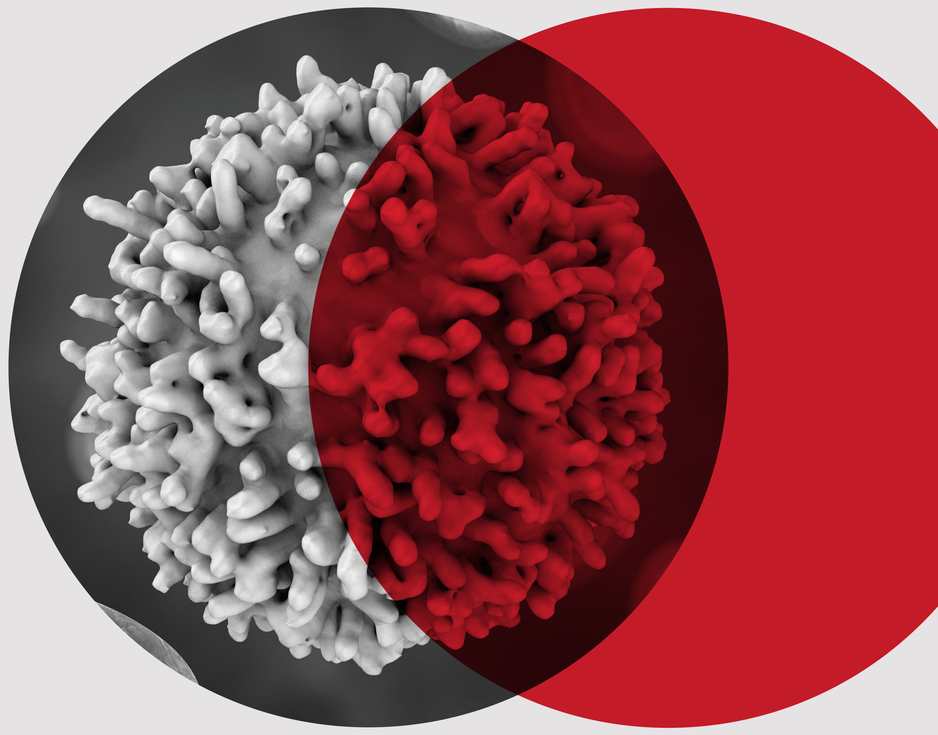
Inter-laboratory variation in B cells subsets reporting and its clinical implications



Katrina Hong, Zoe Vayanos, Peter Graham

The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP), St Leonards, Sydney.

Introduction

Common Variable Immunodeficiency Disorder (CVID) is a type of primary immunodeficiency caused by defective B cell differentiation[1]. CVID affects approximately 1 in 30,000 individuals and is characterised by recurrent infections[1]. Clinical presentations and laboratory anomalies guide the diagnosis of CVID[2]. The European Society for Immunodeficiency (ESID) includes low switched memory B cells (<70% of age adjusted reference interval) as one of the diagnostic criteria for CVID[2]. In addition, the European consensus classification categorises patients with CVID into subgroups relying on 1% of B cells (among PBL), 2% of switched memory B cells (among total B cells), 9% of transitional B cells (among total B cells) and 10% of CD21 low B cells (among total B cells) as the clinical cut-offs. Each of the subgroup is associated with different pathogenesis and clinical presentations (e.g., autoimmune cytopenia, granuloma, splenomegaly and lymphadenopathy)[3].

We sought to assess if the performance of laboratories in the B cell subsets program offered by RCPAQAP was fit for purpose for CVID classifications.

Method

The mean, standard deviation (SD) and coefficient of variance (CV) from all method groups from 2020 to 2022 were compared. The CVs were analysed by single factor ANOVA. A p-value of <0.05 was considered statistically significant.

Results

The CV in the reporting of memory B cells as a percentage of peripheral blood lymphocytes (PBL), switched memory B cells as a percentage of B cells and switched memory B cells as a percentage of PBL showed statistically significant improvement from 2020 to 2022 (Table 1). The CV in the reporting of transitional B cells and CD21 low cells showed no significant difference across the years. Reassuringly, none of the measurands showed any significantly increased variation between 2020 and 2022.

Discussion

The variation (CV) in the reporting of B cell subsets is high in general. The results provided in Table 1 were derived from healthy volunteers. In patients with CVID, abnormally low population in certain B cell subsets may be associated with even higher variation. The level of variation in the reporting of B cell subsets between laboratories may affect the diagnosis and treatment of patients with CVID.

Conclusion

While the inter-laboratory imprecision in the reporting of some B cell sub-populations has significantly improved, the level of variation should still be considered when assessing and monitoring CVID.

Table 1. The analytical performance of all method groups in B cell subsets program offered by RCPAQAP.

Year	2020			2021			2022			
	Mean	SD	CV(%)	Mean	SD	CV(%)	Mean	SD	CV(%)	p value
B cells (% of PBL)	8.7	1.7	21	9.6	1.5	17	12.7	1.9	15	0.2
Memory B Cells (% B Cells)	-	-	-	33	5	15	28	5	21	0.3
Memory B Cells (% PBL cells)	-	-	-	3.1	0.9	32	2.6	0.5	22	<0.05
Switched memory B cells (% B cells)	14.6	8.9	65	15.6	3.7	24	12.6	3.6	31	0.005
Switched memory B cells (% PBL cells)	1.3	0.8	64	1.5	0.5	33	1.2	0.3	31	<0.005
Transitional B cells (% B cells)	2.1	1.5	71	1.6	1.2	80	2	1.3	65	0.29
Transitional B cells (% PBL cells)	0.2	0.1	73	0.2	0.1	107	0.3	0.2	72	0.3
CD21 low cells (% B cells)	8.7	5.3	67	7	2.5	37	6.4	3.2	66	0.33

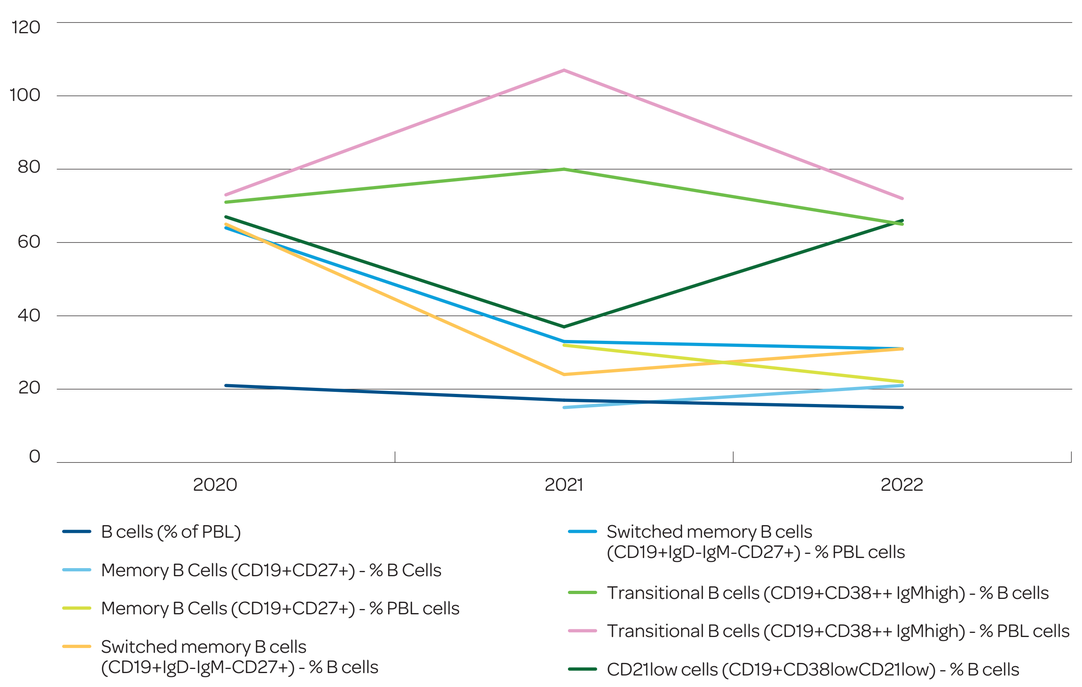


Figure 1. The CVs from all methods for the measurement of B cell subsets from 2020 to 2022.

References:

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3. Wehr C, Kivioja T, Schmitt C, Ferry B, Witte T et al. The EUROclass trial: defining subgroups in common variable immunodeficiency. Blood. 2008 Jan 1;111(1):77-85.

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The Royal College of Pathologists of Australasia
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