

# July 2014 REBELCast Episode 1 Show Notes

## Topic #1: Clinically Important Biphasic Anaphylaxis

**Clinical Question:** How long do I really need to monitor a patient for who has presented with anaphylaxis and has complete resolution of symptoms after administration of medications?

### Article

Grunau BE et al. Incidence of Clinically Important Biphasic Reactions in Emergency Department Patients with Allergic Reactions or Anaphylaxis. Ann of EM 2014 63(6): 736-44. PubMed ID: [24239340](#)

**Background:** Standard teaching in Emergency Medicine holds that patients who present with allergic reactions, especially anaphylactic ones, should be monitored for 6-8 hours after symptoms resolve in order to ensure that the patient does not have a biphasic anaphylactic response. However, this recommendation is based on minimal, if any, evidence.

### Details

- Retrospective review of 430,000 patients over 5 years
- Found 2800 with allergic reactions (496 with anaphylaxis)
- 5 patients (0.18%) had significant biphasic reactions
- 2 patients had biphasic reactions during initial hospital visit
- 3 patients had significant biphasic anaphylaxis after discharge (28, 35 and 143 hours after initial presentation)
- 0 patients died from biphasic anaphylaxis

### Weaknesses

- Retrospective – outcomes known to researchers
- Follow up – possible that patients represented elsewhere but unlikely given the healthcare system this study was performed in

**For More Information, see also:** [The SGEM #57](#): Should I Stay or Should I Go (Biphasic Anaphylactic Response)

## **Bonus Article**

Rohacek M, Edenhofer H, Bircher A. Biphasic anaphylactic reactions: occurrence and mortality. Eur J All Clin Imm 2014; 69(6): 791-7. PubMed ID: [24725226](#)

### Details

- Retrospective review of 300,000 patients
- Found 1300 with allergic reactions (495 with anaphylaxis)
- 25 patients (4.5%) had biphasic reactions
- 12 patients (2.3%) required treatment for their biphasic reaction
- 0 patients died from biphasic anaphylaxis

### **Weaknesses**

- Retrospective – outcomes known to researchers
- Follow up – possible that patients represented elsewhere but unlikely given the healthcare system this study was performed in

Additionally, these researchers differentiate between long (> 8 hours) and short (< 8 hours) observation lengths and found no difference in the occurrence of biphasic responses.

**Clinical Bottom Line: Prolonged observation is likely unnecessary in patients who's symptoms resolve with therapy in the ED. Biphasic reactions are rare and can occur anywhere from 10 minutes up to 6 days.**

**For More Information:** [SGEM #57](#): Should I Stay or Should I Go (Biphasic Anaphylactic Response).

### **References**

1. Grunau BE et al. Incidence of Clinically Important Biphasic Reactions in Emergency Department Patients with Allergic Reactions or Anaphylaxis. Ann of EM 2014 63(6): 736-44.
2. Rohacek M, Edenhofer H, Bircher A. Biphasic anaphylactic reactions: occurrence and mortality. Eur J All Clin Imm 2014; 69(6): 791-7.

**Topic #2:** Total Lymphocyte Count as a Surrogate Marker for CD4 Count

**Clinical Question:** Can we Use Total Lymphocyte Count as a surrogate marker for CD4 Counts in HIV/AIDs patients?

**Total Lymphocyte Count (TLC) Calculation:**

TLC Calculation = (% lymphocytes x WBC count)/100

If a patient has 10% lymphocytes and a WBC count of 4000...the TLC would be (10 x4000)/100 = 400

**Article:**

Obirikorang C et al. Total Lymphocyte Count as a Surrogate Marker for CD4 Count in Resource-Limited Settings. BMC Infectious Diseases Journal 2012; 12 (128): 1 - 5.

**PMID:** 22676809

**What they did:**

An observational study of 184 patients with confirmed seropositive HIV. Blood samples were taken at the same time to estimate CD4 counts and total lymphocyte counts.

Patients were categorized into 3 categories of CD4 counts as defined by the Centers for Disease Control and Prevention (CDC):

CD4  $\geq$  500 cells/mm<sup>3</sup>

CD4 200 – 499 cells/mm<sup>3</sup>

CD4 <200 cells/mm<sup>3</sup>

There are 2 cut-offs in my mind that stick out here....CD4 <350 is typically the number used to initiate HIV therapy, and CD4 < 200 is when we as ED physicians should consider opportunistic infections.

**Patients Excluded:**

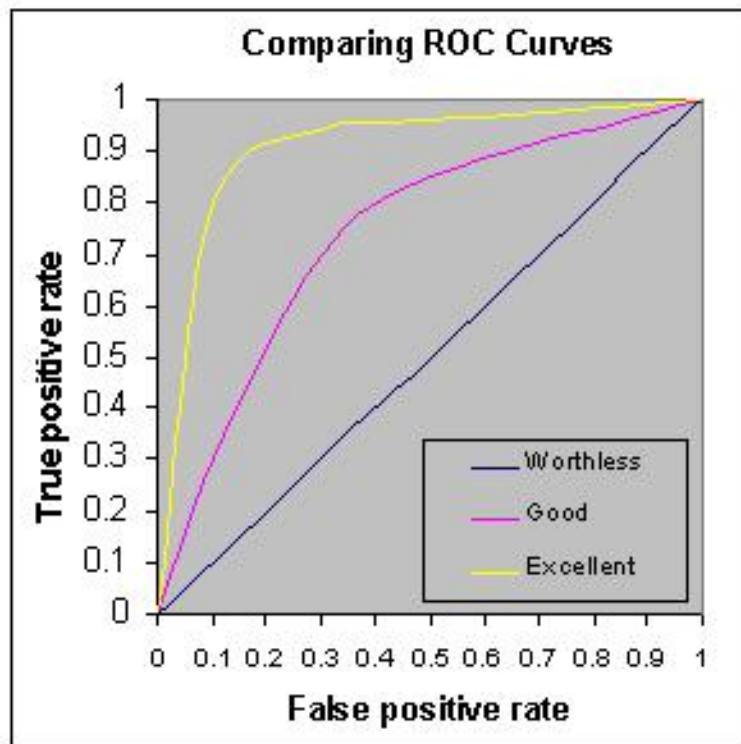
Patients on antiretroviral therapy and comorbidities such as tuberculosis, endocarditis, and acute viral infections were excluded as all of these can greatly affect hematologic counts.

### What TLC correlates with what CD4 Counts:

- TLC 1200 cells/mm<sup>3</sup> correlated with CD4 count of < 200 cells/mm<sup>3</sup> with a maximal sensitivity of 72.2%, and specificity of 100%
- TLC 1500 cells/mm<sup>3</sup> correlated with CD4 count of 200 – 499 cells/mm<sup>3</sup> with a maximal sensitivity of 96.7% and specificity of 100%
- TLC 1900 cells/mm<sup>3</sup> correlated with CD4 count of ≥ 500 cells/mm<sup>3</sup> with a maximal sensitivity of 98.5% and specificity of 100%

The above numbers were also assessed with Area Under the Curve (AUC) Analysis and the AUC of TLC predicting CD4 counts < 200 was 0.98.

### Area Under the Curve (AUC)



- Ratio of Sensitivity (True Positive Rate) vs 1 – Specificity (False Positive Rate)
- 0.5 = No better than chance

- $\geq 0.8$  = Strong predictor of identifying those within a group and those that are not
- 1 = Perfectly identifies those within a group and those that are not

## **Conflicting Reports of TLC as Surrogate for CD4:**

### **Studies consistent with:**

1. Kumarasamy N et al. Total Lymphocyte Count (TLC) is a Useful Tool for the Timing of Opportunistic Infection Prophylaxis in India and Other Resource-Constrained Countries. *J Acquir Immune Defic Syndr.* 2002; 31 (4): 378 – 83
  - 405 Patients: TLC  $< 1400$  cells/mm<sup>3</sup> sensitivity 73% and specificity 88% for CD4  $< 200$  cells/mm<sup>3</sup>.
2. Spacek et al. Total Lymphocyte Count and Hemoglobin Combined in an Algorithm to Initiate the Use of Highly Active Antiretroviral Therapy in Resource-Limited Settings. *AIDS* 2003; 17 (9): 1311 – 7.
  - 3,269 Patients: Combined TLC  $< 1200$  cells/mm<sup>3</sup> and Hb  $< 12$  g/dL had a sensitivity 70.7% and specificity of 81.7% for CD4  $< 200$  cells/mm<sup>3</sup>.
3. Badri M et al. Usefulness of Total Lymphocyte Count in Monitoring Highly Active Antiretroviral Therapy in Resource-Limited Settings. *AIDS* 2003; 17 (4): 541 – 545.
  - 266 Patients: A change in TLC had a sensitivity 73% and specificity 88% for the same decreases in CD4.

**Conclusion:** The studies above showed a Sensitivity 70.7% - 73% and Specificity 81.7% - 88% for TLC as a surrogate for CD4

### **Studies contradictory with:**

1. Daka D et al. Relationship Between Total Lymphocyte Count (TLC) and CD4 Count Among Peoples Living with HIV, Southern Ethiopia: A Retrospective Evaluation. *AIDS Res Ther* 2008, 5: 26.
  - 2,019 Patients: TLC < 1200 cells/mm<sup>3</sup> predicts CD4 count < 200 cells/mm<sup>3</sup> had a sensitivity 41% and specificity 83.5%
2. Akinola NO et al. The Search for a Predictor of CD4 Cell Count continues: Total Lymphocyte Count is Not a Substitute for CD4 Cell Count in Management of HIV-Infected Individuals in a Resource-Limited Setting. *Clin Infect Dis* 2004; 39(4): 579 – 581.
  - 109 Patients: CD4 cell counts of <200 cells/mm<sup>3</sup> were found in 42 cases (37.8%) with TLCs of  $\geq$ 1200 cells/mm<sup>3</sup>.
3. Angelo AL et al. Evaluating Total Lymphocyte Counts as a Substitute for CD4 Counts in the Follow up of AIDS Patients. *Braz J Infect Dis* 2007; 11 (5): 466 – 470.
  - 1,174 Patients: TLC of < 1,000 cells/mm<sup>3</sup> for CD4 < 200 cells/mm<sup>3</sup>, had a sensitivity 29% and specificity 98%.

**Conclusion:** The studies above showed a Sensitivity 29% - 41% and Specificity 83.5% - 98% for TLC as a surrogate for CD4

**Take Home Message:** TLC can be used as a rough surrogate marker of CD4 counts in patients when CD4 counts are not available in patients who are not on antiretroviral therapy, but use caution in using this marker as the sole absolute cut-off value in making decisions