking place in the lab aiming at better disease understanding, diagnosis and management. Finally, even though the Immunology department at The Royal London does have a dedicated ward in the hospital, unlike any other Immunology centre in the country, inpatients are also allocated to other wards according to their immediate needs (e.g. respiratory ward, renal etc.). Thus, care of inpatients is split among Immunologists and other specialties, all of whom liaise regularly for a complete patient care.

On a personal level, I really enjoyed my time at this elective placement, and I have managed to achieve all personal objectives I had set beforehand and are listed on question (d) above, through seeing patients in the ward and clinics (both sitting in/attending only, and clerking patients independently), be it adult immunodeficiency, paediatric outpatients, or allergy clinics, and the ward. As I aspire to follow a Clinical Academic career in Immunology, my placement here has further benefited me via i) familiarising myself with the strict protocols an NHS lab has to work under, ii) appreciating the professionalism of research and healthcare NHS staff in patient direct and indirect care, and also iii) understanding the hierarchical organisation of such a setting. Furthermore, by attending the weekly MDT meetings and staff briefings further enhanced my appreciation of such an approach to the management of immunological conditions. Finally, I will be continuing collaboration with the team, as I have undertaken to write a case report for publication on an

interesting case seen in the clinic, which is in addition to a review draft I have already written for Dr Grigoriadou, thus further improving my understanding of important immune phenomena and enhancing my CV for the future. My experience here has greatly helped me widen my career horizons.

## References


1) Edgar JD1, Buckland M, Guzman D et al. The United Kingdom Primary Immune Deficiency (UKPID) Registry: report of the first 4 years' activity 2008-2012. Clin Exp Immunol. 2014 Jan;175(1):68-78
2) Chapel H. Classification of primary immunodeficiency diseases by the International Union of Immunological Societies (IUIS) Expert Committee on Primary Immunodeficiency 2011. Clin Exp Immunol 2012; 168:58-9.
3) Keerthikumar S, Raju R, Kandasamy K, Hijikata A et al. RAPID: Resource of Asian Primary Immunodeficiency Diseases. Nucleic Acids Res 2009; 37:D863-7.
4) Herriot R, Sewell WA. Antibody deficiency. J Clin Pathol 2008; 61:994-1000.
5) Cunningham-Rundles C. How I treat common variable immune deficiency. Blood 2010; 116:7-15.
6) Bousfiha AA, Jeddane L, Ailal F, et al. A phenotypic approach for IUIS PID classification and diagnosis: guidelines for clinicians at the bedside. J Clin Immunol. 2013;33(6):1078-1087
7) Rose ME, Lang DM. Evaluating and managing hypogammaglobulinemia. Cleve Clin J Med. 2006;73(2):133-137, 140, 143-134
8) Yomota M, Amano I, Horita N, et al. Serum immunoglobulin G is a marker for the risk of opportunistic infection in steroid-dependent severe asthmatic patients. Intern Med. 2012;51(19):2715-2719
9) Ozaras N, Goksugur N, Eroglu S, Tabak O, Canbakan B, Ozaras R. Carbamazepine-induced hypogammaglobulinemia. Seizure. 2012;21(3):229-231
10) Baris S, Ercan H, Cagan HH, et al. Efficacy of intravenous immunoglobulin treatment in children with common variable immunodeficiency. J Investig Allergol Clin Immunol. 2011;21(7):514-521
11) Quinti I, Soresina A, Guerra A, et al. Effectiveness of immunoglobulin replacement therapy on clinical outcome in patients with primary antibody deficiencies: results from a multicenter prospective cohort study. J Clin Immunol. 2011;31(3):315-322
12) Gunther G, Dreger B. Post-marketing observational study on 5% intravenous immunoglobulin therapy in patients with secondary immunodeficiency and recurrent serious bacterial infections. Microbiol Immunol. 2013;57(7):527-535
13) Castigli E, Geha RS. Molecular basis of common variable immunodeficiency. J Allergy Clin Immunol. 2006;117(4):740-746


**Word Count (excl. References and Titles)**: 1246