Biochemical Tests in Clinical Medicine

Med 4  2010 / 11
Medical Biochemistry / Clinical Biochemistry / Chemical Pathology ? Use in Future

- Breadth
- Role in Medical Practice
- Diagnosis
- Prognosis
- Monitoring of Disease Progression
- Monitoring of Treatment
- Screening
- Reference Ranges
- Interpretation.
Introduction

Clinical Biochemistry

- Dissolved elements in body fluids
- Concentration and type e.g. glucose, electrolytes, hormones and significance of levels and interpretation.
- Accurate and precise laboratory measurements can aid in diagnosis and management of disease
Use of Biochemical Tests

- **Diagnosis**
  - **History** and **Physical Examination** of patient -- form **Differential Diagnosis** i.e. Hypothesis
  - Lab tests and Radiology to support or reject hypothesis. Limitations of tests must be appreciated
  - Interpretation must be carefully done in context of clinical details
Monitoring

- Monitor effectiveness of treatment glucose levels in diabetic patients in response to insulin treatment.
- Follow natural history of the disease.
- Development of complications and side effects of treatments.
- Toxicity / TDM.
Screening

- Detection of sub-clinical
- Neonatal screening PKU, CHT
- Criteria for same.
- Natural history known
- Acceptable tests no false negatives, few false positives
- Ease of treatment
- Positive outcome
Variation

Patient Variables:
- Age, gender, fasting, time of day, exercise, posture, need to document these.

Biological Variation

Pre-Analytical Variation
- Sample site, type of bottle
- Transportation to lab.
- Stability of analyte aging with time

Analytical Variation

Post Analytical Variation
- Interpretation
Prognosis

- Serial tests to identify progressive disease creatinine in renal failure
- Tests to identify risks of disease in future in certain groups cholesterol in “at risk families”
- Calculation of risk depends on epidemiological data
- Likely outcome of disease
Sampling

Test Request
- Clinician requests that analysis be conducted.

Requirements
- Name, DOB, Gender, Hos. No. MRN
- Ward, Address
- Requesting Clinician
- Hypothesis / Problem
- Tests sought, time of sampling, date
- Clinical details, Drugs or Therapy.
Sampling Issues.

- Patient Centred Factors
- Age
- Gender
- Posture
- Physiological State
- Pregnancy
- Exercise
- Fasting / Fed
- Time
Sampling contd.

- Plasma, serum
- Bottle and preservative, anti coagulant used
- Age of sample
- Time of sampling
- Guidance from lab on sample requirements
- Correct label
- Transport
- High risk spec.
Analysis

- Accuracy
- Precision
- Detection limits
- Specificity
- Cost Effective
- Rapid Turnaround Time
Reporting

- Analytical vs Biological Variation
- Reporting
- Interpretation
- Ward reporting by computer

Point of Care Testing

- Clinical Users
- Laboratory
- System Suppliers
- Medico-legal issues
- Guidelines - Governance
Errors

- Pre-analytical
- Analytical
- Post-analytical,
- Interpretation,
- Delays
- Wrong records
Interpretation

- Is Result Normal?
- Has it changed?
- Does it support the clinical hypothesis?
Does it Support the Hypothesis?

- Consistent and supports diagnosis
- Inconsistent needs explanation
- Error in sampling, patient labelling analysis, or reporting.
- Repeat test
- ? Diagnosis
- Statistical random event abnormal test can indicate no disease.
- Diagnostic Utility: Sensitivity, Specificity
Screening

- Natural history of disease
- Acceptable and reliable screening Tests, FP issues
- Therapy available
- Prevalence
- Entire population
- or “at risk groups”
## Is It Different?

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Analytical variation</th>
<th>Biological variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>sodium</td>
<td>1.1 mmol/L</td>
<td>2.0 mmol/L</td>
</tr>
<tr>
<td>potassium</td>
<td>0.1 mmol/L</td>
<td>0.19 mmol/L</td>
</tr>
<tr>
<td>bicarbonate</td>
<td>0.5 mmol/L</td>
<td>1.3 mmol/L</td>
</tr>
<tr>
<td>urea</td>
<td>0.4 mmol/L</td>
<td>0.85 mmol/L</td>
</tr>
<tr>
<td>creatinine</td>
<td>5.0 μmol/L</td>
<td>4.1 μmol/L</td>
</tr>
<tr>
<td>calcium</td>
<td>0.04 mmol/L</td>
<td>0.04 mmol/L</td>
</tr>
<tr>
<td>phosphate</td>
<td>0.04 mmol/L</td>
<td>0.11 mmol/L</td>
</tr>
<tr>
<td>total protein</td>
<td>1.0 g/L</td>
<td>1.66 g/L</td>
</tr>
<tr>
<td>albumin</td>
<td>1.0 g/L</td>
<td>1.44 g/L</td>
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<tr>
<td>aspartate transaminase</td>
<td>6.0 IU/L</td>
<td>8.0 IU/L</td>
</tr>
<tr>
<td>alkaline phosphatase</td>
<td>4.0 IU/L</td>
<td>15.0 IU/L</td>
</tr>
</tbody>
</table>

\[ SD^2 = \sqrt{SD_{anal}^2 + \sqrt{SD_{biol}^2}} \]
Gaussian distribution

number of subjects

-3SD  -2SD      mean      +2SD  +3SD

test result
1 Diagnostic Sensitivity

2 Diagnostic Specificity

1 Positive test result in presence of disease.

2 Negative test result with no disease.

Diagnostic Sensitivity = \frac{TP}{TP + FN}

Diagnostic Specificity = \frac{TN}{FP + TN}
A graph illustrates the relationship between the number of tests and various test results. The x-axis represents the test result, ranging from the reference range on the left to false positives and false negatives on the right. The y-axis represents the number of tests. The graph shows distributions of values in health and disease, with highlighted areas indicating false positives and false negatives.

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12/12/2010
Diagnostic Sensitivity = \( \frac{TP}{TP + FN} \)
The graph illustrates the relationship between the number of tests and the test result, with a diagnostic cut-off point. The x-axis represents the test result, with a peak indicating high specificity and another peak indicating low specificity. The y-axis represents the number of tests, with a peak indicating the optimal test result. The graph shows that as the test result approaches the diagnostic cut-off, the specificity increases, while sensitivity decreases.
Diagnostic Specificity = \frac{TN}{FP+TN}
ROC CURVES A, B, C

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Test Efficiency and Predictive Values

\[
TE = \frac{TP + TN}{Total \ No. \ of \ Tests} \times 100
\]

\[
PV_{\text{Pos}} = \frac{TP}{TP + FP} \times 100
\]

\[
PV_{\text{Neg}} = \frac{TN}{TN + FN} \times 100
\]
Features of PD pos. and PD neg.

- Prevalence of disease in population.
- Low prevalence with less than 100% specificity high FP will result in low PV
- Screening with follow up testing should have a high PV neg.
Likelihood Ratios

- LR pos = Sens. / 1 – Spec.
- LR neg = Spec. / 1 - Sens.
AUDIT

- Patient Centred
- Quality and Continuously improving Service
- Efficient
- Review of Practice
- Changes to Improve service
- Measure Improvement
- Standards and Protocol Based
- Continuous Review of Practice
Evidence Based Clinical Biochemistry

- Experience and Intuition used to interpret
- Evidence Based Medicine ought to use outcomes as assessed by the PV, TE, LR and other concepts as outlined
- Will be case in future.