

The purpose of the MRCPPath Part I exam is to assess a candidate's core knowledge base, basic laboratory skills, and ability to integrate laboratory data with clinical scenarios. The practical examination of this exam tests routine laboratory issues, including interpretation of laboratory data and calculations, basic analytical problem solving, understanding of quality assurance, and clinical interpretation of laboratory results. Areas of strength or weakness highlighted by the written answers may be explored in the viva component of the exam.

For each exam, the model answers and examination standards are agreed in advance by at least 2 examiners. In order to assist exam preparation, we are publishing a sample of questions from a recent examination, with model answers and examiner's notes. We hope that these are useful to you.

Unofficial Top Tips for the MRCPPath Practical Exam:

- Always read the question!
- Common things are common – even in the MRCPPath
- Be concise in your answer: less is often more

MRCPath Part 1 (Dry Practical)

In this exam, there were 7 questions, of which 4 questions and model answers are given here

General Comments

- Answer all questions.
- All candidates should work on their own and are advised not to discuss answers to the exam questions with other candidates.
- Please do not remove and question papers or answer books from the examination rooms.
- You will be required to read and interpret some immunofluorescence slides. Before the start of the exam, you will be assigned a specific time slot to view these to enable you to plan your time. If you are not familiar with the microscope please seek advice. As you will have to share the equipment please be considerate of other users.
- Biological materials provided are not known to be biohazardous. However, good laboratory practice is essential.
- All written answers should be succinct and to the point.

The Examination Questions

Section A2. Practical Simulation: ELISA data

Question

You are provided with the raw data (Optical density in duplicate (OD1 and OD2)) on anti-MPO and anti-PR3 antibody ELISAs.

1. Construct appropriate standard curves using the graph paper provided.
2. Evaluate controls. Target values are
Anti-MPO: control 1 positive 45-65 units, control 2 negative <10
Anti-PR3: control 1 positive 50-70 units, control 2 negative <10
3. Interpolate samples using the standard curve to derive quantitative ELISA results. Interpret a result of <15 units as negative in either assay.
4. Provide interpretive comment for each sample based on the combined immunofluorescence and ELISA data.

Anti-MPO ELISA

units	OD1	OD2	Mean	Units from graph	Comment
300	1.697	1.754	1.726		
100	0.771	0.760	0.766		
30	0.314	0.321	0.318		
10	0.181	0.175	0.178		
3	0.087	0.090	0.089		
0	0.035	0.037	0.036		
control 1	0.432	0.457	0.445		
control 2	0.066	0.074	0.070		
Sample 1	2.141	2.098	2.120		
sample 2	0.213	0.254	0.573		
sample 3	0.088	0.090	0.089		
sample 4	0.179	0.173	0.176		
sample 5	0.093	0.091	0.092		
sample 6	0.038	1.280	0.659		
sample 7	0.842	0.931	0.887		

Anti-PR3 ELISA

units	OD1	OD2	Mean	Units from graph	Comment
300	1.986	1.878	1.932		
100	0.954	1.057	1.006		
30	0.609	0.638	0.624		
10	0.257	0.249	0.253		
3	0.112	0.114	0.113		
0	0.050	0.052	0.051		
control 1	0.803	0.789	0.796		

control 2	0.101	0.097	0.099
sample 1	0.113	0.134	0.124
sample 2	0.078	0.080	0.079
sample 3	1.584	1.626	1.605
sample 4	0.164	0.148	0.156
sample 5	0.253	0.257	0.255
sample 6	0.312	0.308	0.310
sample 7	0.704	0.711	0.708

Clinical details and reporting

Patient	Gender	Age (years)	Clinical details	ANCA Immunofluorescence	Report
1	M	54	Pulmonary infiltrates & rash - ?vasculitis	P-ANCA positive	
2	F	48	pain in joints	Obscured by ANA	
3	M	49	Acute renal failure	C-ANCA	
4	M	35	?Irritable bowel	Atypical P-ANCA	
5	M	68	?Wegener's	Negative	
6	F	38	RA vasculitis	Negative	
7	M	26	Acute renal failure. Haemoptysis Anti-GBM positive	P-ANCA positive	

Question A3. Functional complement assays

Question

You are provided with the raw data (well diameters) from two commercial assays for the assessment of functional complement pathways. These are both founded on the principle of red cell lysis in agarose gel media (haemolytic complement assays for the classical (CH50) and alternate (AP50) pathways).

You are asked to construct standard curves and interpolate data accordingly. You are provided with brief details on the samples received. Comment on the performance of the assay and provide interpretive comment on the samples.

CH50				
Sample	Value (%normal)	Diameter (mm)	Age/Gender	Clinical details
Standard 1	120	9.8		
Standard 2	60	7.5		
Standard 3	30	5.4		
Control	Expected range 90 – 110%	8.9		
Patient 1		6.2	6/F	septic
Patient 2		8.3	13/M	Meningitis x3
Patient 3		8.1	32/F	SLE
Patient 4		8.7	4/F	?immunodeficiency
Patient 5		10.0	35/M	Father of patient 6 Familial HUS?
Patient 6		No lysis	5/M	Son of patient 5 Familial HUS?
Patient 7		5.0	55/F	Recurrent infection (sample received by first class post)

AP50				
Sample	Value (%normal)	Diameter (mm)	Age/Gender	Clinical details
Standard 1	120	7.9		
Standard 2	60	4.3		
Standard 3	30	3.3		
Control	Expected range 65 – 80%	5.0		
Patient 1		3.5	6/F	septic
Patient 2		No lysis	13/M	Meningitis x3
Patient 3		4.8	32/F	SLE
Patient 4		6.2	4/F	?immunodeficiency
Patient 5		7.0	35/M	Father of patient 6 Familial HUS?
Patient 6		No lysis	5/M	Son of patient 5 Familial HUS?
Patient 7		4.0	55/F	Recurrent infection (sample received by first class post)

Clinical results

	CH50	AP50	Notes
Control	96	72	
Patient 1	42	36	
Patient 2	80	<30	
Patient 3	76	68	
Patient 4	92	92	
Patient 5	>120	104	
Patient 6	No lysis	No lysis	
Patient 7	<30	52	

Question B4. Flow Cytometry

You are provided with a short history, laboratory results and flow cytometry plots. For each case a scatter plot is provided and associated 2-colour flow cytometry plots gated on lymphoid cells.

For each of the 5 cases below please provide

- 1) Provide a short interpretation of the data provided,
- 2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary
- 3) Potential diagnoses.

Case 1

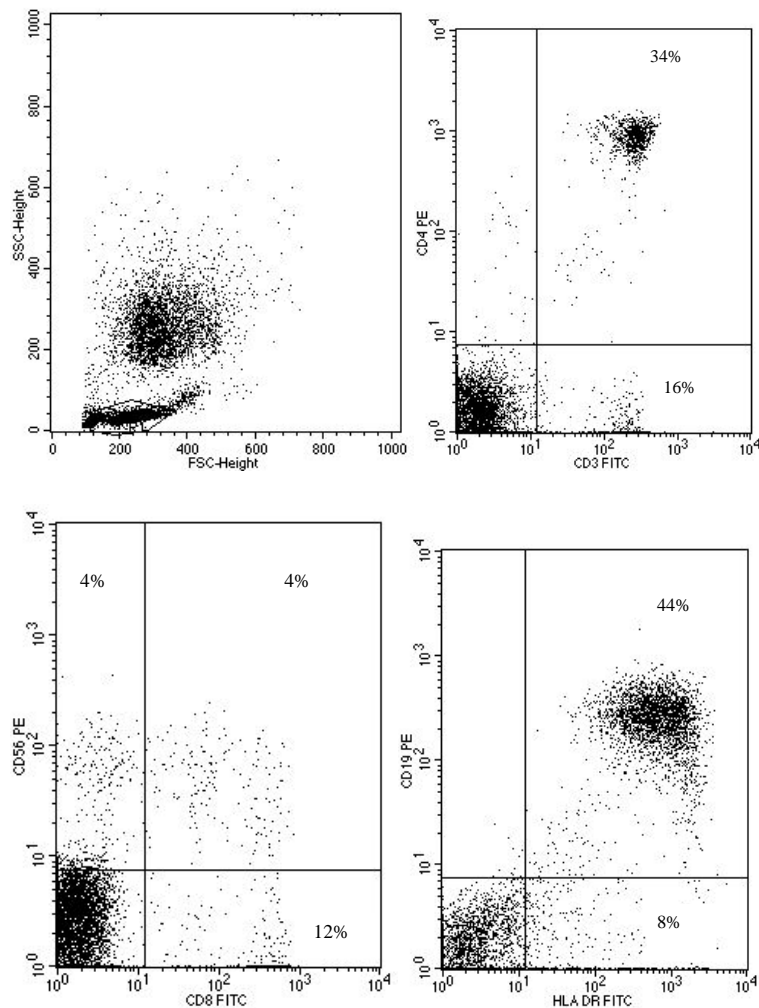
A 54-year-old male is referred from general practice with a history of recurrent chest infections. As part of the investigation immunoglobulins were measured:

IgG = 2.4g/l (Reference range 6.8-15.6g/l)

IgA = 0.12g/l (Reference range 1.0-5.0g/l)

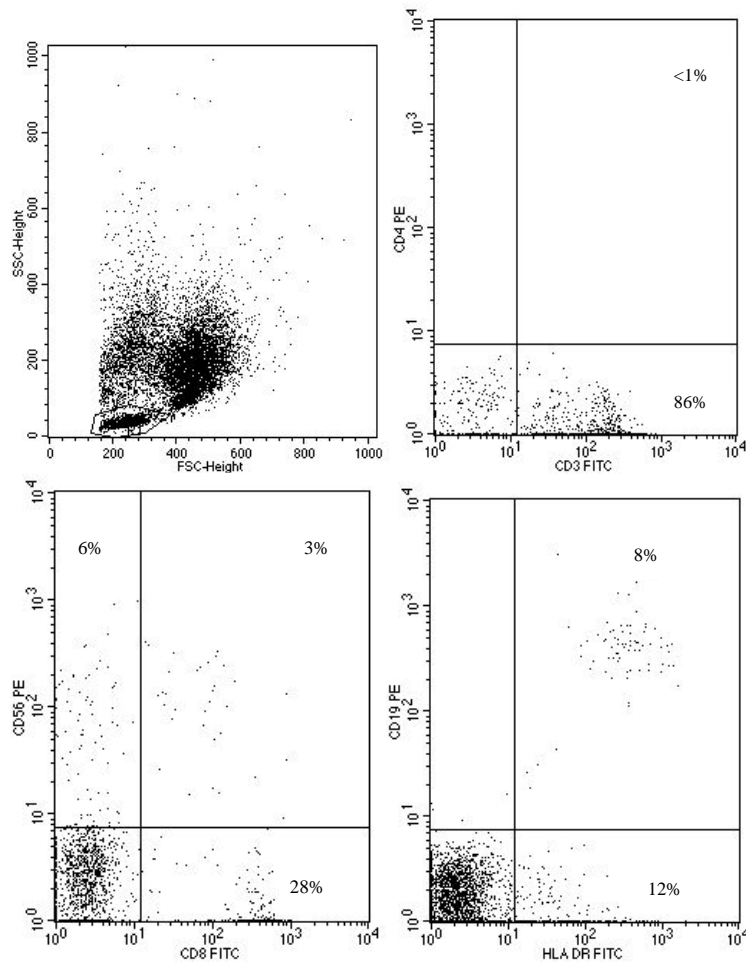
IgM = 1.6g/l (Reference range 0.5-2.8 g/l)

Flow cytometry was performed, total lymphocyte count $4.6 \times 10^9/l$:



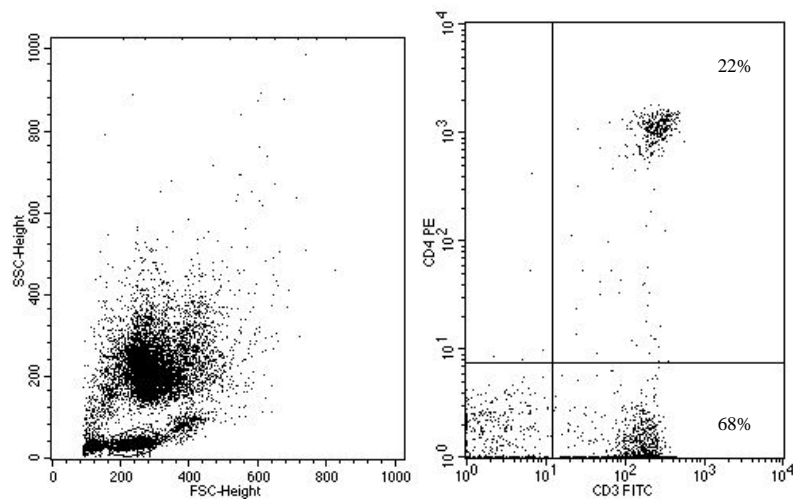
Case 2

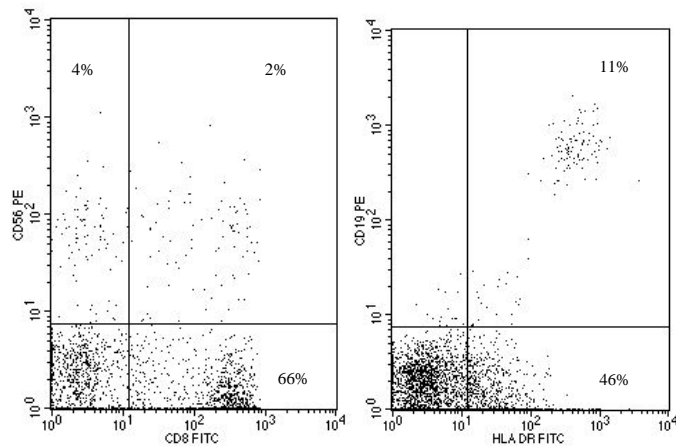
A 24-year-old female is referred with a history of recurrent oral candidiasis. As part of the laboratory investigation flow cytometry was performed, total lymphocyte count $1.6 \times 10^9/l$:



Case 3

A 28-year-old male is referred with a history of recurrent oral candidiasis. As part of the laboratory investigation flow cytometry was performed, total lymphocyte count $0.9 \times 10^9/l$:



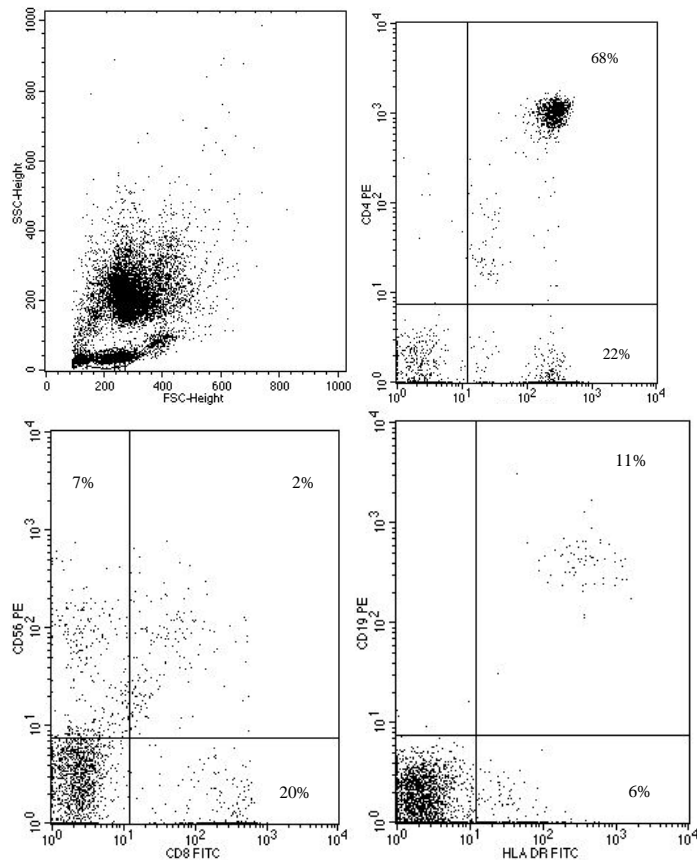


Case 4

A 6-month-old male is admitted in respiratory distress. A previous male sibling died at a similar age from pneumonia. As part of the investigation, immunoglobulins are performed:

IgG = 0.3g/l (Reference range 2.9-8.5g/l)
 IgA = <0.05g/l (Reference range 0.1-0.5g/l)
 IgM = 0.26g/l (Reference range 0.1-0.7 g/l)

Flow cytometry was performed, total lymphocyte count $13.9 \times 10^9/l$:

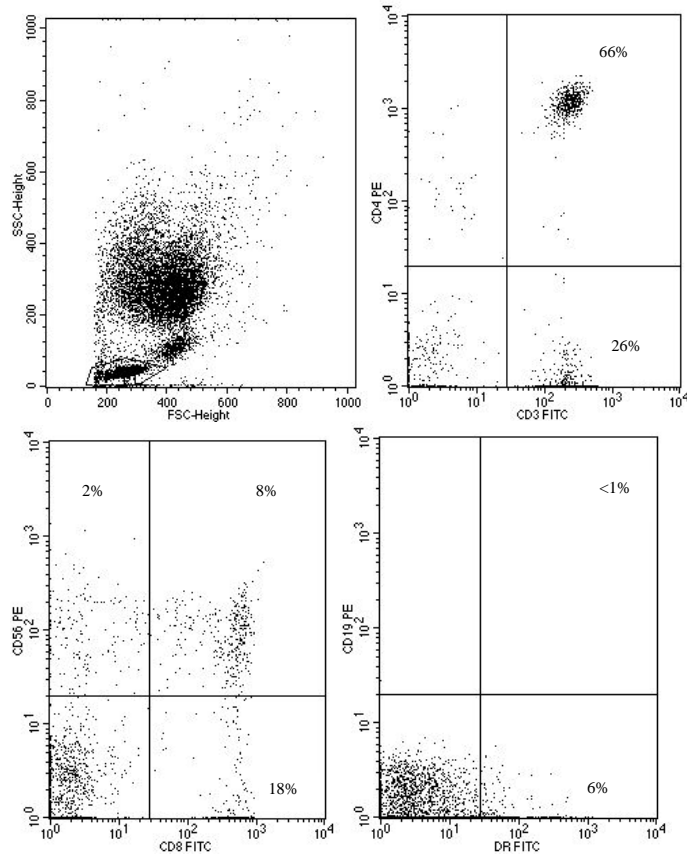


Case 5

A 6-year-old male is referred with a history of recurrent ear infections causing excessive loss in school time. There is no family history of recurrent infections.

IgG = 2.6 g/l (Reference range 6.8 – 15.6g/l)
IgA = 0.15g/l (Reference range 0.4 – 2.4g/l)
IgM = 0.1g/l (Reference range 0.5 – 2.1 g/l)

Flow cytometry was performed, total lymphocyte count $3.6 \times 10^9/l$:



Question B5. Reporting

The following are simulations of printed reports for clinical approval before sending to the requestor. Please supply appropriate clinical comment and indicate further immunological investigations required

Question A:

Name	Patient 1	Age/Sex	66 / M
Source	Rheumatology		
Clinical Details; RA, rash			
		reference ranges	
C3	0.63 g/L	0.8 - 1.6	
C4	0.08 g/L	0.15 - 0.55	
Rheumatoid Factor	878 IU/mL	<10	
Autoimmune profile	Antinuclear antibody positive		

Question B:

Name	Patient 2	Age/Sex	12/ M
Source	Pediatric Nephrology		
Clinical Details; Acute renal failure			
		reference ranges	
C3	0.33 g/L	0.8 - 1.6	
C4	0.43 g/L	0.15 - 0.55	
ANCA	negative		
Autoimmune profile	negative		

Question C:

Name	Patient 3	Age/Sex	29/ F
Source	Fertility clinic		
Clinical Details; recurrent miscarriage			
		reference ranges	
IgG anti-cardiolipin	3 AU	0-14	
IgM anti-cardiolipin	38 AU	0-10	

Question D:

Name	Patient 4	Age/Sex	30/F
Source	GP		
Clinical Details; Anaemia ?cause			
IgA Anti-tissue transglutaminase	26 AU	reference ranges	<15 AU
Serum IgA	0.8		1.0 – 5.0

The Questions and Model Answers

Model answer: Section A2. Practical Simulation: ELISA data

Question

You are provided with the raw data (Optical density in duplicate (OD1 and OD2)) data on anti-MPO and anti-PR3 antibody ELISAs.

5. Construct appropriate standard curves using the graph paper provided.
6. Evaluate controls. Target values are
Anti-MPO: control 1 positive 45-65 units, control 2 negative <10
Anti-PR3: control 1 positive 50-70 units, control 2 negative <10
7. Interpolate samples using the standard curve to derive quantitative ELISA results. Interpret a result of <15 units as negative in either assay.
8. Provide interpretive comment for each sample based on the combined immunofluorescence and ELISA data.

Examiners comments

Candidates are expected to produce standard curves; to comment on the acceptability of duplicates; and to interpolate data from the graph.

- Note two poor replicate samples in anti-MPO ELISA.
- Controls are all within acceptable limits.

This answer will be marked in 2 parts:

Part 1: Curve

Pass = Appropriately constructed standard curves with derived quantitative answer within 10% of defined value

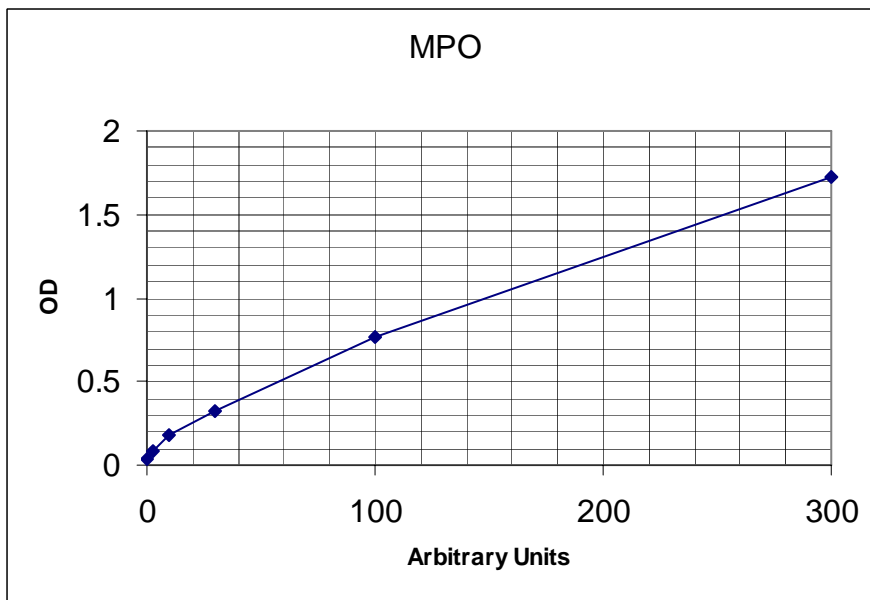
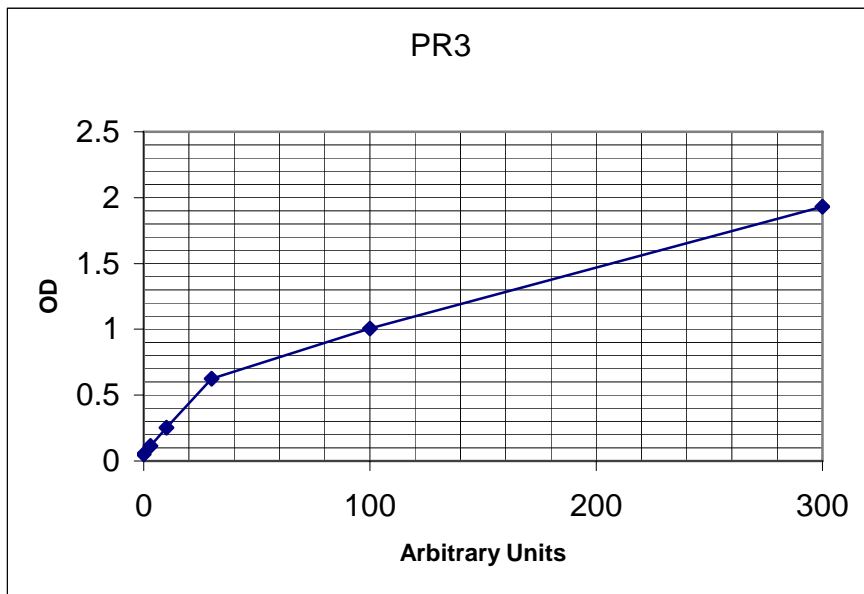
Fail = Failure to get at least 10/14 quantitative values OR
Failure to identify very poor duplicate on sample 7

Part 2: Clinical Interpretation

Pass = 5/7 correct interpretations to include sample 7 (see above) and sample 3 (important to comment on interfering ANA and possible significance of MPO ELISA positivity)

Fail = Systematic omission of interpretive comment or incorrect interpretive comment

Standard Curves



Anti-MPO ELISA

units	OD1	OD2	Mean	Units from graph	Comment
300	1.697	1.754	1.726		
100	0.771	0.760	0.766		
30	0.314	0.321	0.318		
10	0.181	0.175	0.178		
3	0.087	0.090	0.089		
0	0.035	0.037	0.036		
control 1	0.432	0.457	0.445	50	Acceptable
control 2	0.066	0.074	0.070	2	Acceptable
Sample 1	2.141	2.098	2.120	>300	Strong positive
sample 2	0.213	0.254	0.573	12	Negative

sample 3	0.088	0.090	0.089	3	Negative
sample 4	0.179	0.173	0.176	10	Negative
sample 5	0.093	0.091	0.092	3	Negative
sample 6	0.038	1.280	0.659		Very poor duplicate. Probably no sample in first well. Repeat.
sample 7	0.842	0.931	0.887	128	Relatively poor duplicate but both positive. Repeat if used for quantification (e.g.monitoring therapy)

Anti-PR3 ELISA

units	OD1	OD2	Mean	Units from graph	Comment
300	1.986	1.878	1.932		
100	0.954	1.057	1.006		
30	0.609	0.638	0.624		
10	0.257	0.249	0.253		
3	0.112	0.114	0.113		
0	0.050	0.052	0.051		
control 1	0.803	0.789	0.796	60	Acceptable
control 2	0.101	0.097	0.099	2	Acceptable
sample 1	0.113	0.134	0.124	4	Negative
sample 2	0.078	0.080	0.079	1	Negative
sample 3	1.584	1.626	1.605	216	Strong positive
sample 4	0.164	0.148	0.156	6	Negative
sample 5	0.253	0.257	0.255	10	Negative
sample 6	0.312	0.308	0.310	14	Negative
sample 7	0.704	0.711	0.708	47	Positive

Clinical details and reporting

Patient	Gender	Age (years)	Clinical details	ANCA Immunoflourescence <i>(reading these was part of a previous question)</i>	Report
1	M	54	Pulmonary infiltrates & rash - ?vasculitis	P-ANCA positive	Strongly positive MPO antibody with positive P-ANCA. In conjunction with the clinical history, this suggests Churg Strauss vasculitis. Other possibilities include Goodpasture's syndrome or Wegener's granulomatosis, especially if renal function is normal. Suggest check eosinophil count, anti-GBM antibody. (I would telephone this result)
2	F	48	pain in joints	Obscured by ANA	The presence of a positive ANA obscures ANCA immunoflourescence. However, the negative MPO and PR3 antibodies makes systemic vasculitis unlikely.

					Suggest further lupus serology, including ANA titre & pattern, anti-DNA antibodies and anti-ENA antibodies
3	M	49	Acute renal failure	C-ANCA	Positive C-ANCA with strongly positive anti-PR3 antibody in the context of acute renal failure is very suggestive of Wegener's granulomatosis. (I would telephone this result)
4	M	35	?Irritable bowel	Atypical P-ANCA	Atypical P-ANCA with negative anti-MPO and anti-PR3 antibody. Atypical P-ANCA are frequently found in ulcerative colitis, but their clinical significance is uncertain. This combination of antibody patterns is not suggestive of systemic vasculitis.
5	M	68	?Wegener's	Negative	Negative ANCA with negative anti-MPO and anti-PR3 antibodies makes the diagnosis of Wegener's unlikely
6	F	38	RA vasculitis	Negative	Repeat anti-MPO antibody before reporting (poor duplicates) However, ANCA is generally not useful in the investigation of RA vasculitis
7	M	26	Acute renal failure. Haemoptysis Anti-GBM positive	P-ANCA positive	P-ANCA with positive MPO (poor duplicates) and positive PR3. The anti-GBM antibody is also positive. Although dual positivity, most usually anti-GBM and anti-MPO/ANCA, can occasionally occur in both Goodpasture's syndrome and Microscopic Polyarteritis, the presence of <i>three</i> antibodies is suggestive of either laboratory error, or a heterophil or contaminating antibody. Before reporting, I would recheck all tests. If all three antibodies remain positive, I would check serum IgM, protein electrophoresis and cryoglobulins.

Model Answers A3. Functional complement assays

Question

You are provided with the raw data (well diameters) from two commercial assays for the assessment of functional complement pathways. These are both founded on the principle of red cell lysis in agarose gel media (haemolytic complement assays for the classical (CH50) and alternate (AP50) pathways).

You are asked to construct standard curves and interpolate data accordingly. You are provided with brief details on the samples received. Comment on the performance of the assay and provide interpretive comment on the samples.

CH50				
Sample	Value (%normal)	Diameter (mm)	Age/Gender	Clinical details
Standard 1	120	9.8		
Standard 2	60	7.5		
Standard 3	30	5.4		
Control	Expected range 90 – 110%	8.9		
Patient 1		6.2	6/F	septic
Patient 2		8.3	13/M	Meningitis x3
Patient 3		8.1	32/F	SLE
Patient 4		8.7	4/F	?immunodeficiency
Patient 5		10.0	35/M	Father of patient 6 Familial HUS?
Patient 6		No lysis	5/M	Son of patient 5 Familial HUS?
Patient 7		5.0	55/F	Recurrent infection (sample received by first class post)

AP50				
Sample	Value (%normal)	Diameter (mm)	Age/Gender	Clinical details
Standard 1	120	7.9		
Standard 2	60	4.3		
Standard 3	30	3.3		
Control	Expected range 65 – 80%	5.0		
Patient 1		3.5	6/F	septic
Patient 2		No lysis	13/M	Meningitis x3
Patient 3		4.8	32/F	SLE
Patient 4		6.2	4/F	?immunodeficiency
Patient 5		7.0	35/M	Father of patient 6 Familial HUS?
Patient 6		No lysis	5/M	Son of patient 5 Familial HUS?
Patient 7		4.0	55/F	Recurrent infection (sample received by first class post)

Examiners comments

Candidates are expected to produce standard curves and to interpolate data from the graph.

This question will be marked in 2 parts:

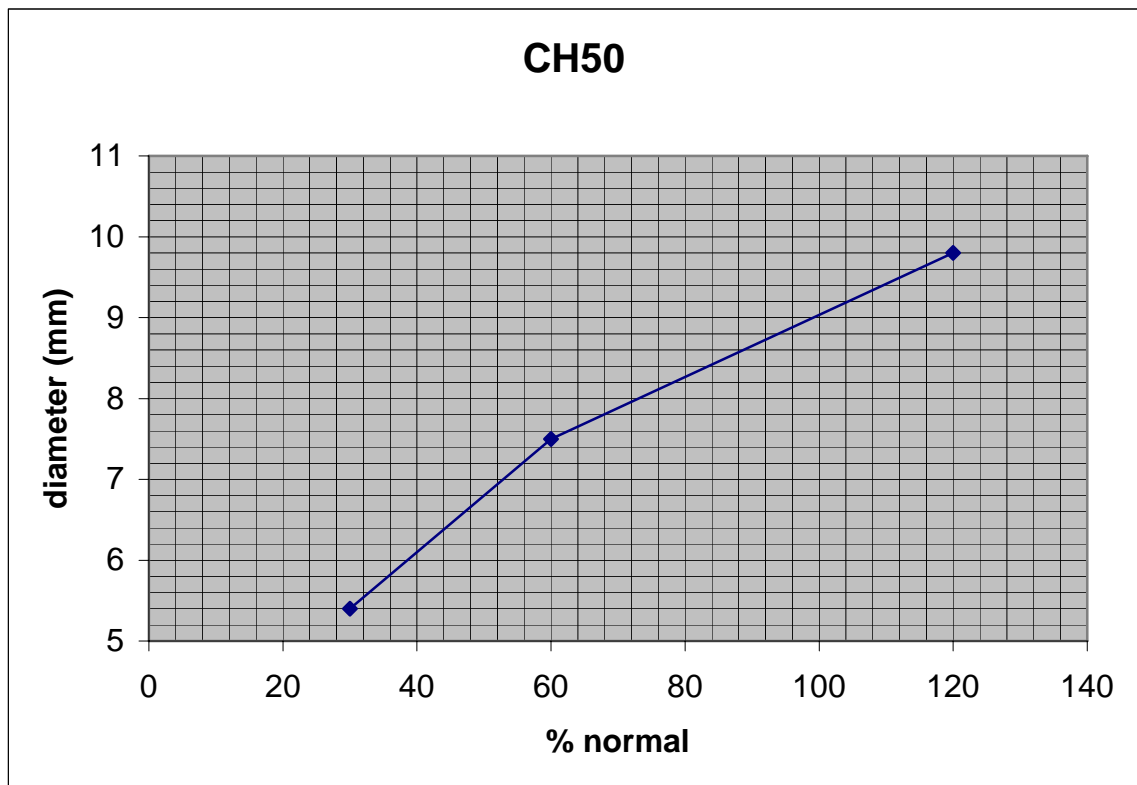
Part 1 Curve Pass = Appropriately construct standard curves and derive quantitative answer within 10% of defined value

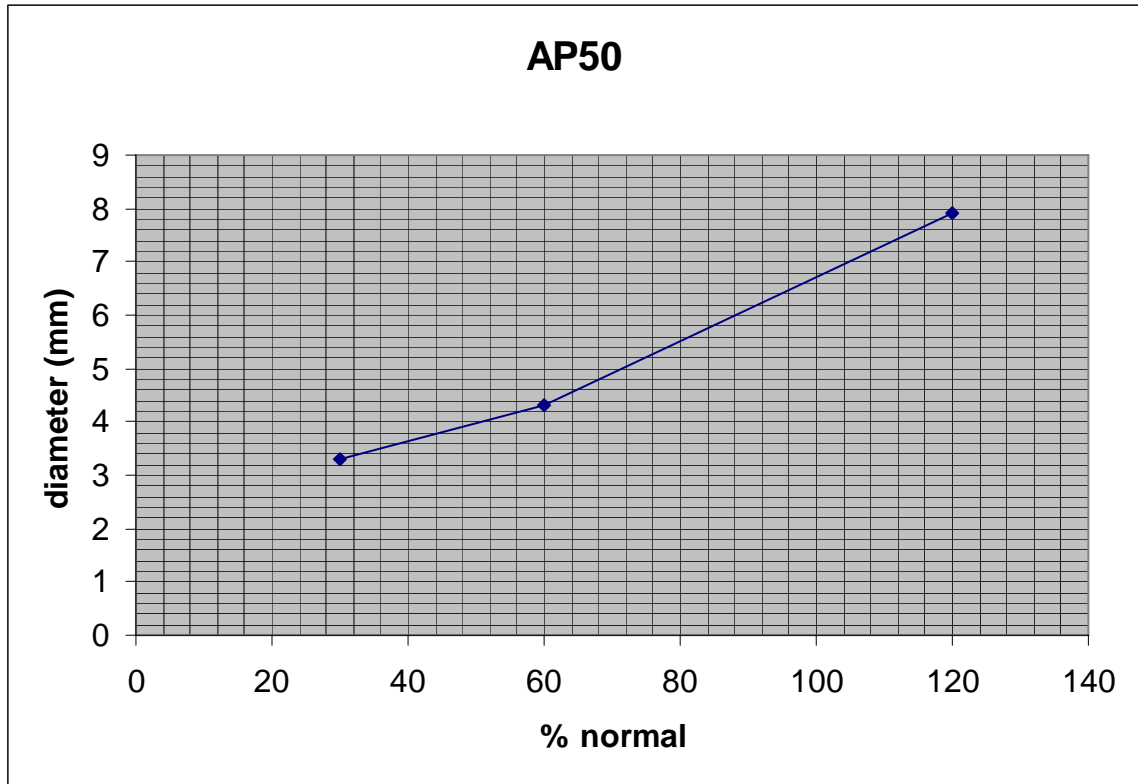
Fail = Failure to get at least 10/14 quantitative values

Part 2 Clinical Interpretation Pass = Patient 2 suspect alternate pathway defect.
Patient 5 not complement deficient.
Patient 6 atypical results in view of family history needs repeat.
Patient 7 atypical results repeat.

Fail = Failure to identify 3 of 4 above.

Standard curve





Clinical results

	CH50	AP50	Notes
Control	96	72	Both controls acceptable.
Patient 1	42	36	Results indicative of activation of both classical and alternate pathways. This is consistent with active infection. Suggest repeat when well if complement deficiency considered
Patient 2	80	<30	Absent alternate pathway. In a patient with 3 episodes of meningitis this is a very significant result. Suggest repeat on a fresh sample – if confirmed, check individual alternative pathway components, particularly properdin
Patient 3	76	68	Normal result. This is an insufficiently accurate assay for SLE disease monitoring – suggest C3 and C4 quantification
Patient 4	92	92	Normal
Patient 5	>120	104	Normal. In a patient with familial HUS, the most common pattern is an alternate pathway defect (factor H or I)
Patient 6	No lysis	No lysis	Unexpected result – was the sample applied to plate? Repeat before result reported.
Patient 7	<30	52	Undetectable CH50 and low AP50 is probably the result of delayed sample transit. Suggest repeat on a fresh (<24hr) sample. Please phone to discuss how best to transport the sample to the laboratory.

Model Answers B4. Flow Cytometry (Overall flow section pass = 4 of 5 cases correct)

Question

You are provided with a short history, laboratory results and flow cytometry plots. For each case a scatter plot is provided and associated 2-colour flow cytometry plots gated on lymphoid cells.

For each of the 5 cases below please provide

- 1) Provide a short interpretation of the data provided,
- 2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary
- 3) Potential diagnoses.

Case 1

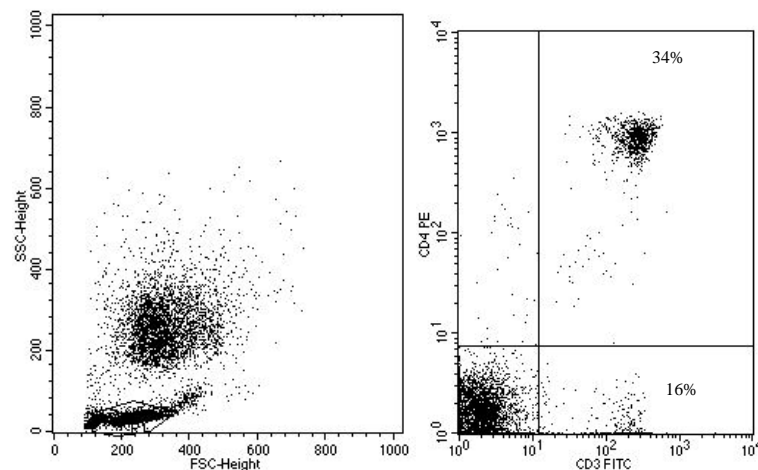
A 54-year-old male is referred from general practice with a history of recurrent chest infections. As part of the investigation immunoglobulins were measured:

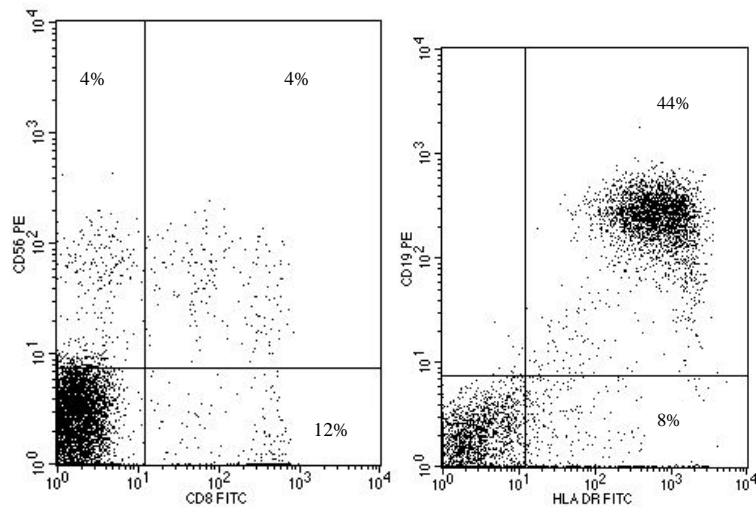
IgG = 2.4g/l (Reference range 6.8-15.6g/l)

IgA = 0.12g/l (Reference range 1.0-5.0g/l)

IgM = 1.6g/l (Reference range 0.5-2.8 g/l)

Flow cytometry was performed, total lymphocyte count $4.6 \times 10^9/l$:





1) Provide a short interpretation of the data provided,

- Low serum IgG and IgA with normal IgM
- Increased number of CD19+HLA-DR+ cells i.e. B cells
- Normal total lymphocyte count.
- In a patient of this age, this pattern is suggestive of hypogammaglobulinaemia secondary to B cell malignancy

2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary

- Serum and urine electrophoresis.
- Kappa and lambda staining of B cells to identify clonal expansion
- Bone marrow aspirate, CT scanning may be indicated depending upon the results of the above
- For bonus points: additional markers for B cell malignancy including CD5, CD10, CD79b, CD103.

3) Potential diagnoses

- Chronic lymphocytic leukaemia
- Non-Hodgkin's lymphoma

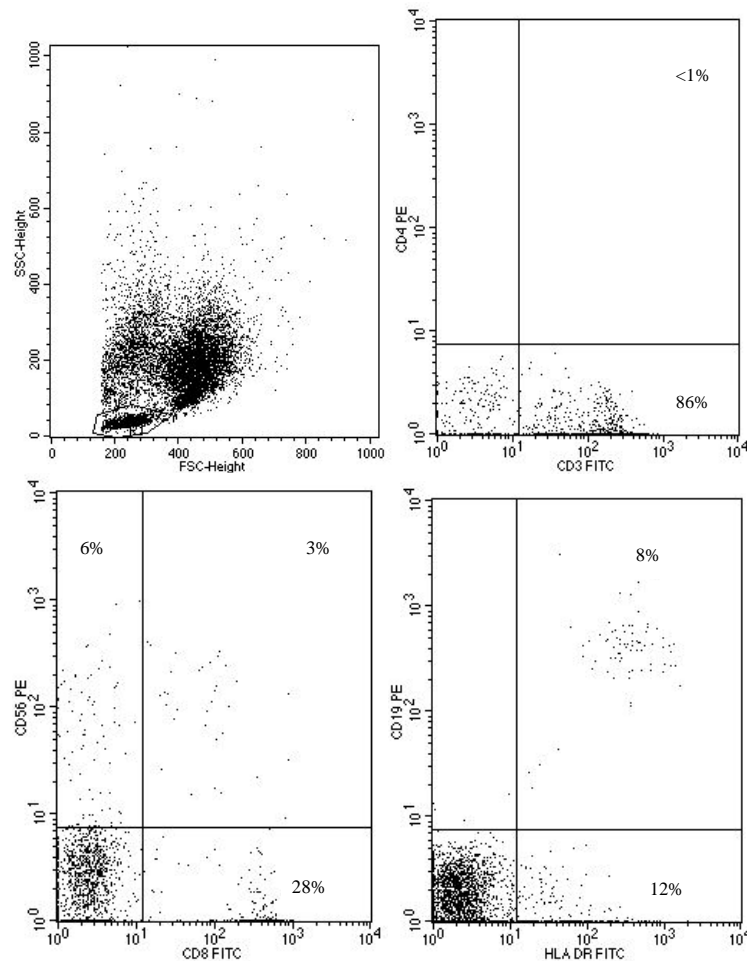
Examiners comments

Pass = Identification of hypogammaglobulinaemia with raised B cells
?haematological malignancy.

Fail = No comment on possibility of clonal B cell population.

Case 2

A 24-year-old female is referred with a history of recurrent oral candidiasis. As part of the laboratory investigation flow cytometry was performed, total lymphocyte count $1.6 \times 10^9/l$:



1) Provide a short interpretation of the data provided,

- Normal total lymphocyte count
- Absolutely no CD4+ cells
- CD3+ cells = 86% but CD4 cells + CD8+CD56- cells = 28%
- This is suggestive of laboratory error (omission of anti-CD4 reagents)

2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary

- Repeat assay

3) Potential diagnoses

- Laboratory error
- An alternative explanation could be expansion of a $\gamma\delta$ or double null T cell population, but given the complete absence of CD4 cells, laboratory error is much more likely.

Examiners comments

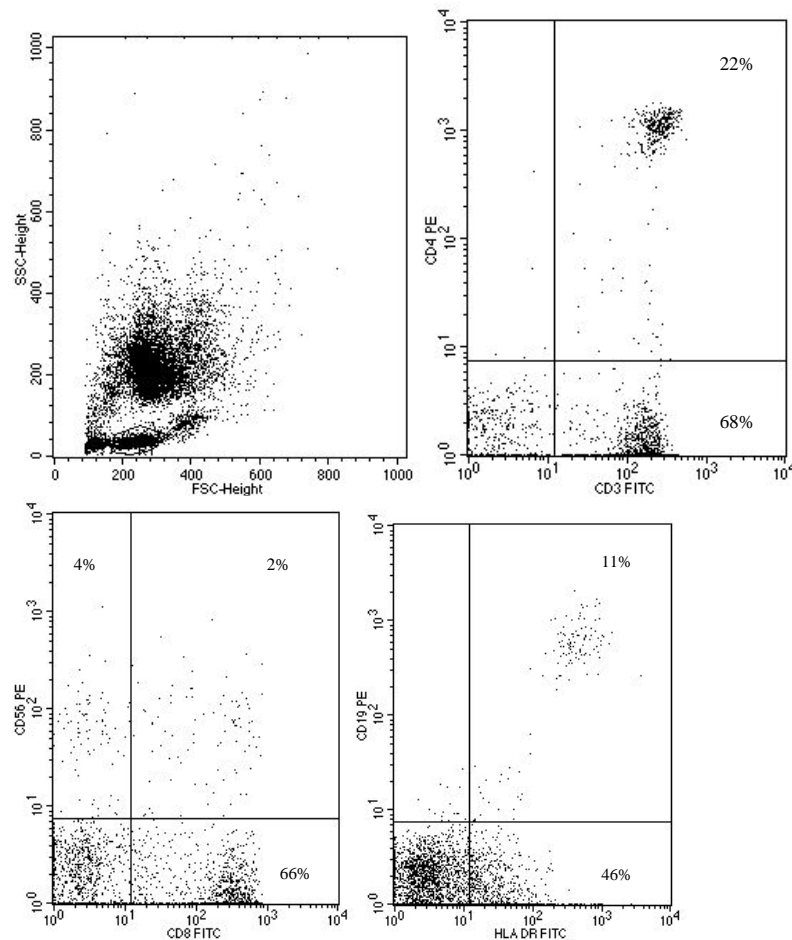
Key Points: CD3 does not equal CD4 + CD8. Consider technical problem or null population ($\gamma\delta$). Needs repeat.

Pass = CD3 does not equal CD4 + CD8. Needs repeat.

Fail = Identification of low CD4 count as caused by HIV.

Case 3

A 28-year-old male is referred with a history of recurrent oral candidiasis. As part of the laboratory investigation flow cytometry was performed, total lymphocyte count $0.9 \times 10^9/l$:



1) Provide a short interpretation of the data provided,

- Low total lymphocyte count
- Total number CD4+ cells = $22 \times 0.9 = 0.198 \times 10^9/l$
- Reversal of CD4:CD8 ratio

2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary

- HIV antibody test; if positive follow with viral load PCR

3) Potential diagnoses

- HIV infection
- CD4 lymphopenia secondary to corticosteroids, immunosuppressive drugs, chronic viral infection especially CMV
- Diagnosis of exclusion: idiopathic CD4 lymphopenia

Examiners comments

Key Points: Reversed CD4:CD8 with low absolute CD4 count. ? HIV

Pass = Identification of Reversed CD4:CD8 with low absolute CD4 count. ? HIV

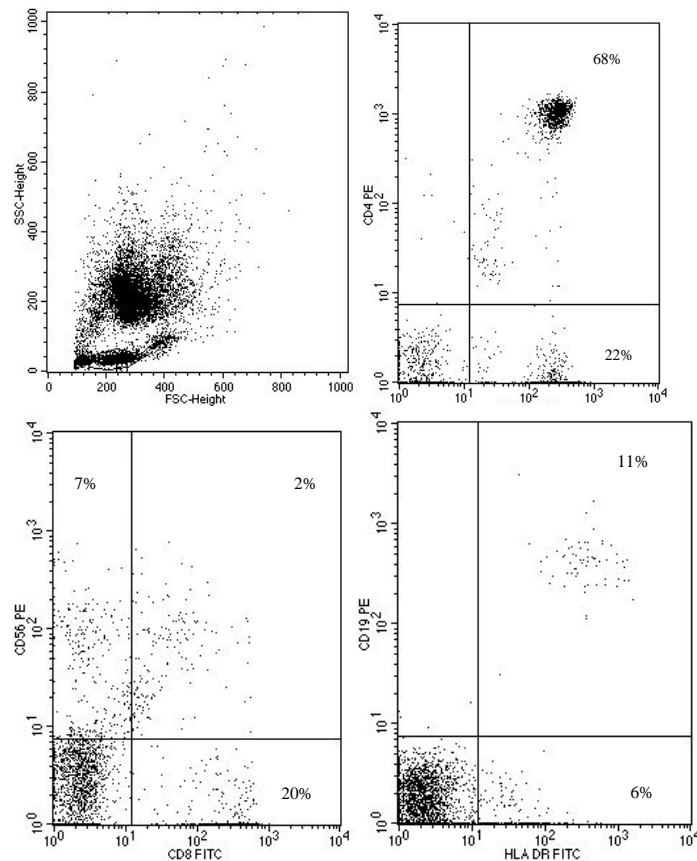
Fail = No consideration of HIV

Case 4

A 6-month-old male is admitted in respiratory distress. A previous male sibling died at a similar age from pneumonia. As part of the investigation, immunoglobulins are performed:

IgG = 0.3g/l (Reference range 2.9-8.5g/l)
IgA = <0.05g/l (Reference range 0.1-0.5g/l)
IgM = 0.26g/l (Reference range 0.1-0.7 g/l)

Flow cytometry was performed, total lymphocyte count $13.9 \times 10^9/l$:



1) Provide a short interpretation of the data provided,

- History suggestive of immune deficiency, possibly X-linked
- Profound hypogammaglobulinaemia with absent IgA but normal IgM
- Normal limited flow cytometry

2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary

- CD40 and CD40 Ligand assessment
- T cell proliferation studies
- Anti-Tetanus antibody determination

3) Potential diagnoses

- Hyper IgM syndrome (despite normal IgM)
- Severe combined immune deficiency

- (Hypogammaglobulinaemia of infancy should only be considered after all other possibilities have been excluded, given the family history)

Examiners comments

Key Points: Flow normal. Strong history ? X Linked. Hypogammaglobulinaemia with normal IgM. Needs more tests ? SCID ? Hyper IgM.

Pass = Suspect inherited immune deficiency. Suggest appropriate further tests (Hyper IgM, T cell Function)

Fail = Identification of abnormal flow cytometry features. Failure to identify possibility of inherited immune deficiency requiring further characterization.

Case 5

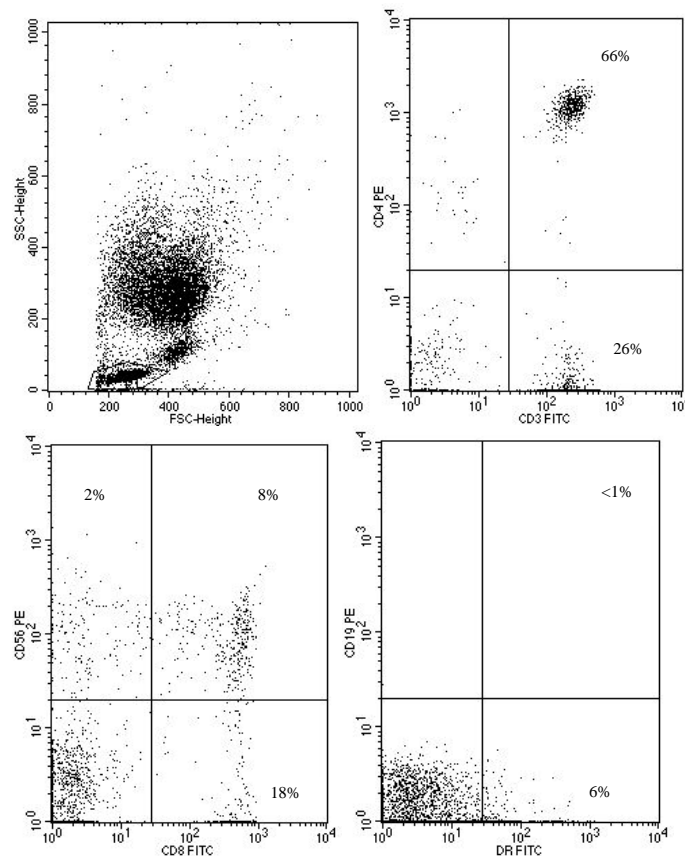
A 6-year-old male is referred with a history of recurrent ear infections causing excessive loss in school time. There is no family history of recurrent infections.

IgG = 2.6 g/l (Reference range 6.8 – 15.6g/l)

IgA = 0.15g/l (Reference range 0.4 – 2.4g/l)

IgM = 0.1g/l (Reference range 0.5 – 2.1 g/l)

Flow cytometry was performed, total lymphocyte count $3.6 \times 10^9/l$:



1) Provide a short interpretation of the data provided,

- History of recurrent infections
- Moderate hypogammaglobulinaemia with low IgA and low IgM
- Absent CD19+ B cells

2) Further laboratory tests (Immunology & other pathology tests if appropriate) that you feel are necessary

- Confirm absence of B cells on additional sample and with additional B cell antibodies (CD20, CD22)
- Antibodies to Tetanus, Hib, Measles, diphtheria (if available); anti-blood group antibody determination
- Btk analysis

3) Potential diagnoses

- Bruton's agammaglobulinaemia

Examiners comments

Pass = Identification of, pan hypogammaglobulinaemia, absent B cell suspect XLA
Fail = Failure to recognize absent B cells with hypogammaglobulinaemia. Failure to consider XLA

B5. Reporting

The following are simulations of printed reports for clinical approval before sending to the requestor. Please supply appropriate clinical comment and indicate further immunological investigations required

Examiners comment: To pass this section, 3 of 4 questions must be answered correctly

Question A:

Name	Patient 1	Age/Sex	66 / M
Source	Rheumatology		
Clinical Details; RA, rash			
		reference ranges	
C3	0.63 g/L	0.8 - 1.6	
C4	0.08 g/L	0.15 - 0.55	
Rheumatoid Factor	878 IU/mL	<10	
Autoimmune profile	Antinuclear antibody positive		
<u>Comment</u> Note low C4: in a patient with RA, consider cryoglobulin or rheumatoid vasculitis. Alternative diagnoses include RA/SLE overlap etc. Please phone to discuss			
<u>Further tests</u> 1) Cryoglobulins 2) anti-DNA antibodies, anti-ENA, hepatitis C antibody, CRP			

Pass = Identification of at least 2 of the following possible diagnoses: cryoglobulin, rheumatoid vasculitis, RA/SLE overlap. Identification of 2 of 4 follow up tests to include cryoglobulin, anti-DNA antibody, anti-ENA antibody, hepatitis C antibody
Fail = Failure to consider cryoglobulin.

Question B:

Name	Patient 2	Age/Sex	12/ M
Source	Pediatric Nephrology		
Clinical Details; Acute renal failure			
		reference ranges	
C3	0.33 g/L	0.8 - 1.6	
C4	0.43 g/L	0.15 - 0.55	
ANCA	negative		
Autoimmune profile	negative		
<u>Comment</u> ***** A significant result***** Note low C3 with normal C4. Does this child have post-streptococcal glomerulonephritis? Other possibilities include gram negative sepsis.			

C3 nephritic factor to follow
(suggest phone this result to discuss)

Further tests

- 1) C3 nephritic factor
- 2) ASO titre, C3 degradation products, CRP

Pass = Identify low C3; identify at least one of post-strep GN and C3 nephritic factor as possible diagnoses; and recommend C3 nephritic factor.

Fail = To consider neither diagnosis

Question C:

Name	Patient 3	Age/Sex	29/ F
Source	Fertility clinic		
Clinical Details; recurrent miscarriage			
		reference ranges	
IgG anti-cardiolipin	3 AU	0-14	
IgM anti-cardiolipin	38 AU	0-10	
<u>Comment</u> Raised IgM anti-cardiolipin antibody. This may indicate primary or secondary anti-phospholipid syndrome, but this result should be confirmed by repeat testing in 6-8 weeks as false positive results are common.			
<u>Further tests</u> 1) Repeat IgG and IgM anti-cardiolipin antibodies 2) Lupus anticoagulant, Anti-nuclear antibody, complement C3 and C4			

Pass = Identification of possible antiphospholipid syndrome and further tests required

Fail = Failure to repeat cardiolipin at later time point.

Question D:

Name	Patient 4	Age/Sex	30/F
Source	GP		
Clinical Details; Anaemia ?cause			
		reference ranges	
IgA Anti-tissue transglutaminase	26 AU	<15 AU	
Serum IgA	0.8	1.0 – 5.0	
<u>Comment</u> Weak positive IgA anti-tissue transglutaminase antibody with borderline low serum IgA. This may indicate coeliac disease but should be confirmed by further testing			
<u>Further tests</u> Anti-endomysial antibody. If positive, the diagnosis of coeliac disease should be confirmed by duodenal biopsy			

Pass = Consideration of coeliac disease.

Fail = To imply confirmed coeliac disease or to fail to mention coeliac disease.