

Incidental G-6-PD Identification Using the PerkinElmer GSP Neonatal GALT Kit

APHL NBS> Symposium
October 28, 2014

Project Initiation

Instrumentation



AutoDelfia



GSP



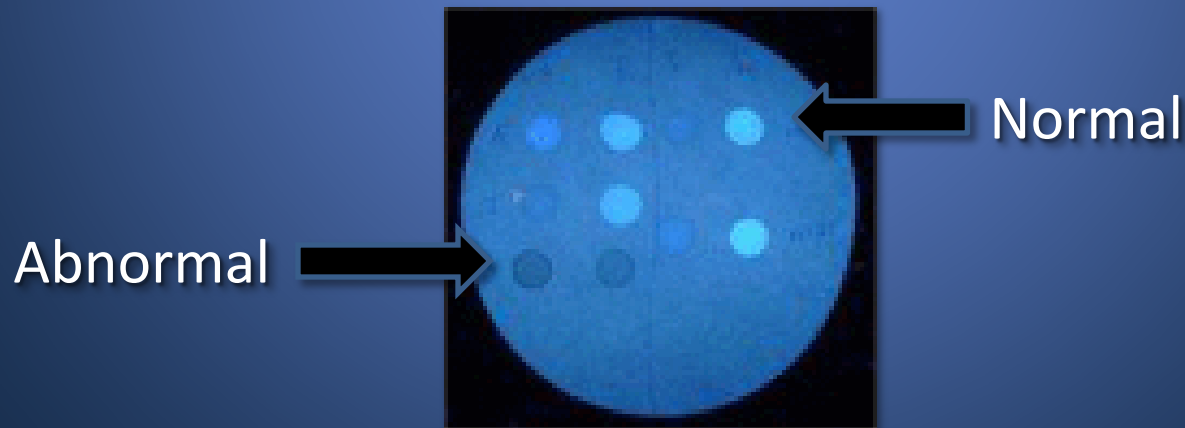
Instrumentation

- PerkinElmer AutoDelfia
 - » T4, TSH, 17-OHP and IRT
- Introduction of Genetic Specimen Processor (GSP)
 - » Transfer of AutoDelfia tests
 - » Expansion capability to add GALT and Biotinidase
- Decision made to add GALT to GSP using the PerkinElmer Neonatal GALT kit

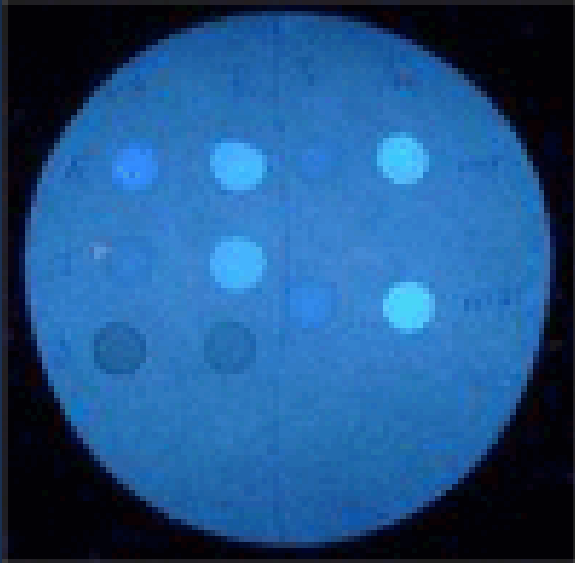
Beutler Assay to GSP GALT

Screening for Galactosemia

- 1964 to February 2012 – Beutler assay
- Detection of galactose-1-uridylyltransferase (GALT) enzyme
- Presence or absence of fluorescence
- Results read visually using a UV light box



Beutler Assay



- Manual method
- In-house reagents
- Visually read
- Qualitative
- Subjective

PE GSP GALT Assay

- Automated method
- Manufactured reagents
 - » Adaptation of Beutler/Baluda assay
- Instrument read
- Quantitative
- Objective



Validation

- Beutler to GSP Neonatal GALT Kit comparisons
- 2,800 blood spot specimens
 - » 1,411 first screen specimens (zero to 7 days of age)
 - » 1,359 second screen specimens (>7 days of age)
 - » All Beutler normal
- CDC PT samples
 - » Beutler normal, reduced or no fluorescence



Validation Results

- First specimens - zero through 7 days of age
 - » Mean 12.58 U/dL
 - » Standard deviation 3.92
- Second specimens - > 7 days of age
 - » Mean of 12.43 U/dL
 - » Standard deviation of 11.30
 - » Higher variability
- CDC specimens – Interpretation matched Beutler GALT test results



Validation Results

- Classic galactosemia specimens
 - » GSP GALT values < 1.5 U/dL
- Reduced fluorescence specimens
 - » GSP GALT values ≤ 5.50 U/dL
- Proposed cutoffs
 - » Abnormal < 2.5 U/dL
 - » Borderline 2.5 to 3.49 U/dL
 - » Normal ≥ 3.50 U/dL



Validation Results

- False Positive Predictions
 - » < 2.50 U/dL would produce 11 false positives in addition to the true positives
- Borderline range
 - » < 3.00 U/dL – 15 false positives
 - » < 4.00 U/dL – 1 false positive
 - » Selected cutoff of < 3.50 U/dL – 8 more borderline positives



Assay Implementation

Screening Results

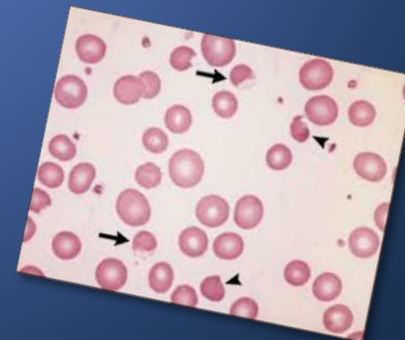
- Increased number of presumptive positives with the GSP GALT
 - » 120 in 2011 (Beutler assay)
 - » 681 in 2012
- Mainly reduced fluorescence values
- Majority from Hawaii
- Asian and Pacific Islander population

Diagnostic Results

- Galactosemia false positives
- Confirmation of glucose-6-phosphate dehydrogenase deficiency (G-6-PD)
- Already well known to be common in the Hawaiian population
- Testing routinely performed in the state

G-6-PD

- Deficiency in glucose-6-phosphate dehydrogenase
- Insufficient amounts – red blood cell destruction
- Triggered by infections, severe stress, certain foods or drugs



Assay Evaluation

Cutoff Analysis and Revision

- 6 month data review
- Evaluation of confirmed cases
 - » GALT deficient
 - » D/G
 - » Duarte
 - » Carrier
 - » Other variant



Cutoff Analysis and Revision

- Beutler assay classic Galactosemia specimens
 - » GSP GALT values < 1.5 U/dL
- Beutler assay reduced fluorescence specimens
 - » GSP GALT values ≤ 5.50 U/dL
- Revised cutoffs
 - » Abnormal < 2.5 U/dL \Rightarrow < 2.0 U/dL
 - » Borderline 2.5 to 3.49 U/dL \Rightarrow 2.0 to 3.49 U/dL
 - » Normal ≥ 3.50 U/dL \Rightarrow No change

Beutler Assay to GSP GALT Statistics

Beutler vs. GSP GALT Cases

	Beutler			GSP GALT		
	2009	2010	2011	2012	2013	As of 10/2014
Presumptive Positive	189	108	120	681	922	660
Classic Galactosemia	0	3	2	1	3	1
G-6-PD	0	0	0	0	5	46
Duarte Variant	43	14	9	12	30	14
G/N Heterozygote	8	2	1	0	12	4
Specimens Screened	315,670	301,897	293,405	292,372	291,946	216,480
Average PP Frequency	1:1,094			1:197		

Summary

Summary

- GSP Neonatal GALT Kit
 - » Greater sensitivity than Beutler in G-6-PD detection
 - » Unexpected increase in presumptive positives with population bias
 - » Increased short-term follow-up
 - » Increased diagnostic costs – GALT and G-6-PD analysis vs. GALT alone

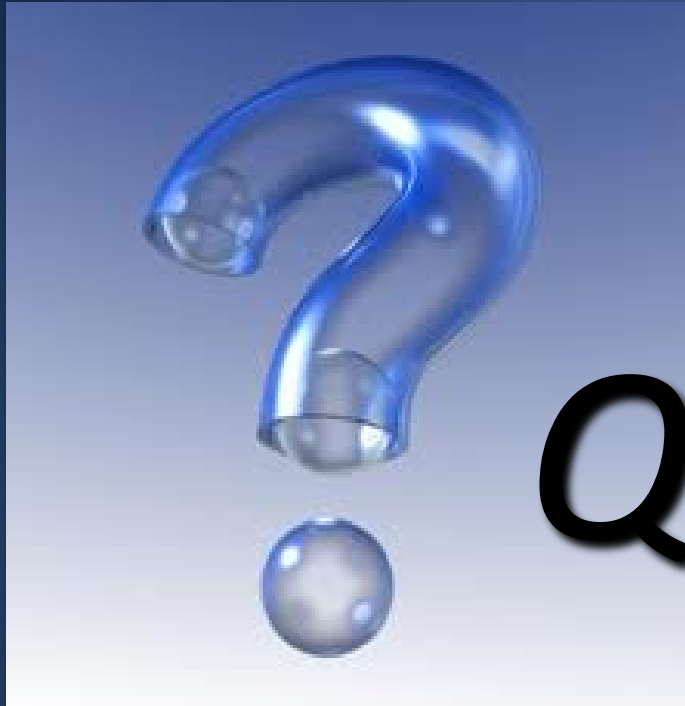
Incidental vs. Supplemental Findings



Definitions

- in·ci·den·tal
 - » *adjective* \,in(t)-sə-'den-t^ə\ : happening as a minor part or result of something else
- sup·ple·men·tal
 - » *adjective* \,sə-plə-'men-t^ə\ : added to something else to make it complete





Questions

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