

# PKU Screening: Simple Idea, Complex Realities

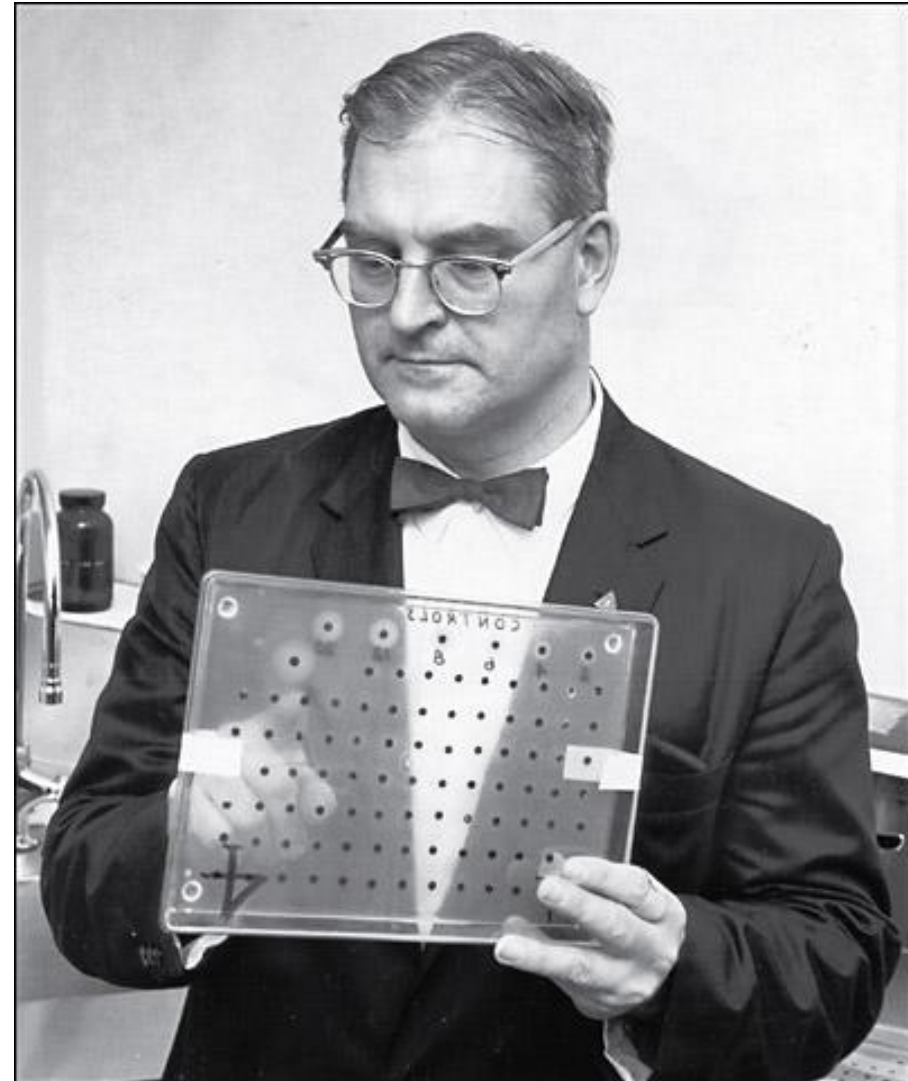
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Washington State Department of Health



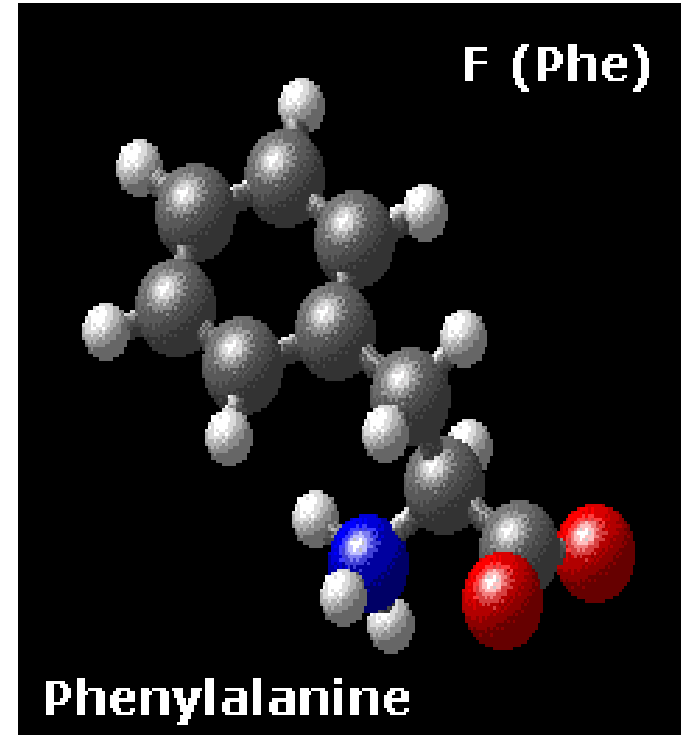
# Simple Idea

Identify  
newborns with  
elevated  
phenylalanine  
levels &  
initiate dietary  
therapy



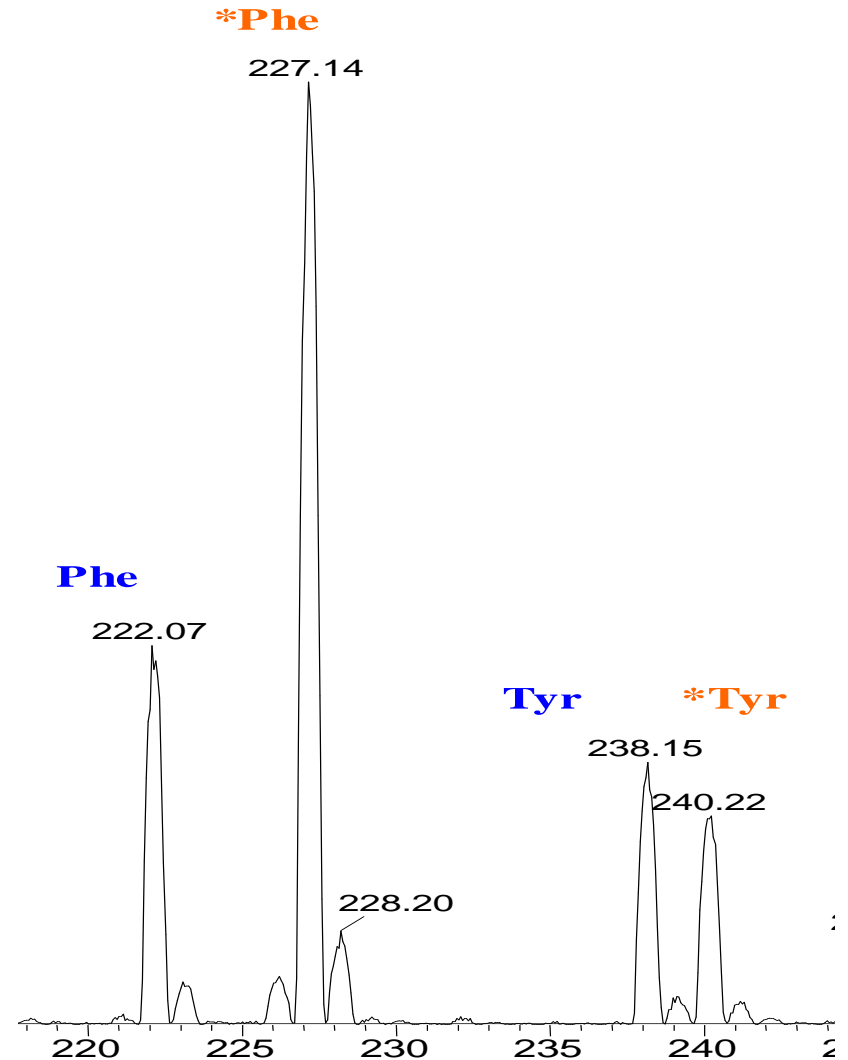
# Known Realities

- Safe Blood Levels
- Lifetime Diet
- Maternal PKU
- Biopterin Defects
- >500 mutations



# Simple Idea

mild mutations  
(phe levels  
<360 $\mu$ M)  
don't require  
dietary therapy



# Reality

Pt.#1 - 3655g White ♂

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
27 hours	283	2.5

# Reality

Pt.#1 - 3655g White ♂

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
27 hours	283	2.5
1 month	255	3.3
6 months	283	3.9

# Reality

Pt.#1 - 3655g White ♂

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
27 hours	283	2.5
1 month	255	3.3
6 months	283	3.9
12 months	221	4.5
18 months	340	4.4

# Reality

Pt.#1 - continued monitoring

<b>Age (months)</b>	<b>Phe (<math>\mu\text{M}</math>)</b>	<b>Phe/Tyr</b>
24	<b>370</b>	4.6
30	<b>368</b>	3.7



# Reality

Pt.#1 - continued monitoring

Age (months)	Phe ( $\mu\text{M}$ )	Phe/Tyr
24	370	4.6
30	368	3.7
34	509	5.6

Started formula



at 34 months!

# Similar Cases

who “appeared” to have benign hyperphe

<b>Pt.</b>	<b>Phe (<math>\mu\text{M}</math>)</b> (1 <sup>st</sup> abnormal screen)	<b>Phe/Tyr</b> <b>ratio</b>	<b>Tx Started</b> (months)
#2	272	3.0	10
#3	194	6.3	11
#4	244	6.8	14
#5	298	4.1	15
#6	230	3.5	16
#7	159	4.2	34

# Similar Cases

Pt. #1  
phe/tyr= 2.5

all had phe/tyr ratios >2.5!

<b>Pt.</b>	<b>Phe (<math>\mu\text{M}</math>)</b> (1 <sup>st</sup> abnormal screen)	<b>Phe/Tyr</b> <b>ratio</b>	<b>Tx Started</b> (months)
#2	272	3.0	10
#3	194	6.3	11
#4	244	6.8	14
#5	298	4.1	15
#6	230	3.5	16
#7	159	4.2	34

# True Benign Hyperphe

(not requiring treatment)

difference: lower phe/tyr ratio!

<b>Pt.</b>	<b>Phe (<math>\mu\text{M}</math>)</b> (1 <sup>st</sup> abnormal screen)	<b>Phe/Tyr</b> <b>ratio</b>	<b>Current Age</b> (months)
#8	183	1.9	11
#9	180	1.9	25
#10	162	2.3	31
#11	162	2.4	34
#12	200	2.1	60

# Awaiting Reality ...

Pt.#13 - 3544g White ♀

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
11 hours	223	4.6
12 months	204	4.4
36 months	341	5.2

# Awaiting Reality ...

Pt.#14 - 408 Ig White ♀

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
13 hours	282	4.2
12 months	224	3.7
36 months	296	5.2
60 months	287	4.8

# Questions ...

How long do you monitor phe  
levels  $< 360 \mu\text{M}$ ?

When can you close the case?



# Another Simple Idea





# Interfering Substances

babies in the NICU on IV feedings can have falsely elevated phe levels



# Interfering Substances

of 107 babies on HA/TPN with elevated phe levels in one year:

	<b>Phe</b>	<b>Phe/Tyr</b>
<b>Median</b>	<b>187</b>	<b>2.5</b>
<b>Mean</b>	<b>232</b>	<b>2.9</b>

# Interfering Substances

of 107 babies on HA/TPN with elevated phe levels in one year:

	<b>Phe</b>	<b>Phe/Tyr</b>
Median	187	2.5
Mean	232	2.9
<b>Low</b>	<b>152</b>	<b>0.3</b>
<b>High</b>	<b>1213</b>	<b>24.0</b>

# Reality

median 187  
mean 232

Pt.#15 - 1330g White ♂

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
1 hour (on HA/TPN)	165	2.3

# Reality

Pt.#15 - 1330g White ♂

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
1 hour (on HA/TPN)	165	2.3
9 days (off HA/TPN?)	2964	42.7

# Reality

Pt.#15 - 1330g White ♂

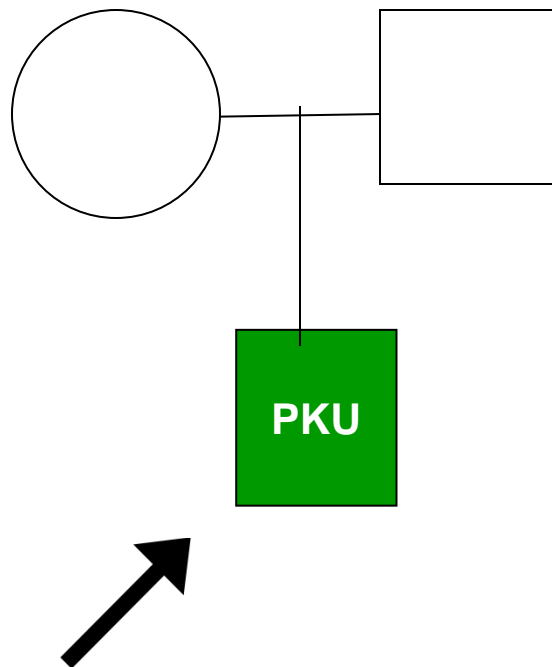
Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
1 hour	165	2.3
9 days	<b>2964</b>	<b>42.7</b>

diagnostic serum  
@ 12 days:  
Phe = 3199  $\mu\text{M}$   
Phe/Tyr = 28.3

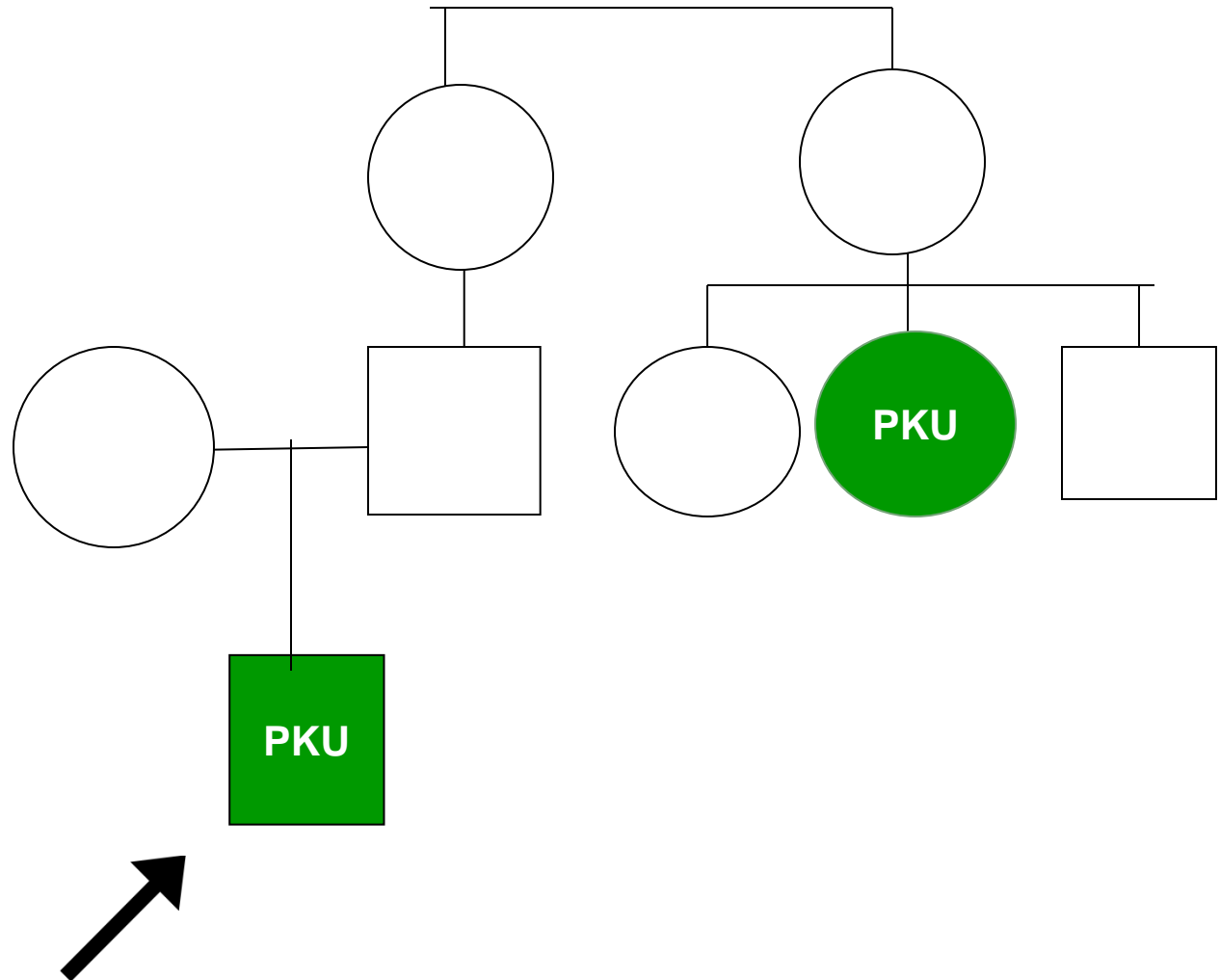


*Yikes*

# Family History ...

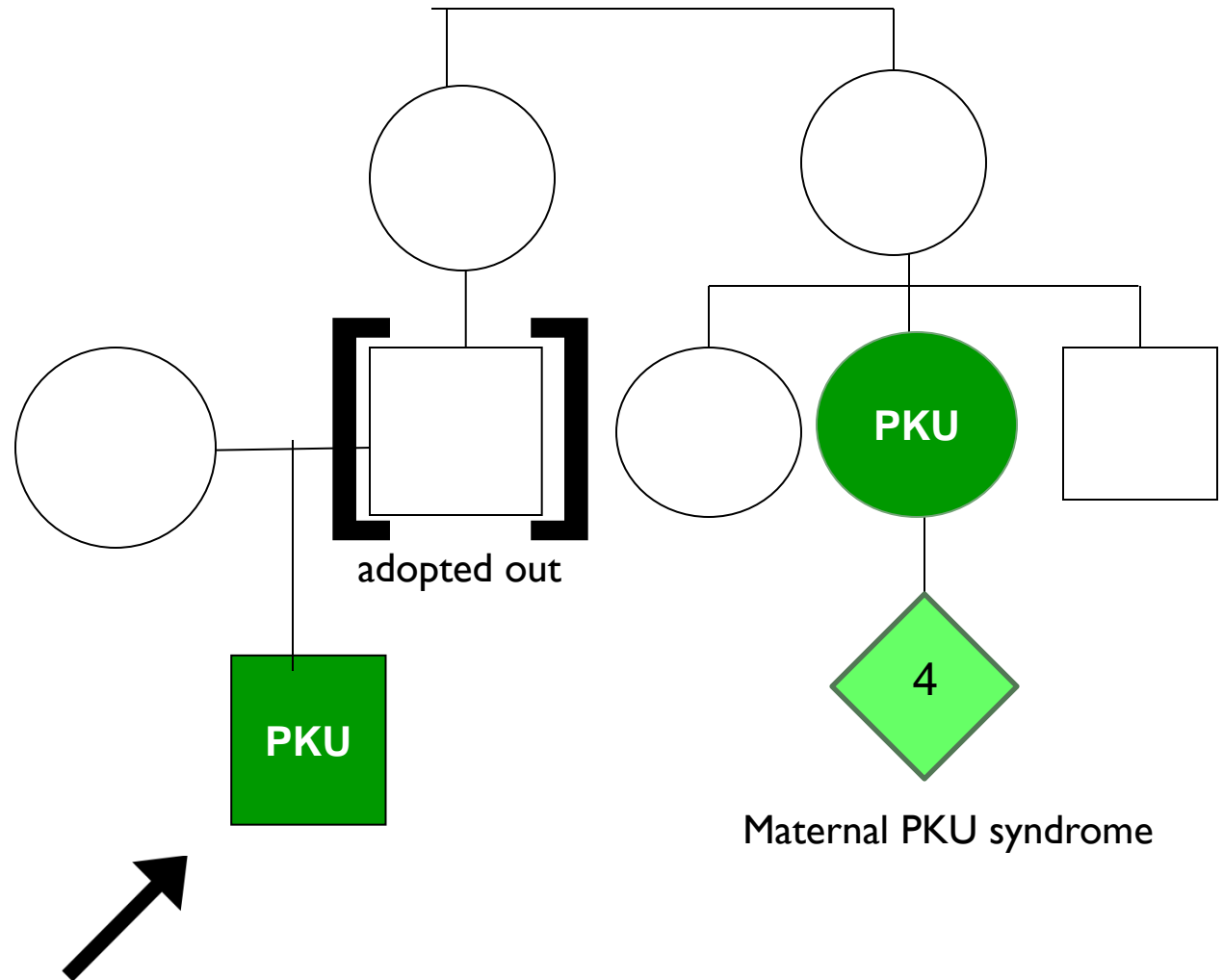


# Family History of PKU!

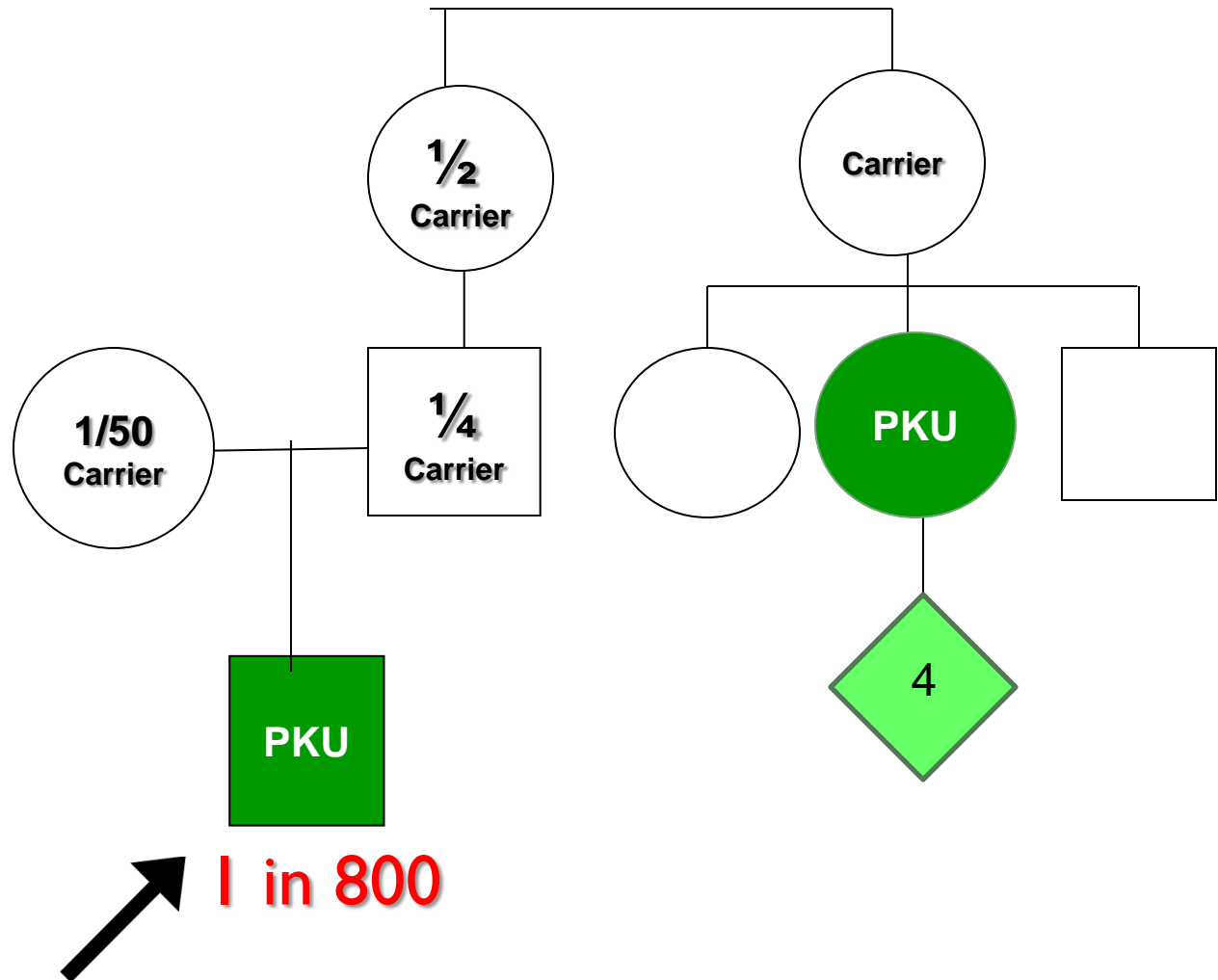




# Family History Uncovered



# Increased Risk for PKU



# Question ...

How aggressive do we need to be when babies on HA/TPN have elevated phe levels?

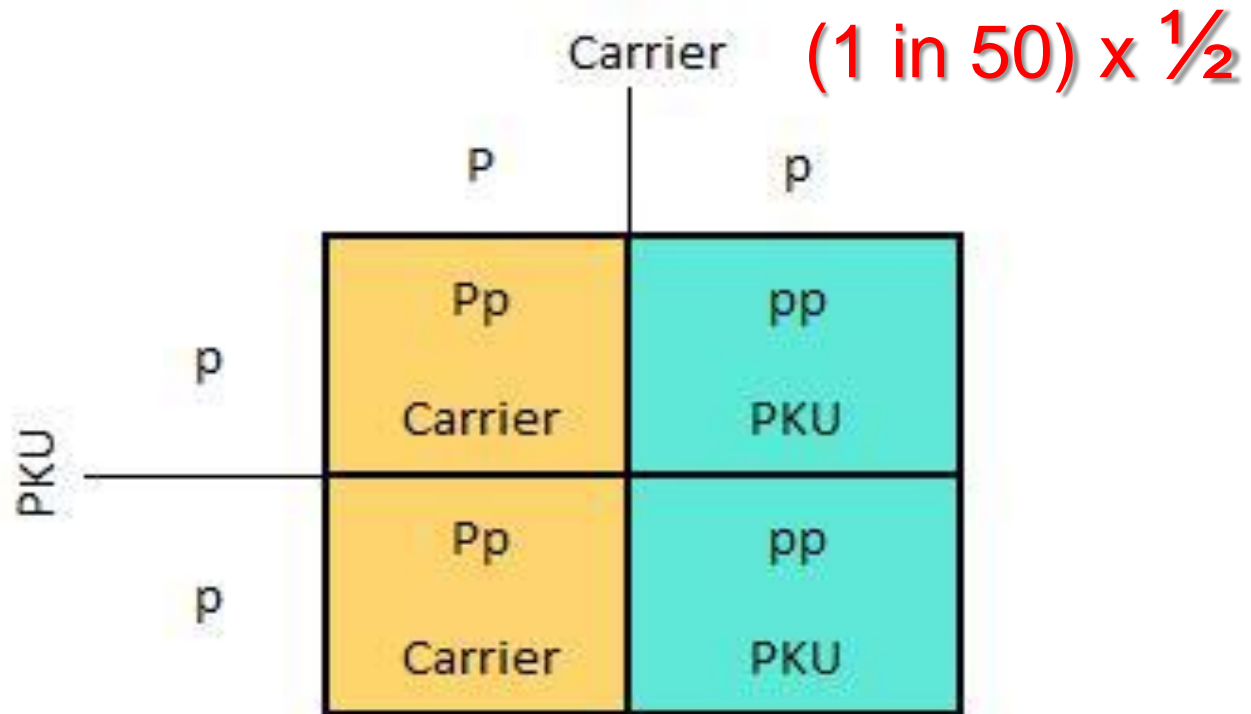


# Another Simple Idea



# Maternal PKU

Most women with PKU **do not** have children with PKU (~1% chance)



# Reality

but ... babies of women with PKU  
can have elevated phe levels at birth

Pt.#16 - 2870g White ♀

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
4 hours	<b>489</b>	2.3

# Reality

but ... babies of mothers with PKU can have elevated phe levels at birth

Pt.#16 - 2870g White ♀

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
4 hours (cord blood)	489	2.3
4 days	89	2.2

# Reality

but ... babies of mothers with PKU can have elevated phe levels at birth

Pt.#16 - 2870g White ♀

Age	Phe ( $\mu\text{M}$ )	Phe/Tyr
4 hours (cord blood)	<b>489</b>	2.3
4 days	89	2.2
10 days	96	1.0
16 days	74	1.0



# Question ...

Can we expect hospitalists to understand all of the issues related to maternal PKU?



# My Thoughts ...



# ...“Bottom” Line Realities



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As Newborn Screeners we must:

- Monitor elevated phe levels long-term



# ...“Bottom” Line Realities

As Newborn Screeners we must:

- Monitor elevated phe levels long-term
- Resolve results from babies on HA/TPN



# ...“Bottom” Line Realities

As Newborn Screeners we must:

- Monitor elevated phe levels long-term
- Resolve results from babies on HA/TPN
- Continually provide NBS education



# Acknowledgements

WA State NBS Laboratory,  
Follow-up, & Support staff



University of Washington  
PKU Clinic staff & families





**TIME FOR**

**QUESTIONS**