UK NEQAS (H)

Perspective on performance: The Haemoglobinopathies

Barbara Wild

Haemoglobinopathies

Perspective on Performance:
Performance assessment process

DNA diagnostics for Haemoglobinopathies scheme
Outcomes of shadow scoring exercise

Abnormal Haemoglobins A_2/F/S scheme
Plan for performance assessment of interpretive comments

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UKNEQAS(H) Quality assessment schemes for the Haemoglobinopathies

- Sickle cell screening
- Abnormal Haemoglobins HbA_2/F
- Liquid Newborn specimens

- Newborn sickle screening on dried blood spots

- DNA diagnostics for the Haemoglobinopathies

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Haemoglobinopathy schemes

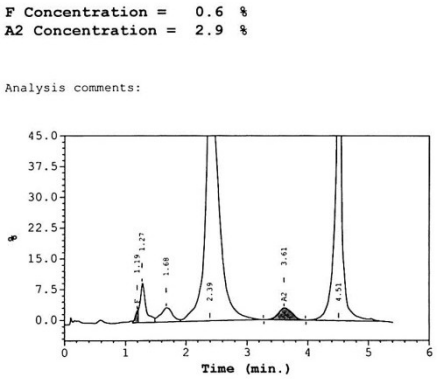
- Sickle screening

  Solubility test

Specimens:
Whole blood

- Abnormal haemoglobins +HbA_2/F

Haemoglobin electrophoresis
High Performance Liquid Chromatography
Capillary electrophoresis



Liquid newborn samples

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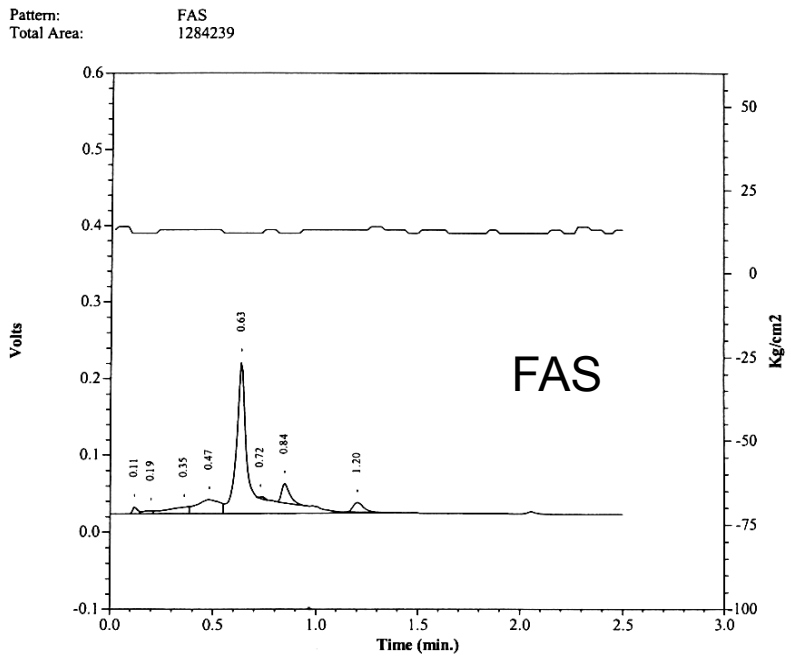
Haemoglobinopathy schemes

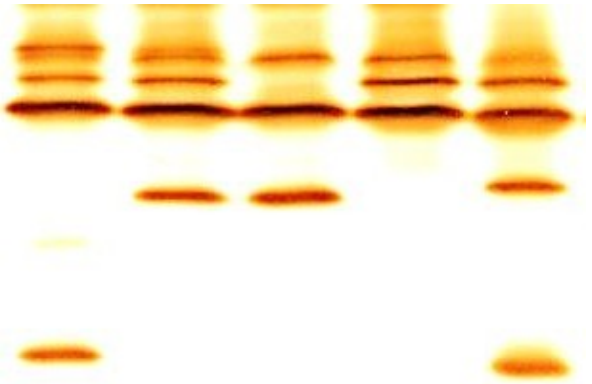
- Newborn screening for sickle cell disease

High Performance Liquid Chromatography



Specimens:
Dried blood spots

Isoelectric focusing



FAC FAS FS FA AFDC

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Mass Spectrometry

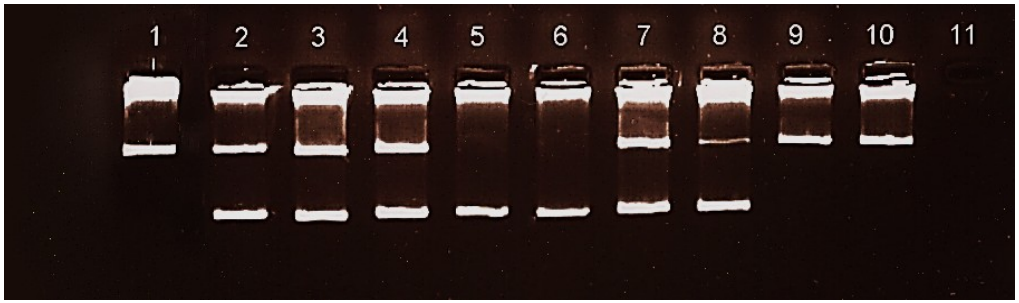
Haemoglobinopathy schemes

- DNA diagnostics

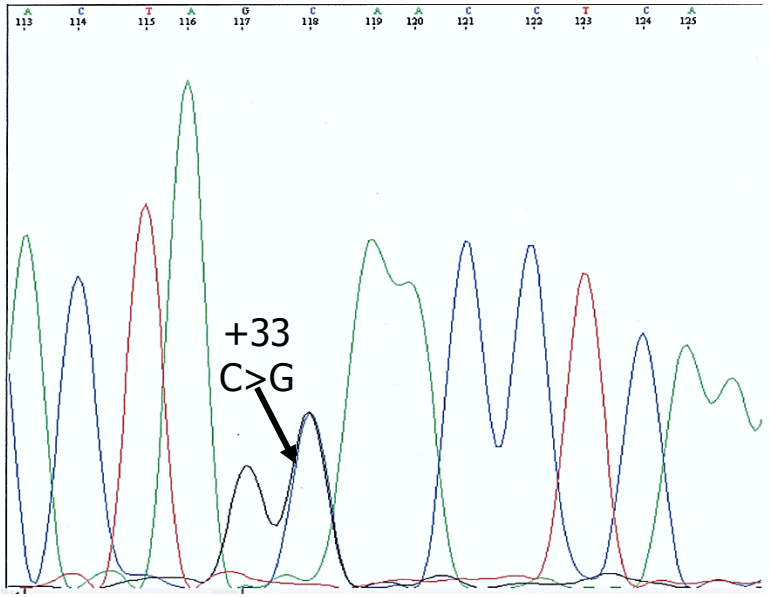
Suitable for all DNA diagnostic techniques

Specimens:
Extracted DNA in buffer

Amplification Refraction Mutation System



DNA fluorescent sequencing



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DNA scheme: Plan

- *Develop schedule for regular surveys*
- *Develop Performance Assessment*
- Apply for accredited status of scheme

DNA Scheme: History

Scheme commenced in 2002 as a pilot scheme

Purpose:

- To assess the quality of DNA analyses for the haemoglobinopathies within the UK

Participants:

- The 3 Prenatal Diagnosis laboratories
- Any other UK laboratory undertaking α/β genotyping

Surveys:

- 12 surveys over 10 year period

Outcome:

- Summary reports, no scoring undertaken

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Current process

Schedule developed

3 surveys per with 2 specimens per year, commenced 2011

Specimens issued with:

Age/gender

Full blood count data

Haemoglobinopathy screening data

Reason for referral

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Current participants

Australia	1	Israel	2
Austria	2	Ireland	2
Belgium	3	Portugal	3
Cyprus	1	Poland	1
France	7	Spain	1
Germany	2	Sweden	2
Greece	1	Switzerland	4
Netherlands	2	UK	9

Total = 43 participants

16 different countries

Current process

Start

- Specimens and instructions dispatched
- Participants given 4 weeks to complete

Data Analysis

- Summary report written → participants
- ***Results shadow scored***

Outcomes

- Results and recommendations→
- Expert advisors, SSAG + NQAAP

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Shadow scoring

>Scoring requires internal and external expert

>Model answer agreed by experts

>Assessment undertaken at UKNEQAS(H)

>Independent scoring by external assessor

>Meeting to finalise participants' scores

Tariff of penalties

Aspect	Penalty	
Non participation	50	
Incorrect analytical results: α genotype	50	
Incorrect analytical results: β genotype	50	
Incorrect annotation: α genotype	35	
Incorrect annotation: β genotype	35	
Incorrect interpretation re case details	50	
Incorrect annotation of interpretation	35	
Inadequate/absent/incorrect recommendations	50	
HGVS nomenclature incorrect/not used	35	

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Cases shadow scored

Date	Genotypes : Specimen 1	Genotypes : Specimen 2
July 2012	$--^{SEA}/-\alpha^{3.7}$: β^A/β^E	$-\alpha^{4.2}$ /αα : $\beta^A/\beta^{IVS1-5\ (G>C)}$
November 2012	αα /αα : $\beta^A/\beta^{Fr\ 41-42(-TCTT)}$	$-\alpha^{3.7}/-\alpha^{3.7}$: β^A/β^S
February 2013	$-\alpha^{3.7}$/αα : $\beta^A/\beta^{IVS\ II\ 654(C>T)}$	αα /αα : β^A/β^A
July 2013	αα /αα : $\beta^A/\beta^{Cd8/9(+G)}$	$-\alpha^{3.7}$/αα : $\beta^A/\beta^{-88(C>T)}$

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Example

Sample 1202DN1 was from a 1.5 year old female of Vietnamese origin. Referred for elucidation of FBC results:

FBC: Hb: 98 g/L
RBC: 6.43 x 10^{12}/L
MCV: 52 fl
MCH: 17 pg

Haemoglobinopathy screen:

Hb A + fraction eluting in Hb A_2 window
Hb A_2=13.7%; Hb F=2.0%

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Expected results:
Criteria for the model answer

Mutation analysis:	Alpha genotype: $-\alpha^{3.7}/--^{SEA}$
	Beta genotype: β^{A}/β^{E}
Interpretation using case details:	
	HbH disease plus Hb E trait (carrier)
Recommendations on report:	Child should be referred for follow-up
	Parental testing recommended
HGVS nomenclature	HBB:c.79G>A

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RESULTS	1202DN1	1202 DN2	1301 DN1	1301DN2
No participants	35	35	41	41
Incorrect analysis: α genotype	$-\alpha^{3.7}/--^{SEA}$ 4	$-\alpha^{4.2}/\alpha\alpha$ 4	$-\alpha^{3.7}/\alpha\alpha$ 2	$\alpha\alpha/\alpha\alpha$ 2
Incorrect analysis: β genotype	$\beta^{A}/\beta^{Cd26(G>A)}$ 0	$\beta^{A}/\beta^{IVS1,5(G>C)}$ 1	$\beta^{A}/\beta^{IVSII\ 654(C>T)}$ 4	$\beta\beta/\beta\beta$ 1
Incorrect annotation: α genotype	6	2	12	1
Incorrect annotation: β genotype	3	3	10	1
Incorrect interpretation	1	1	1	2
Incorrect annotation of interpret	0	0	3	0
Inadequate/absent/incorrect recommendations	21	12	12	3
HGVS nomenclature incorrect/absent	9	5	11	16
Labs with ZERO penalties	2	6	3	6

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Participation

Survey	Total number of participants in scheme	Number of Non-participants
1202DN	35	3
1203DN	37	3
1301DN	41	6
1302DN	43	3

Ranges of penalties accrued per sample

	1202 DN1	1202 DN2	1203 DN1	1203 DN2	1301 DN1	1301 DN2	1302 DN1	1302 DN2
Ranges of points given	0–190	0–190	0–255	0–240	0–220	0–135	0–255	0–255
% labs with no points	9	16	6	6	9	18	10	10

Scoring – outcomes

- Labs are given a score
  0 = No penalties

- Persistent unsatisfactory performance
  = 2 or more errors in 3 surveys

(usual score accumulated = 100 or more)

Accredited Scheme: PUP referred to a professional overseeing organisation

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Outcomes of shadow scoring project

- Report of shadow scoring for participants

- Guidelines / user reference compiled
  - What's required in the report (...already provided)
  - Example of model answer
  - Reference websites for guidance
    - Globin gene server
    - ITHANET
    - HGVS
  - Examples of 'ideal reports'

Meeting for participants to discuss these

Assistance –upgrade

- Incorrect mutation analysis discussed with participant as soon as survey closes
- Model answer issued within a week of survey closure
- International experts available for discussion on inconsistencies or out of consensus results

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Interestingly……

- Annotation can be addressed
- Is interpretation not a usual process?
- Are recommendations not a usual process?
- How do the latter work for different countries'
  - culture
  - economy
  - healthcare systems

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Finally

Understanding that *from non-UK labs*
this approach *could* be for NEQAS reports only

Shadow scoring exercise – accepted
commences November 2014

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Performance assessment of the Abnormal Haemoglobins HbA_2/F Scheme

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Performance assessment: Abnormal Hbs, A_2/F scheme

Extension of performance assessment

- Fraction identification
- Interpretive comments

Project to commence 2015

Performance assessment: Abnormal Hbs, A_2/F scheme

The process

Likely that the process will be similar to that of the DNA diagnostics

The aim is to achieve:

Performance assessment of the whole analytical, analytical and reporting outcomes

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Performance assessment: Abnormal Hbs, A_2/F scheme

There are significant differences to be considered: each individual laboratory's level of operation, -how they define their role and purpose

- Primary screening, then refer
- Presumptive identification of common variants, then refer
- Comprehensive diagnostic service
- Referral service

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Performance assessment: Abnormal Hbs, A_2/F scheme

UKNEQAS(H) needs

- more information instrumentation and techniques
- diagnostic protocols

in order to 'categorise' laboratories

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Performance assessment: Abnormal Hbs, A_2/F scheme

- Consideration of the following

  Modification of the results proforma to encompass all categories of operation

  A good example: Has the 'Non-specific fraction' outlived itself

The level of operation will obviously affect interpretive comments made by participants

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Performance assessment: Abnormal Hbs, A_2/F scheme

- Participation – being purist about it…..

- Reasons for repeated non-participation
- Incomplete participation
- Failure to request repeat samples
- Joint participation=one report

Performance assessment: Abnormal Hbs, A_2/F scheme

- Where to start?
- Questionnaire to participants–early next year
- Create participant 'Groups'
- Modify: results proformas
  create model answers
  create new penalty tariff
  udjust IT accordingly

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Performance assessment

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