When are Test Results Significantly Different?

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Case 1
- 42 y female has a TSH performed on day 1 with a result of 6.18 mIU/L (0.2 to 4.01 mIU/L)
- The test is repeated 30 days later with a result of 2.57 mIU/L
When are Test Results Significantly Different?

Explanations
• The lab has messed up (again)
• TSH is a difficult test to measure accurately
• TSH can change that much

Case 2
• Two patients, both diabetic, have their HbA$_{1c}$ tested on day 1 with both patients having a HbA$_{1c}$ result of 7.0%.
• 120 days later both have the HbA$_{1c}$ repeated and patient A has a HbA$_{1c}$ result of 6.5% and patient B has a HbA$_{1c}$ result of 7.5%.
• Is patient B more successful than patient A in controlling their diabetes?
Critical Difference Calculation

\[ C = Z \sqrt{\frac{2 \times V_{\text{biological}}^2 + V_{\text{analytical}}^2}{2}} \]

Where \( c \) = critical difference

\( Z \) = confidence statistic (ie. 1.96 for 95%)

\( V_{\text{VARIATION}} \) = biological variation

\( V_{\text{ANALYTICAL}} \) = analytical variation

Calculated Critical Differences for Some Chemistry Parameters

<table>
<thead>
<tr>
<th>Test</th>
<th>Biological CV</th>
<th>Analytical CV</th>
<th>CD as %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>4.7</td>
<td>1.9</td>
<td>9.9</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>5.8</td>
<td>2.0</td>
<td>17.0</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>8.6</td>
<td>3.0</td>
<td>25.2</td>
</tr>
<tr>
<td>Urea</td>
<td>10.3</td>
<td>1.6</td>
<td>28.9</td>
</tr>
<tr>
<td>Total Protein</td>
<td>2.6</td>
<td>3.1</td>
<td>11.2</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.6</td>
<td>3.1</td>
<td>11.2</td>
</tr>
<tr>
<td>Calcium</td>
<td>1.6</td>
<td>1.5</td>
<td>6.1</td>
</tr>
<tr>
<td>In Phosphorus</td>
<td>4.8</td>
<td>1.3</td>
<td>13.8</td>
</tr>
<tr>
<td>T. Bilirubin</td>
<td>16.5</td>
<td>4.7</td>
<td>47.5</td>
</tr>
<tr>
<td>Alk. Phosphate</td>
<td>6.5</td>
<td>3.6</td>
<td>37.1</td>
</tr>
<tr>
<td>LD</td>
<td>12.9</td>
<td>1.5</td>
<td>35.0</td>
</tr>
<tr>
<td>AST</td>
<td>8.2</td>
<td>5.7</td>
<td>27.7</td>
</tr>
</tbody>
</table>
When are Cholesterol Results Clinically Significantly Different?

- The critical difference is 17.0%
- At an initial value of 5.2 mmol/L the subsequent value may be between 4.3 and 6.1 mmol/L due solely to analytical variation

When are Liver Enzyme Values Changes Significant?

- Critical difference for AST is 27%. Therefore a result of 200U/L for AST can vary between 146 and 254 U/L due to analytical and biological variation
- AST is A Stupid Test
When are TSH Results Clinically Different?

- For TSH analytical variation is 10% and biological variation is giving a critical difference of 63%
- In case 1 63% of 6.18 mIU/L is 3.89 so the critical difference range is 2.29 mIU/L to 10.07 mIU/L the second result of 2.57 mIU/L is within the critical difference

When are HbA\textsubscript{1c} Results Different?

- For HbA\textsubscript{1c} the biological variation id 2% and the ideal analytical variation is 2%
- The critical difference at a HbA\textsubscript{1c} of 7% is a change in value of 0.5
- The National Academy of Clinical Biochemistry has stated that a difference of 0.5 or greater for HbA\textsubscript{1c} is clinically significant
Summary

• A patient's results can change as the result of biological and analytical change
• These changes can make a significant impact on the laboratory value
• Physicians need to be aware of the effect of analytical and biological factors on laboratory results