Using LOINC and HL7 to standardize hemoglobinopathy screening result reporting

Swapna Abhyankar, MD
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Swapna Abhyankar¹
Brad Therrell²
Roger Eaton³
Carla Cuthbert⁴

Jelili Ojodu⁵
Sara Copeland⁶
Rebecca Goodwin¹
Clem McDonald¹

¹ National Library of Medicine, NIH, Bethesda, MD, ² National Newborn Screening and Genetics Resource Center, Austin, TX, ³ New England Newborn Screening Program, University of Massachusetts Medical School, Jamaica Plain, MA, ⁴ Newborn Screening and Molecular Biology Branch, CDC, Atlanta, GA, ⁵ Association of Public Health Laboratories, Silver Spring, MD, ⁶ Genetic Services Branch, HRSA, Rockville, MD
Background
Hemoglobin disorders and NBS

• 1987 - Universal newborn hemoglobinopathy screening formally recommended by an NIH Consensus Development Panel

• 2006 - SACHDNC’s Recommended Uniform Screening Panel created
  ▫ Core conditions - Hb SS, Hb SC, Hb SβTh
  ▫ Secondary conditions – various other hemoglobinopathies

• 2006 - All of the U.S. NBS programs have sickle cell anemia on their screening panel
Hemoglobin nomenclature

- 1953 – NIH panel recommendations

<table>
<thead>
<tr>
<th>Recommended name</th>
<th>Previous name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb A</td>
<td>Hb N, Hb a</td>
</tr>
<tr>
<td>Hb F</td>
<td>Hb f</td>
</tr>
<tr>
<td>Hb S</td>
<td>Hb b</td>
</tr>
<tr>
<td>Hb C</td>
<td>Hb c, Hb III, Hb X</td>
</tr>
<tr>
<td>Hb D</td>
<td>Hb d</td>
</tr>
</tbody>
</table>

*New hemoglobin variants should be named in order starting with E*

- As >26 Hb types identified, began naming in part on geographic location in which they were discovered
- New nomenclature system based on molecular information is under development
Hemoglobin identification

- Hb identification depends on the methodology used as well as available controls
- Lab methodologies
  - Isoelectric focusing (IEF)
  - High pressure liquid chromatography (HPLC)
  - Citrate agar gel electrophoresis
  - Mutation analysis
- Combination of these methods is often used
- Hb controls
  - Limited number of commercially available controls
  - Local controls based on the samples previously analyzed in that lab
Reporting NBS hemoglobinopathy results – the old way

- Until recently, mostly paper reports with hemoglobin screening results reported as a text string listing all of the Hb types found in descending concentration
  - Hb FA – normal newborn Hb pattern
  - Hb AF – specimen likely taken after blood transfusion
  - Hb FAS – sickle cell trait
  - Hb FS – sickle cell disease, sickle beta⁰ thalassemia
  - Hb FSA – sickle beta⁺ thalassemia
Electronic reporting of NBS results

- Recent push for electronic health record (EHR) adoption and electronic transmission of clinical data
- HRSA/NLM guidance for reporting NBS results
- Nationally-accepted standard vocabularies
  - LOINC (Logical Observation Identifiers Names and Codes) – codes for lab tests and other clinical measures
  - HL7 (Health Level Seven) – standards for electronic messaging of clinical data
Reporting hemoglobinopathy results – the new way, take 1

• The first attempt to create an electronic method tried to replicate the text string and assign one LOINC answer code per Hb pattern per method

(this is an excerpt from the original list for electrophoresis)
Reporting hemoglobinopathy results – the new way, take 1

- We soon realized - assigning a code to each pattern is not sustainable
- 20 types of Hb with 2 types found in one sample – 380 permutations
- 20 types of Hb with 3 types found in one sample - 6,840 permutations!
- And >700 Hb variants have been identified to date

So...we needed a new solution
Methods
The task and the players

- Create a straightforward, sustainable method for reporting NBS hemoglobinopathy results using LOINC and HL7
- NBS Hemoglobinopathy workgroup
  - Federal – NLM, HRSA, CDC
  - State – multiple NBS programs and laboratories
- Face-to-face meeting in 5/2010 followed by multiple phone calls
Results
New focus

• Our final method focuses on the individual types of Hb found in one sample rather than the overall result (i.e., Hb combination or pattern)
• One LOINC code for each Hb found and its relative concentration
• To date, a maximum of 5 Hb types have been found in a single sample, so we created 5 LOINC codes
<table>
<thead>
<tr>
<th>Observation</th>
<th>LOINC code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most predominant hemoglobin</td>
<td>64117-5</td>
</tr>
<tr>
<td>Second most predominant hemoglobin</td>
<td>64118-3</td>
</tr>
<tr>
<td>Third most predominant hemoglobin</td>
<td>64119-1</td>
</tr>
<tr>
<td>Fourth most predominant hemoglobin</td>
<td>64120-9</td>
</tr>
<tr>
<td>Fifth most predominant hemoglobin</td>
<td>64121-7</td>
</tr>
</tbody>
</table>
Hemoglobin answer list

- Although >700 Hb variants have been identified, only a small subset are identified on NBS.
- The workgroup came to a consensus on a list of 20 Hb types:
  - Mostly single Hbs
  - Hb D/G for labs that cannot separate those two
  - Hb unidentified (currently also called Hb V or Hb X)
<table>
<thead>
<tr>
<th>Hemoglobin type</th>
<th>Answer code</th>
<th>Hemoglobin type</th>
<th>Answer code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb F</td>
<td>LA16208-3</td>
<td>Hb D-Punjab</td>
<td>LA16216-6</td>
</tr>
<tr>
<td>Hb A</td>
<td>LA16209-1</td>
<td>Hb D/G</td>
<td>LA16217-4</td>
</tr>
<tr>
<td>Hb A - indeterminate</td>
<td>LA16210-9</td>
<td>Hb E</td>
<td>LA13005-6</td>
</tr>
<tr>
<td>Hb A2</td>
<td>LA16211-7</td>
<td>Hb G</td>
<td>LA16218-2</td>
</tr>
<tr>
<td>Hb A2 - elevated</td>
<td>LA16212-5</td>
<td>Hb G-Philadelphia</td>
<td>LA16219-0</td>
</tr>
<tr>
<td>Hb Bart's - low level</td>
<td>LA16213-3</td>
<td>Hb H</td>
<td>LA16220-8</td>
</tr>
<tr>
<td>Hb Bart's - highly elevated</td>
<td>LA16214-1</td>
<td>Hb Lepore Boston</td>
<td>LA16221-6</td>
</tr>
<tr>
<td>Hb C</td>
<td>LA13002-3</td>
<td>Hb O-Arab</td>
<td>LA16222-4</td>
</tr>
<tr>
<td>Hb Constant Spring</td>
<td>LA16215-8</td>
<td>Hb S</td>
<td>LA13007-2</td>
</tr>
<tr>
<td>Hb D</td>
<td>LA13003-1</td>
<td>Hb unidentified</td>
<td>LA16223-2</td>
</tr>
</tbody>
</table>
Reporting an unidentified Hb

- If Hb unidentified is reported, the lab must also report which Hb types it *can* identify.
- This will narrow down the possibilities for what the unidentified Hb could be.

| Hemoglobin that can be presumptively identified based on available controls | 64122-5 |
Reporting local recommendations

- Each lab’s unique interpretation or recommendation can be included using the Hb comment/discussion code

| Hemoglobin disorders newborn screening comment-discussion | 57703-1 |
Example – F,A vs. F,A,S

Hb F,A
OBX|1|CE|64117-5^ Most predominant hemoglobin ^LN^^^ |1|LA16208-3^Hb F^LN |||||F||| 20090714145203
OBX|2|CE|64118-3^Second most predominant hemoglobin^LN^^^ |1|LA16209-1^Hb A^LN |||||F||| 20090714145203

Hb F,A,S
OBX|1|CE|64117-5^ Most predominant hemoglobin ^LN^^^ |1|LA16208-3^Hb F^LN |||||F||| 20090714145203
OBX|2|CE|64118-3^Second most predominant hemoglobin^LN^^^ |1|LA16209-1^Hb A^LN |||||F||| 20090714145203
OBX|3|CE|64119-1^Third most predominant hemoglobin ^LN^^^ |1| LA13007-2^Hb S^LN |||||F||| 20090714145203

*Please note – for purposes of simplicity, the entire HL7 OBR/OBX structure is not shown
Example – Hb unidentified

**Hb F,A,unidentified (lab that identifies A, F, C and S)**

| OBX | CE | 64117-5^ | Most predominant hemoglobin ^LN^^^ | 1 | LA16208-3^Hb F^LN | |||||F| || 20090714145203 |
| OBX | CE | 64118-3^ | Second most predominant hemoglobin ^LN^^^ | 1 | LA16209-1^Hb A^LN | |||||F| || 20090714145203 |
| OBX | CE | 64119-1^ | Third most predominant hemoglobin ^LN^^^ | 1 | LA16223-2^Hb unidentified^LN | |||||F| || 20090714145203 |

| OBX | CE | 64122-5^ | Hemoglobins that can be presumptively identified based on available controls ^LN^^^ | 1 | LA16209-1^Hb A^LN | |||||F| || 20090714145203 |
| OBX | CE | 64122-5^ | Hemoglobins that can be presumptively identified based on available controls ^LN^^^ | 1 | LA16208-3^Hb F^LN | |||||F| || 20090714145203 |
| OBX | CE | 64122-5^ | Hemoglobins that can be presumptively identified based on available controls ^LN^^^ | 1 | LA13002-3^Hb C^LN | |||||F| || 20090714145203 |
| OBX | CE | 64122-5^ | Hemoglobins that can be presumptively identified based on available controls ^LN^^^ | 1 | LA13007-2^Hb S^LN | |||||F| || 20090714145203 |
Example – Hb unidentified (cont.)

- This result is from the same exact sample as the last slide, but it was run in a lab that can identify the unidentified Hb as Hb O-Arab
- In this case, the lab doesn’t need to report the list of Hb it can identify

Hb F,A,O-Arab

|OBX|CE|64117-5|Most predominant hemoglobin |LN| |1|
|LA16208-3|Hb F|LN| |20090714145203|
|OBX|CE|64118-3|Second most predominant hemoglobin |LN| |20090714145203|
|LA16209-1|Hb A|LN| |20090714145203|
|OBX|CE|64119-1|Third most predominant hemoglobin |LN| |20090714145203|
|LA16222-4|Hb O-Arab|LN| |20090714145203|
Example – Lab-specific comment

Hb F,A,S
OBX|1|CE|64117-5^ Most predominant hemoglobin^LN^^^|1| LA16208-3^Hb F^LN |||||F||| 20090714145203
OBX|2|CE|64118-3^Second most predominant hemoglobin^LN^^^|1|LA16209-1^Hb A^LN |||||F||| 20090714145203
OBX|3|CE|64119-1^Third most predominant hemoglobin^LN^^^|1|LA13007-2^Hb S^LN |||||F||| 20090714145203
OBX|4|ST|57703-1^Hemoglobin disorders newborn screening comment-discussion^LN^^^|1|^Likely sickle cell trait. Recommend confirmatory testing at 9-12 months of age.^|)|||||F||| 20090714145203
Discussion
Flexible

- A NBS lab can use anywhere from 1 to 5 LOINC codes as necessary for reporting the Hbs found in one specimen
- The comment-discussion code can be used to send custom local text
- A set of segments specifying the variants a lab can identify only has to be created once
  - It can be automatically included in any result that contains an unidentified Hb
  - If at some point the lab can identify another variant, only a simple update is needed to add the segment containing that answer code to the set
Easy to maintain

- If someday a lab identifies more than 5 types of Hb in one specimen, we can add a LOINC code for “Sixth most predominant hemoglobin”
- If labs identify a Hb that is not on the current answer list, we can add a LOINC answer code for that Hb
Challenges

• Major challenge was reaching consensus on list of Hb types
• Some labs report the result that comes directly from the instrument, but this result may not follow the accepted nomenclature
  ▫ a for indeterminate Hb A
  ▫ B and b for varying levels of Hb Bart’s
• Different labs can distinguish different levels of granularity
  ▫ Hb D vs Hb G
Challenges

• We created codes to cover these cases
  ▫ Hb A-indeterminate
  ▫ Hb Bart’s – low level, Hb Bart’s – highly elevated
  ▫ Hb D
  ▫ Hb G
  ▫ Hb D/G

• Labs can report both these codes as well as the result that comes directly from the machine using the comment-discussion code if necessary
Next (even bigger?) challenge – condition and NBS interpretation codes

- Thalassemias - beta versus beta\(^0\) and beta\(^+\)
  - Could create 3 codes for each thalassemia disorder
    - Hb S beta thalassemia, Hb S beta\(^0\) thalassemia, Hb S beta\(^+\) thalassemia
    - Hb C beta thalassemia, Hb C beta\(^0\) thalassemia, Hb C beta\(^+\) thalassemia
- One result can map to multiple conditions (F,S)
- Labs identify different sets of variants, which creates exponential number of combinations
  - e.g., Hb carrier other than C,S,[D],[G],[D/G],[Constant Spring],[O-Arab],[H],[D-Punjab],[Lepore Boston]...
- We need a sustainable method for coding NBS interpretations and conditions
Conclusion

- We created a method for reporting NBS hemoglobinopathy results that is straightforward and simple to maintain.
- The SACHDNC’s Laboratory Standards and Procedures Subcommittee has accepted this method as best approach for reporting hemoglobinopathy results.
- We have incorporated this method into the HRSA/NLM guidance.
- We need to work together to decide how to code NBS interpretations and conditions.
Thank you!
Any questions?


swapna.abhyankar@nih.gov