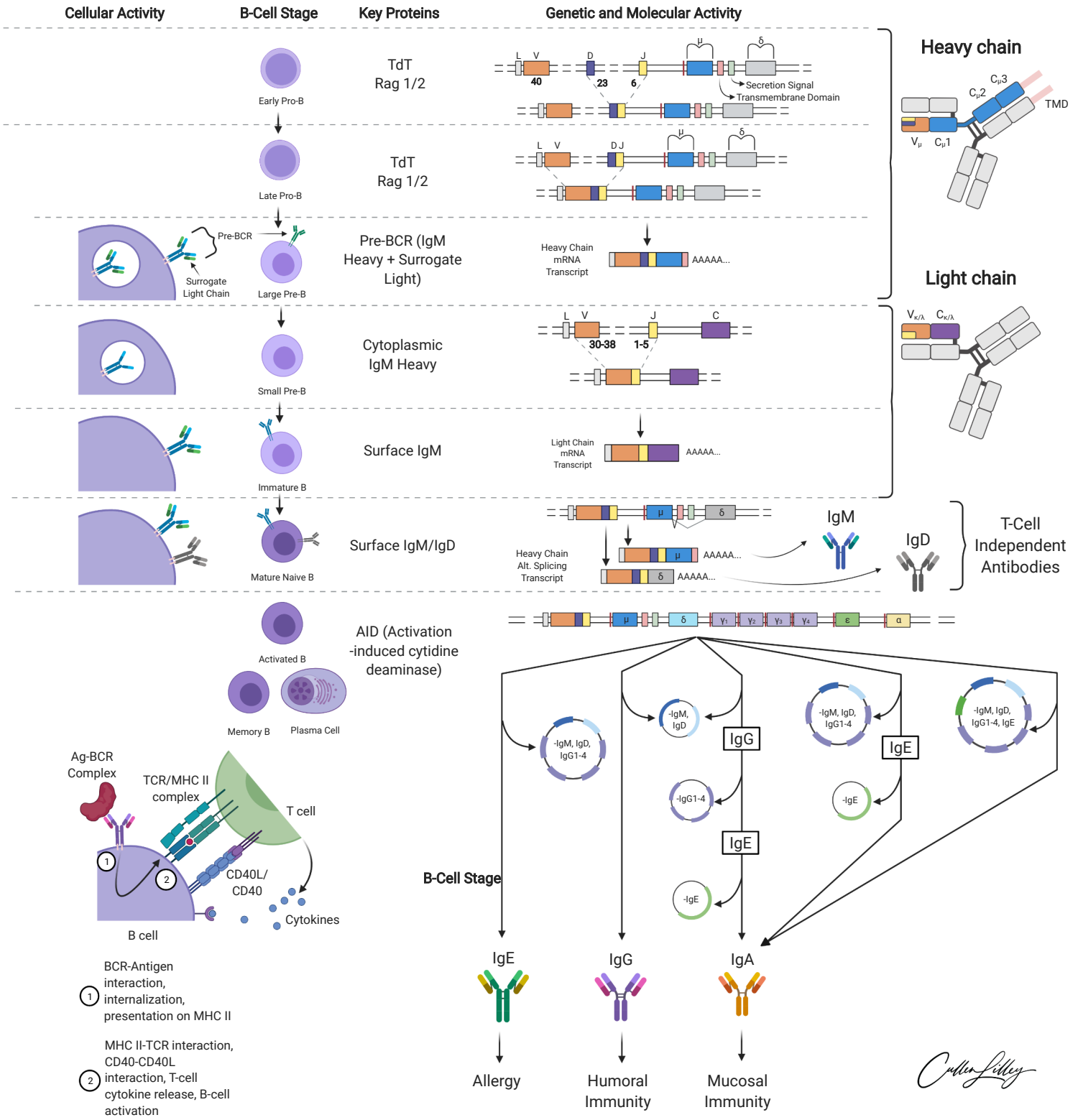
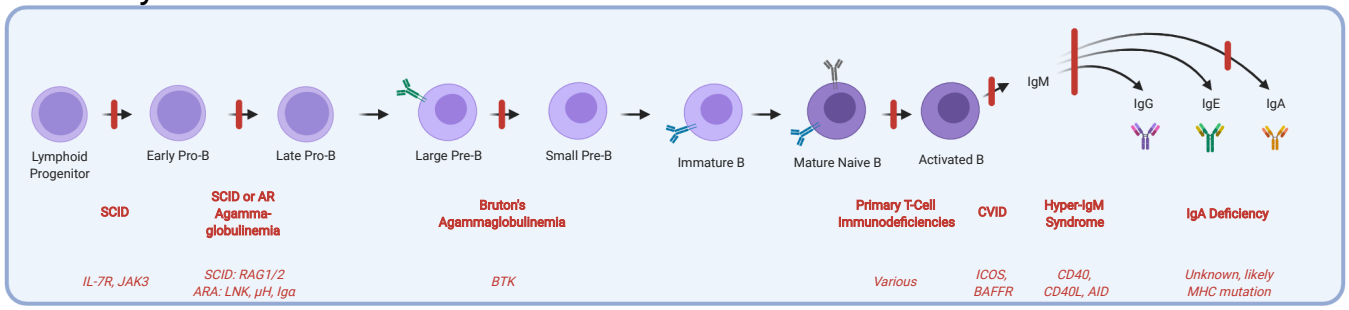
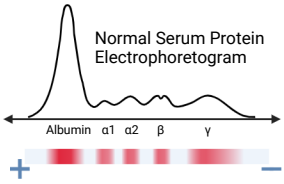
B-Cell Development and Activation



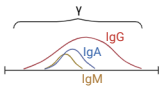
Primary B-cell Immunodeficiencies

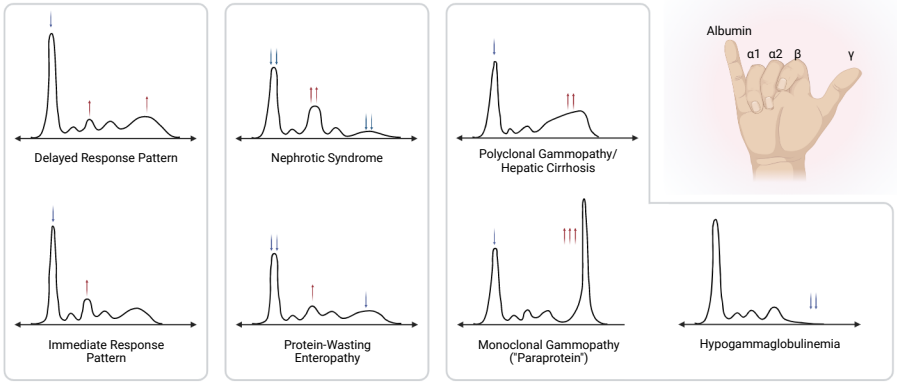


Serum Protein Electrophoresis (SPEP)



Peak	Protein Content	Normal
α1	α_1-Antitrypsin (90%), α_1-lipoprotein, and α_1-acid glycoprotein	0.1-0.3 g/dL
α2	α_2-macroglobulin, haptoglobin, and ceruloplasmin	0.6-1.0 g/dL
β	transferrin, hemopexin, C3, and β-lipoproteins	0.7-1.2 g/dL
γ	IgG, IgA, IgD, IgE, and IgM	0.7-1.6 g/dL

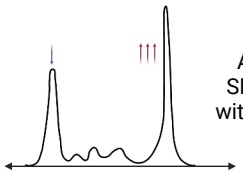




Patterns of Immune Activation | Patterns of Protein Loss | Patterns of Aberrant B-cell Function or Immunoglobulin Production

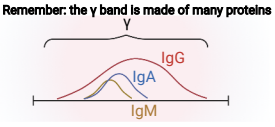
	Albumin	α1	α2	β	γ
↑	Dehydration	Inflammatory states, pregnancy	Inflammatory states, nephrotic syndrome, OCTs, corticosteroids, hyperthyroidism, adrenal insufficiency, diabetes mellitus	Hyperlipidemias, hemoglobinopathies, iron deficiency, biliary cirrhosis, carcinoma, Cushing's disease, DM, hypothyroidism, malignant HTN, nephrosis, polyarteritis nodosa, pregnancy	Polyclonal: liver disease, chronic inflammation, lymphoid malignancy, RA, connective tissue diseases, sarcoid Monoclonal: MM, MGUS, Waldenström macroglobulinemia, amyloidosis
↓	Cachexia, chronic infections, hemorrhage, burns, decreased liver synthetic function, malnutrition, nephrotic syndrome, pregnancy	α_1-antitrypsin deficiency	*in vivo* hemolysis, liver disease, malnutritionm, megaloblastic anemia, Wilson's disease	Hypo-β-lipoproteinemia, malnutrition	Agammaglobulinemia, hypogammaglobulinemia

Immunofixation Electrophoresis (IFE)



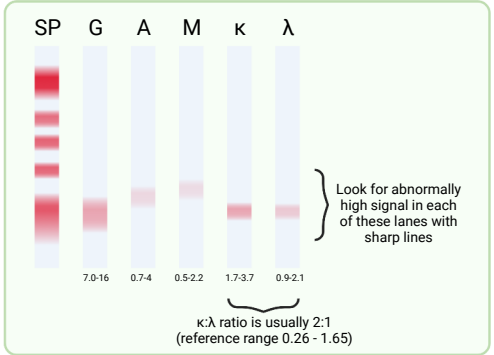
Abnormal SPEP/UPEP with "M-Spike"

Remember: the γ band is made of many proteins



We don't know if this spike is due to IgM, IgA, IgD, IgE, κ or λ

Reflex immunofixation electrophoresis



RESEARCH ARTICLE

Gamma gap thresholds and HIV, hepatitis C, and monoclonal gammopathy

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Table 2. Diagnostic performance of gamma gap for HIV using different gamma gap thresholds, N = 25,680.

Gamma gap (g/dL)	Sn, %	Sp, %	LR +	LR -	Overall AUC (95% CI)
≥ 2.5	94.8	10.5	1.1	0.5	0.80 (95% CI: 0.75, 0.85)
≥ 3.0	84.4	51.9	1.8	0.3	
≥ 3.5	59.3	88.1	5.0	0.5	
≥ 4.0	39.3	98.4	24.2	0.6	
≥ 4.5	19.3	99.6	54.1	0.8	
≥ 5.0	10.4	99.9	139.4	0.9	
≥ 5.5	4.4	100.0	283.9	1.0	

Table 3. Diagnostic performance of gamma gap for HCV using different gamma gap threshold, N = 45,134.

Gamma gap (g/dL)	Sn, %	Sp, %	LR +	LR -	Overall AUC (95% CI)
≥ 2.5	97.8	9.9	1.1	0.2	0.74 (95% CI: 0.72, 0.76)
≥ 3.0	80.8	50.2	1.6	0.4	
≥ 3.5	44.5	86.9	3.4	0.6	
≥ 4.0	19.0	97.8	8.5	0.8	
≥ 4.5	7.0	99.5	13.7	0.9	
≥ 5.0	2.6	99.8	16.3	1.0	
≥ 5.5	1.1	99.9	13.9	1.0	

Table 4. Diagnostic performance of gamma gap for MGUS using different gamma gap thresholds, N = 6,118.

Gamma gap (g/dL)	Sn, %	Sp, %	LR +	LR -	Overall AUC (95% CI)
≥ 2.5	97.6	6.4	1.0	0.4	0.64 (95% CI: 0.60, 0.69)
≥ 3.0	75.7	39.9	1.3	0.6	
≥ 3.5	39.1	80.1	2.0	0.8	
≥ 4.0	15.4	95.4	3.4	0.9	
≥ 4.5	7.7	98.9	6.9	0.9	
≥ 5.0	5.3	99.7	16.7	0.9	
≥ 5.5	3.0	99.8	17.6	1.0	

Conclusions:

- Gamma gap is not a sufficient screening tool (you'd want high sensitivity for a screen)
- An elevated gamma gap warrants further testing for HCV and HIV but not MGUS
- Many patients with HIV and HCV did not have an elevated gamma gap
- HIV and HCV stage of treatment influence the gamma gap

Limitations:

- This study was performed in defined patient populations, so patients with comorbid conditions were not assessed and there was no assessment of a mixed population (HIV, HCV, and MGUS)
- These were outpatients and none had autoimmune conditions, chronic inflammatory conditions, or chronic infections
- When the gamma gap was test further in this study
    - HIV: age > 18
    - HCV: age > 6
    - MGUS: age > 50

Original Article | Published: 30 July 2008

A Clinical Decision Rule to Aid Ordering of Serum and Urine Protein Electrophoresis for Case-Finding of Paraproteins in Hospitalized Inpatients

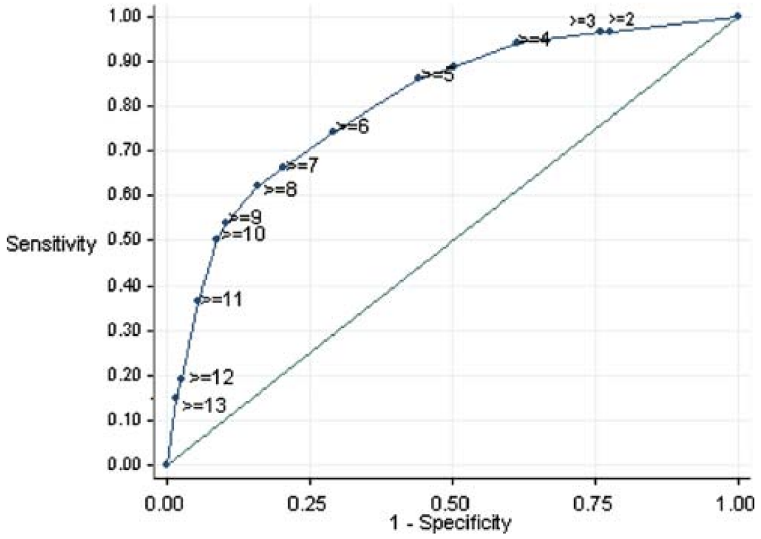
Ammarin Thakkinstian PhD, Huy Tran MB BS, FRACP, Glenn Reeves MB BS, FRACP, Stuart Murch B Med & John Attia PhD, FRCPC, FRACP

Journal of General Internal Medicine **23**, 1688–1692 (2008) | Cite this article

For MGUS use the following equation:

$$Logit\left[\frac{SPE/UPE^{+}}{SPE/UPE^{-}}\right] = -4.4+1.5xglobulin+1.1xage+0.6xhgb+0.4xsex+.2xgfr$$

Variables	OR (95% CI)	Scores
Globulin, g/l		
>41	4.5 (3.8, 5.4)	5
≤41		0
Age, years		
≥60	2.9 (2.4, 3.7)	3
<60		0
Hemoglobin, g/l		
<121	1.9 (1.5, 2.3)	2
≥121		0
Sex		
Male	1.6 (1.4, 1.9)	2
Female		0
eGFR, ml/min/1.73 m^2		
<60	1.3 (1.1, 1.5)	1
≥60		0
Total scores		0–13



Score (prob. of para-protein)	Derivation set				Validation set			
	SPE/UPE		LR^{+}(95% CI)	PPV (%)	SPE/UPE		LR^{+}(95% CI)	PPV(%)
	Positive	Negative			Positive	Negative		
0–5(Low)	207	6,537	1.0	3.1	91	2,797	1.0	3.1
6–10(Med)	303	2,205	2.5(2.4–2.7)	12.1	129	941	2.5(2.3–2.7)	12.1
≥11(High)	294	506	6.7(5.9–7.6)	36.8	127	221	6.6(5.4–79)	36.5