

Using LOINC and HL7 to standardize hemoglobinopathy screening result reporting

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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

Recommended name	Previous name
Hb A	Hb N, Hb a
Hb F	Hb f
Hb S	Hb b
Hb C	Hb c, Hb III, Hb X
Hb D	Hb d

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

NORMATIVE ANSWER LIST:

SEQ#	Answer	Answer ID			
1	Hb F,A (normal)	LA11974-5	22	Hb F,A and other than C,D, E, S, O-Arab	LA12057-8
2	Hb F,A,C	LA11976-0	23	Hb F,A, C and other than D, E, S, O-Arab	LA12968-6
3	Hb F,A,D	LA11977-8	24	Hb F,A, D and other than C, E, S, O-Arab	LA12970-2
4	Hb F,A,E	LA11978-6	25	Hb F,A, E and other than C,D, S, O-Arab	LA12971-0
5	Hb F,A,O-Arab	LA12060-2	26	Hb F,A, S and other than C,D, E, O-Arab	LA12972-8
6	Hb F,A,S	LA11979-4	27	Hb F,A, O-Arab and other than C,D, E, S	LA12973-6
7	Hb F,C	LA11980-2	28	Hb F,A, Barts	LA12974-4
8	Hb F,C,A	LA11981-0	29	Hb Barts, F, A	LA12975-1
9	Hb F,D	LA11982-8	30	Hb Barts, F, A, plus any other band(s)	LA12976-9
10	Hb F,D,A	LA11983-6	31	Hb F,A,C, Barts	LA12977-7
11	Hb F Only	LA11984-4	32	Hb F,A,D, Barts	LA12978-5
12	Hb F,E	LA11985-1	33	Hb F,A,E, Barts	LA12979-3
13	Hb F,E,A	LA11986-9	34	Hb F,A,O-Arab, Barts	LA12980-1
14	Hb F,S	LA11987-7	35	Hb F,A,S, Barts	LA12981-9
15	Hb F,S,A	LA11988-5	36	Hb F,C, Barts	LA12982-7
16	Hb F,S,C	LA11989-3	37	Hb F,C,A, Barts	LA12983-5
17	Hb F,S,D	LA11990-1	38	Hb F,D, Barts	LA12984-3
18	Hb F,S,E	LA11991-9	39	Hb F,D,A, Barts	LA12985-0
19	Hb F,S,O-Arab	LA11992-7	40	Hb F Only, Barts	LA12986-8
20	Hb F,S and other than A,C,D, E, O-Arab	LA11993-5	41	Hb F,E, Barts	LA13017-1
21	Hb F, and other than A,C,D,E, S,O-Arab	LA11994-3	42	Hb F,S, Barts	LA13018-9
			43	Hb F,S,C, Barts	LA13019-7
			44	Hb F,S,D, Barts	LA12990-0
			45	Hb F,S,E, Barts	LA12991-8

(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



Observation	LOINC code
Most predominant hemoglobin	64117-5
Second most predominant hemoglobin	64118-3
Third most predominant hemoglobin	64119-1
Fourth most predominant hemoglobin	64120-9
Fifth most predominant hemoglobin	64121-7



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)



<i>Hemoglobin type</i>	<i>Answer code</i>	<i>Hemoglobin type</i>	<i>Answer code</i>
Hb F	LA16208-3	Hb D-Punjab	LA16216-6
Hb A	LA16209-1	Hb D/G	LA16217-4
Hb A - indeterminate	LA16210-9	Hb E	LA13005-6
Hb A2	LA16211-7	Hb G	LA16218-2
Hb A2 - elevated	LA16212-5	Hb G-Philadelphia	LA16219-0
Hb Bart's - low level	LA16213-3	Hb H	LA16220-8
Hb Bart's - highly elevated	LA16214-1	Hb Lepore Boston	LA16221-6
Hb C	LA13002-3	Hb O-Arab	LA16222-4
Hb Constant Spring	LA16215-8	Hb S	LA13007-2
Hb D	LA13003-1	Hb unidentified	LA16223-2



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

Hemoglobins that can be presumptively identified based on available controls	64122-5
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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
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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|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| LA16223-2^Hb unidentified^LN |||||F|| 20090714145203

OBX|1|CE|64122-5^Hemoglobins that can be presumptively identified based on available controls ^LN^^^ |1| LA16209-1^Hb A^LN |||||F|| 20090714145203

OBX|2|CE|64122-5^Hemoglobins that can be presumptively identified based on available controls ^LN^^^ |1| LA16208-3^Hb F^LN |||||F|| 20090714145203

OBX|3|CE|64122-5^Hemoglobins that can be presumptively identified based on available controls ^LN^^^ |1| LA13002-3^Hb C^LN |||||F|| 20090714145203

OBX|4|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|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|

LA16222-4^ **Hb O-Arab**^LN |||||F|| 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 beta⁰ and beta⁺
 - Could create 3 codes for each thalassemia disorder
 - Hb S beta thalassemia, Hb S beta⁰ thalassemia, Hb S beta⁺ thalassemia
 - Hb C beta thalassemia, Hb C beta⁰ 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?

<http://newbornscreeningcodes.nlm.nih.gov>

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