Pre and post-analytical errors in Haematology

Barbara De la Salle, PhD
Director, UK NEQAS Haematology
Co-Director, UK NEQAS PREPQ
haem@ukneqas.org.uk
Disclosures

• No conflicting interests
Outline of today’s talk

• What is meant by the pre-analytical, analytical and post-analytical phases
• The incidence of errors in the different phases of testing
• Errors peculiar to haematology, with particular reference to automated counting
• Monitoring pre and post-analytical phase errors
Lundberg’s Brain-to-Brain Loop

Lundberg, G.D., 1981. Acting on significant laboratory results. JAMA, 245(17), pp.1762-1763

Total testing process phases

- Pre-analytical
- Analytical
- Post-analytical
Total testing process

Pre-pre-analytical → Pre-analytical → Analytical → Post-analytical → Post-post-analytical
Most errors are not in the analytical phase

The Iceberg of Laboratory Errors

Plebani M et al
Clinical Chemistry and Laboratory Medicine (CCLM). Volume 53, Issue 3, Pages 357–370, ISSN (Online) 1437-4331, ISSN (Print) 1434-6621, DOI: 10.1515/cclm-2014-1051, December 2014
Diagnostic errors cause patient harm:

- Incorrect diagnosis
- Missed diagnosis
- Delayed diagnosis and treatment
- Missed opportunity for screening
- Unsatisfactory patient experience
- Wasted resources (=cost!)

“Get it right first time”

- 1/12 Americans experience a diagnostic error


- Laboratory medicine contributes to this figure

UK NEQAS
International Quality Expertise
Pre-analytical requirements of ISO 15189

• Laboratories should establish quality indicators to evaluate performance throughout the pre-examination, examination and post-examination processes

• Laboratories should have documented procedures for pre-examination processes to ensure validity of results

M Cornes, ACB News: issue 635, 2016
## Incidence of errors by phase

<table>
<thead>
<tr>
<th>TTP phase</th>
<th>Examples of error</th>
<th>Estimated proportion of errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-preanalytical</td>
<td>Test ordering, patient identification, patient preparation, sample collection, sample quality, transportation, storage</td>
<td>46 – 68%</td>
</tr>
<tr>
<td>Preanalytical</td>
<td>Sample sorting, centrifugation, labelling, separation</td>
<td>3-5%</td>
</tr>
<tr>
<td>Analytical</td>
<td>Sample analysis</td>
<td>7 – 13%</td>
</tr>
<tr>
<td>Postanalytical</td>
<td>Validation, interpretation, turnaround time, critical value reporting</td>
<td>13 – 20%</td>
</tr>
<tr>
<td>Post-postanalytical</td>
<td>Interpretation, delayed reaction, lack of follow-up or referral</td>
<td>25- 46%</td>
</tr>
</tbody>
</table>

## Incidence of errors by phase

<table>
<thead>
<tr>
<th>TTP phase</th>
<th>Examples of error</th>
<th>Estimated proportion of errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-preanalytical</td>
<td>Test ordering, patient identification, patient preparation, sample collection, sample quality, transportation, storage</td>
<td>46 – 68%</td>
</tr>
<tr>
<td>Preanalytical</td>
<td>Sample sorting, centrifugation, labelling, separation</td>
<td>3-5%</td>
</tr>
<tr>
<td>Analytical</td>
<td>Sample analysis</td>
<td>7 – 13%</td>
</tr>
<tr>
<td>Postanalytical</td>
<td>Validation, interpretation, turnaround time, critical value reporting</td>
<td>13 – 20%</td>
</tr>
<tr>
<td>Post-postanalytical</td>
<td>Interpretation, delayed reaction, lack of follow-up or referral</td>
<td>25- 46%</td>
</tr>
</tbody>
</table>

Errors common to all disciplines

Pre-analytical phase

- Test selection and ordering (Choosing Wisely!)
- Patient identification
- Wrong blood in tube
- Sample labelling

Post-analytical phase

- Turnaround times for reports
- Appropriate and timely action by clinicians
# Incidence of errors by phase

<table>
<thead>
<tr>
<th>TTP phase</th>
<th>Examples of error</th>
<th>Estimated proportion of errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-preanalytical</td>
<td>Test ordering, patient identification, patient preparation, sample collection, sample quality, transportation, storage</td>
<td>46 – 68%</td>
</tr>
<tr>
<td>Preanalytical</td>
<td>Sample sorting, centrifugation, labelling, separation</td>
<td>3-5%</td>
</tr>
<tr>
<td>Analytical</td>
<td>Sample analysis</td>
<td>7 – 13%</td>
</tr>
<tr>
<td>Postanalytical</td>
<td>Validation, interpretation, turnaround time, critical value reporting</td>
<td>13 – 20%</td>
</tr>
<tr>
<td>Post-postanalytical</td>
<td>Interpretation, delayed reaction, lack of follow-up or referral</td>
<td>25- 46%</td>
</tr>
</tbody>
</table>

From the patient to the laboratory bench

- Sample collection and quality
- Patient preparation
- Transport, storage and preparation
Patient preparation

• Unaccustomed or extreme physical exercise
  – Spurious cell counts
  – Platelet activation
  – RBC fragmentation

• Patient posture
  – Spurious Hb, RBC, Hct

• Fasting status
  – Variation in total and differential counts
  – Lipaemia


Scenario #1: patient posture

• Elderly patient admitted to ER, no apparent bleeding and not treated with IV fluids
• CBC on admission (taken without resting) was within reference interval
• CBC repeated after 2 hours lying down showed a 10-15% reduction in Hb and Hct

Sample collection and quality issues

- Collection site
  - Contamination with infusion fluid
  - Haemolysis in IV catheter samples
- Collection technique
  - Excessive venous stasis
  - Needle gauge
- Anticoagulant / specimen container
- Clotted samples
  - Most common cause of sample rejection in Haematology
- Under and over-filled specimen tubes
- Sample mixing (over and under-mixed)

Transport and handling

- Prolonged transportation and storage time
- Transportation and storage temperatures
- Pneumatic tube delivery systems
- Excessive or inadequate mixing before analysis

Morphological changes, spurious cell counts, MCV changes
Patient-specific causes of spurious CBC results

– Extreme raised WBC
– Lipaemia
– Cryoglobulinaemia
– Cold agglutinins
– Polymorphonuclear cell clumping
– Giant platelets
– Platelet clumping in EDTA
– Platelet satellitism
– WBC fragmentation
– RBC fragments
– Microspherocytes

FOR REVIEW:
Zandecki M et al., 2007. Int J Lab Haematol, 29(1), p.4-20
From the bench to the physician

- Result validation
- Result interpretation
- Critical result reporting
Result validation prior to release

• May detect anomalous results relating to the individual patient

• May detect anomalous results relating to sample collection and quality

• Importance of:
  – Instrument flags
  – Delta checking
  – Reflex testing – e.g. blood film examination
  – Liaison with other disciplines
Scenario #2: sample collection error

- 27 years old female, admitted post RTA
- Hb 81 g/L, Na high normal, extremely low K
- Results of 1 month earlier: Hb 125 g/L, Na 138 & K 4.1 mEq/L

- Classic ‘drip arm’ specimen
- May have resulted in unnecessary transfusion
  – In the UK would have been a reportable haemovigilance incident
Result interpretation: Defining ‘normal’

- Reference intervals
- Action points
  - Thresholds for therapy or investigation
- Impact of (e.g. for Hb):
  - Genetic factors
    • Gender, Ethnicity, Thalassaemia
  - Physiological factors
    • Age, Pregnancy, Diurnal variation
  - Environmental factors
    • Smoking, Altitude
Critical results: policy and alert list

• What should be considered critical?

• How quickly should results be notified?
• How are results notified?
• Who gives/receives results?
• How do you confirm receipt?

• Is information overload a danger?
• What action do you take if you can’t reach the responsible clinician or alternative?
• How do you balance the use of resources?
ICSH Recommendations:
FBC Alert Thresholds – a guide


<table>
<thead>
<tr>
<th>Parameter</th>
<th>Lower alert threshold</th>
<th>Upper alert threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucocytes (x10^9/L)</td>
<td>2.0</td>
<td>100</td>
</tr>
<tr>
<td>Neutrophils (x10^9/L)</td>
<td>0.5</td>
<td>50</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>70</td>
<td>200</td>
</tr>
<tr>
<td>Platelets (x10^9/L)</td>
<td>20-50</td>
<td>1000</td>
</tr>
</tbody>
</table>
ICSH Recommendations: Critical Blood Film Features

Acute Leukaemia (>20% blasts)

Acute Promyelocytic Leukaemia

Parasites, including Malaria

Blood Film consistent with Thrombotic Microangiopathic Anaemia

Blood Film showing bacteria

Images from:
- www.icsh.org/imagebank/
  (Dr J Burthem, Dr M Brereton)
- Dr L Ahmed, Manchester UK
- UK NEQAS Haematology
Total Testing Process and Critical Results Management

Ensure correct contact details

Exclude analytical errors

Exclude pre-analytical errors
Error-monitoring programmes

- CAP Q-Track Monitors
  - Meier FA, Arch Pathol Lab Med 2015; 139: 762-75

- IFCC Model of Quality Indicators project
  - Sciacovelli L, CCLM 2017; 55 (3): 348-357

- RCPA QAP Key Incident Monitoring and Management System (KIMMS)
  - Badrick T, CCLM 2018; 56(2): 264-272

- UK NEQAS PREPQ programme
  - Established 2017
THE QUALITY INDICATORS PARADOX

- Increasing interest of Scientific Societies, International Federations and laboratory professionals
- Availability of a list of harmonized QIs, a specifically developed website, and numerous scientific articles
- Few laboratories are making regular comprehensive data collection

DOI 10.1515/cclm-2015-1080
RCPA QAP KIMMS

• 2008 – 22 labs, 2016 – 69 labs
• Mixture of systems used for recording data (45% manual)
• Data may not be homogeneous
• Determining robust indicators
• Post-analytical data is not collected well
  – Pre-analytical QI participation: 91%
  – Post-analytical QI participation: 69%

_Badrick T et al, 2018. CCLM, 56(2): 264-272_
Why monitor pre and post-analytical errors?

• Because accreditation standards (e.g. ISO15189) say so?

• Monitoring errors alone will not resolve the problem

• Allows the laboratory to identify and prioritise the causes of error and implement corrective actions
Summary

- The laboratory must manage the risks at all phases in the TTP to minimize the contribution of the lab to healthcare risks.
- Although many pre and post-analytical errors are common across disciplines, some are peculiar to haematology and automated counting.
- Monitoring errors in the pre and post-analytical phases is necessary to identify and prioritise the corrective action needed to reduce risk.
Acknowledgements

For UK NEQAS PREPQ Programme:

- Finlay MacKenzie (Co-Director, UK NEQAS PREPQ)
- Dr David Bullock
- Dr Rachel Marrington
- UK NEQAS PREPQ Steering Group
Thank you for your attention

Have a safe trip home!