Recommendations for Dietitians: Dietary Adjustments and BH_4 Responsiveness

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Patient Selection

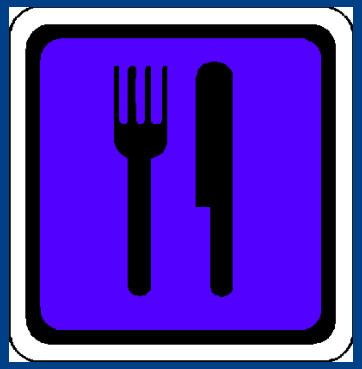
- Age
  - 4 years and older
- Type of PKU
  - Moderate PKU most likely to respond
- Ability to comply
  - Blood specimens
  - Diet records
- Life situation
  - Maternal PKU

Setting Expectations

- BH_4 is not a cure
- Approximately 25% of people respond
- Most people remain on some degree of Phe/protein restriction
  - Average increase in Phe intake in BioMarin study was 29 mg/kg
- Likely that some medical food will be needed

Adequate Trial of BH_4 Responsiveness

- Keep diet intake the same
  - Medical food
  - Phenylalanine intake
- No major lifestyle changes
  - Exercise
  - Dining out
  - Travel
- Not ill
- Trial for 4 weeks recommended



Drug Administration

- Recommended dose of Kuvan™ is 5−20 mg/kg/d
  - Based on actual weight
- 100 mg tablets
  - Swallowed whole or
  - Dissolved in 4−8 ounces of apple juice or water
    - Drink within 15 minutes of dissolving
- Take once a day with food

Determining Dose

- 70 kg patient
- 20 mg/kg = 1400 mg sapropterin dihydrochloride
- 100 mg per tablet = 14 tablets

Determining Responsiveness

- Blood Phe re-checked at 24−48 hours, then 7, 14, 21, 28 days
- Clinical judgment
  - Reduction in blood Phe
    - BioMarin study criteria was a ≥ 30% reduction in blood Phe
      - 1200 to 840 µmol/L (20 to 14 mg/dL)
      - 360 to 252 µmol/L (6 to 4.2 mg/dL)
  - Increased phenylalanine tolerance
  - Improved attention, mood, behavior

Adjusting Diets- It's what we do!

Factors affecting blood phenylalanine

Before BH_4

- Amount of Phe
- Type and amount of protein
- Energy intake
- Weight gain
- Growth spurts
- Illness/Injury
- Exercise

With BH_4

- Amount of Phe
- Type and amount of protein
- Energy intake
- Weight gain
- Growth spurts
- Illness/Injury
- Exercise
- BH_4 Responsiveness

Dietary Phenylalanine Challenge

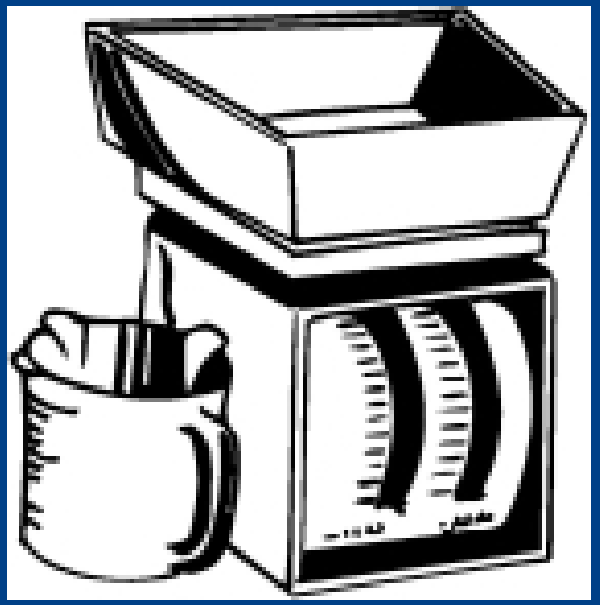
- If blood Phe < 360 µmol/L
  - Add 10 mg/kg dietary Phe
    - 350 mg maximum increase
  - Add as milk or egg powder

Nutrient Composition of Nonfat Dried Milk (NFDM) and Dried Egg White Powder

Protein Source	Energy	Protein (gm)	Phe (mg)
10 grams NFDM Powder	35	3.5	170
21 grams NFDM Powder	74	7.4	350
10 grams Egg Powder	38	8.2	518
7 grams Egg Powder	26	5.8	363

During Diet Adjustments

- Weekly blood Phe determinations
- Diet intake records
  - Assess using usual methods for
    - Energy
    - Protein
    - Phenylalanine
    - Tyrosine
    - Vitamins/Minerals
    - Fluid
- Medical food intake is kept constant



Medical Food Adjustment

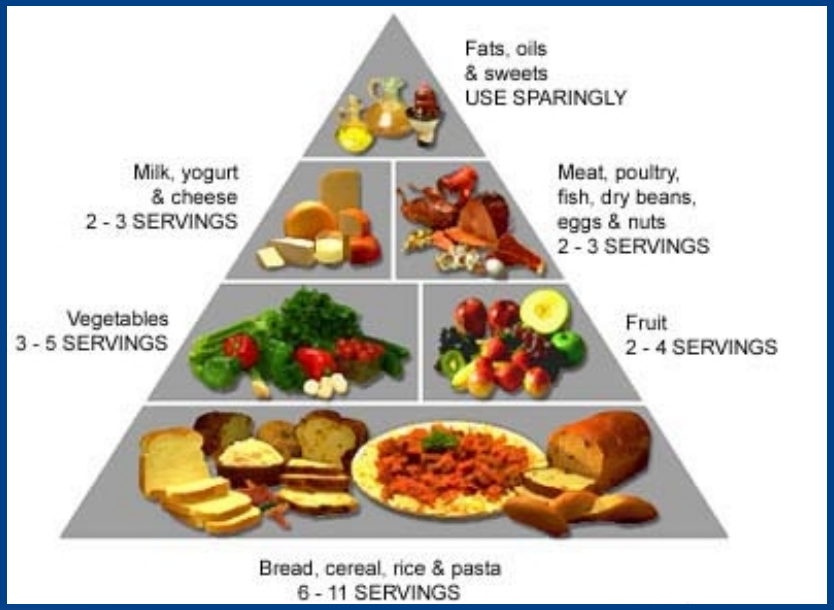
- Consider decreasing protein from medical food
  - By amount of additional protein being provided by milk or egg powder
  - Example—patient tolerates
    - 50 grams of NFDM = 18 g protein = 900 mg Phe
    - Reduce medical food by 18 grams of protein
- Re-evaluate total protein intake compared to DRI

Should Some Medical Food Remain Part of the Diet?

- Advantages of continuing medical food
  - Times when need to decrease Phe and medical food can provide protein
    - Illness
    - Growth spurts
  - Times when BH_4 would be discontinued
    - Pregnancy
    - Drug not tolerated
- Disadvantages
  - Expense
  - Adherence
  - Lifestyle

Adding Phenylalanine as Food

- Patients may be
  - Overwhelmed by amount of extra Phe
  - Fearful of increasing Phe too quickly
  - Hesitant about adding foods that might be taken away
  - Needing diet re-education



Small Steps

- Replace low protein products with regular foods
  - Bread, pasta, cereal, baked goods
- Introduce high protein foods
  - Suggest foods that are easily measured (egg, cheese)
  - Counsel patients that small errors in measuring result in large increases in Phe

Protein Content of Food

Food	Amount	Gram Weight	Protein (g)	Phe (mg)
Milk, low fat	1 ounce (2 TBSP)	30	1	50
Yogurt, low fat	1 ounce (2 TBSP)	30	1.2	65
Cheese, parmesan	1 TBSP	5	2	100
Peanut butter	1 TBSP	16	4	190
Hot dog, beef	1 (10/kg)	45	5	220
Cheese, American	1	21	5	240
Egg, large	1	50	6	340
Tuna, canned	1 ounce (1/8 cup)	29	7	260

SOURCE: USDA DATABASE

Diet 10 yr old—475 mg Phe/day

Diet 1: 10 year old, weight 29 kg: 475 mg phenylalanine (16/kg)				
Food	**Amount**	**Phe (mg)**	**Protein (g)**	**Energy (kcal)**
Phenex-2	1 cup (120 g)	0	35.0	492
Orange juice	½ cup	11	0.9	56
Cheerios	½ cup	80	1.5	55
Non-dairy creamer	¼ cup	57	1.1	37
Low protein toast	1 slice	9	0.2	110
Margarine	1 tsp	1	0.0	34
Jam	1 TBSP	4	0.1	56
French fries	1 sm serving	139	3.5	290
Lettuce	½ cup	8	0.3	5
Tomato	2 slice	20	0.3	5
Cucumber	2 slice	4	0.1	2
Italian dressing	1 TBSP	0	0.0	43
Low protein rice	1/3 cup dry	7	0.2	210
Broccoli	½ cup	70	1.9	114
Low protein cheese	2 slice	56	1.4	120
Low protein choc chip cookie	2 cookies	6	0.4	240

Diet Adjustment 650 mg Phe/day

Food	Amount	Phe (mg)	Protein (g)	Energy (kcal)
Phenex-2	1 cup (120 g)	0	35.0	492
Orange juice	½ cup	11	0.9	56
Cheerios	½ cup	80	1.5	55
Non-dairy creamer	¼ cup	57	.06	37
Wheat toast, regular	½ slice	33	1.4	33
Margarine	2 tsp	2	0.1	70
Jam	2 TBSP	8	0.2	111
French fries	1 sm serving	139	3.5	290
Lettuce	½ cup	8	0.3	5
Tomato	2 slice	20	0.3	5
Cucumber	2 slice	4	0.1	2
Italian dressing	2 TBSP	0	0.0	86
Rice, regular white	2/3 cup	152	2.9	138
Broccoli	½ cup	70	1.9	114
Low protein cheese	2 slice	56	1.4	120
Low protein choc chip cookie	2 cookies	6	0.4	240
TOTAL		**646**	**46.8**	**1854**

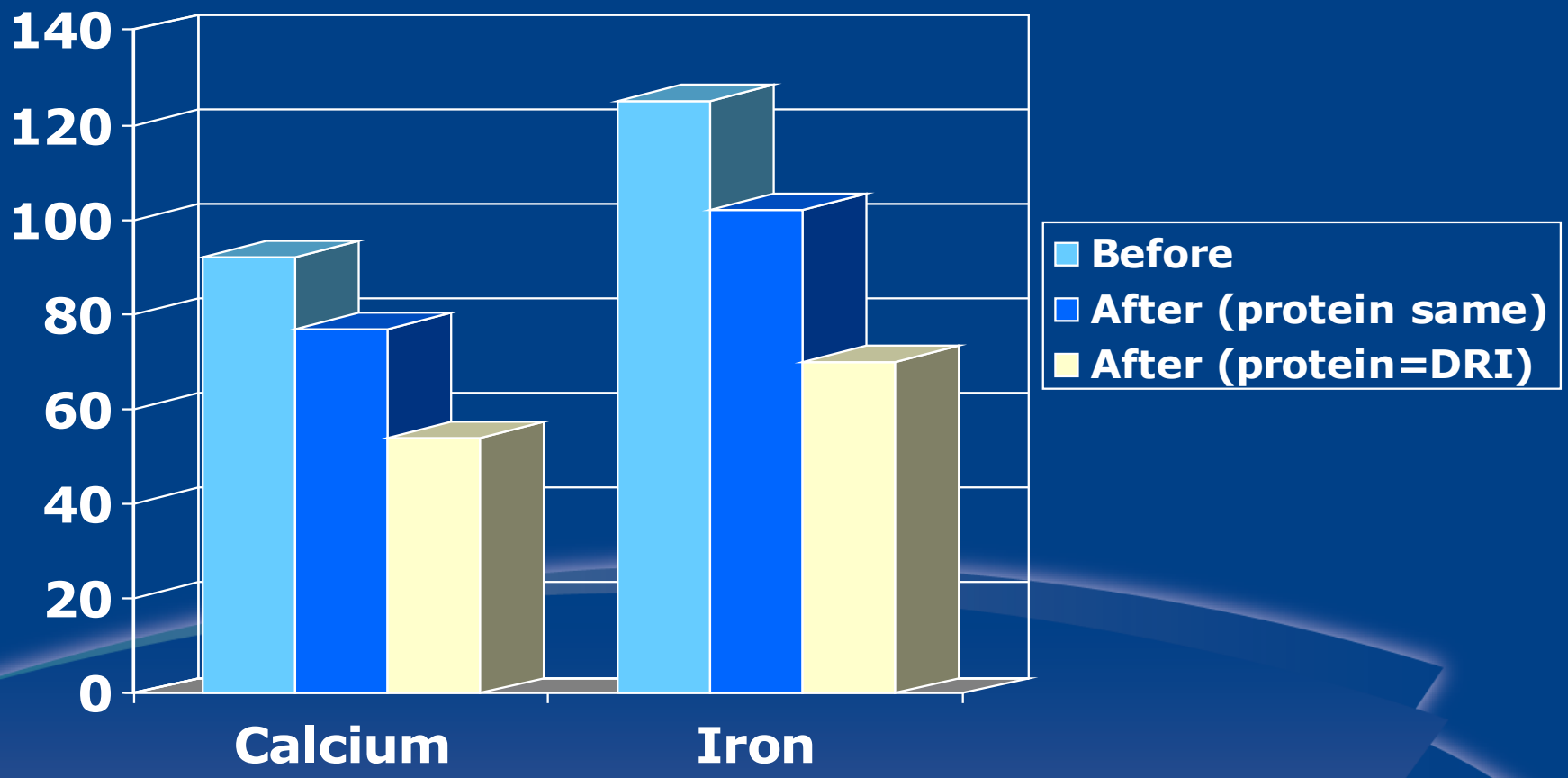
Diet Adjustment 1350 mg Phe/day

Food	Amount	Phe (mg)	Protein (g)	Energy (kcal)
Phenex-2	0.5 cup (60 g)	0	18.0	246
Orange juice	¾ cup	17	1.4	84
Cheerios	1 cup	160	3.0	110
Milk, whole	½ cup	179	3.9	73
Wheat toast, regular	1 slice	66	2.7	66
Margarine	1 tsp	1	0.0	51
Jam	1 TBSP	4	0.1	56
French fries	1 med serving	217	3.5	453
Lettuce	½ cup	8	0.3	5
Tomato	2 slice	20	0.3	5
Cucumber	2 slice	4	0.1	2
Italian dressing	2 TBSP	0	0.0	86
Rice, regular white	2/3 cup	152	2.9	138
Broccoli	½ cup	70	1.9	114
Cheddar cheese	1 ounce	372	6.7	114
Choc chip cookie	2 cookies	73	1.7	137
Cranberry juice	4 ounces	0	0.0	68
TOTAL		**1343**	**46.5**	**1808**

Diet Re-evaluation

- Protein
  - 46 g before and after
    - Ross protocol:≥40 g
    - DRI: 34 g
      - should total protein intake be reduced to meet DRI?
- Vitamins and Minerals likely to be low when animal protein intake is minimal or absent:
  - Iron, Calcium, Zinc, Vitamin D, Vitamin B12

%DRI for calcium and iron before/after diet change

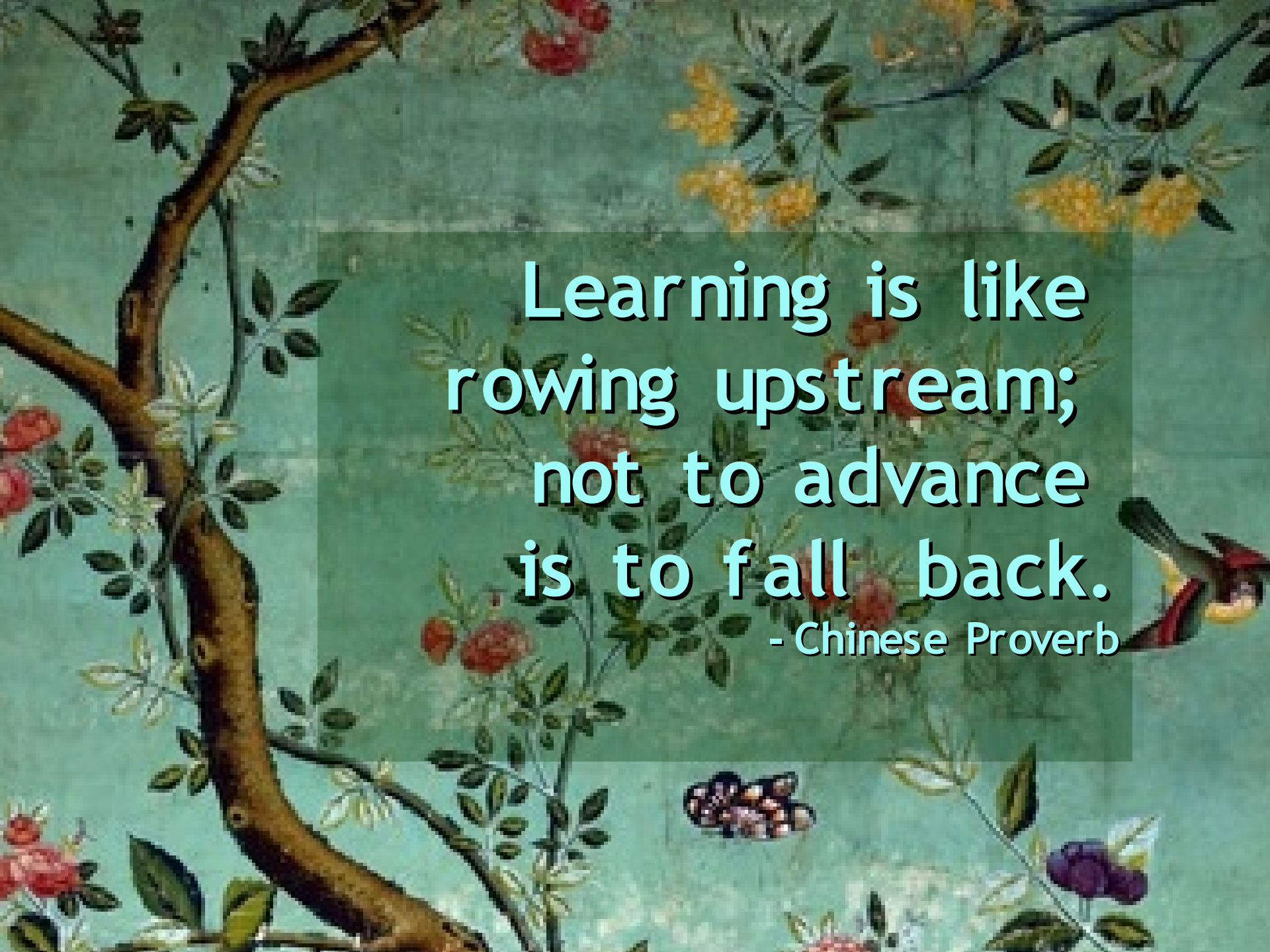


Monitoring

- Anthropometrics
  - Adjust drug dose
- Dietary intake
- Metabolic status
  - Blood Phe/Tyr
  - Plasma Amino Acids
- Nutrient status
  - CBC, albumin, pre-albumin, ferritin, others as needed

Summary

- BH_4 offers the hope that a subset of people with PKU will be able to have
  - Diets containing more natural protein
  - Better control of blood Phe
- Dietitians role
  - Helping to determine which patients respond to BH_4
  - Monitoring blood Phe, diet intake, nutritional status
  - Educating families
- Guidelines are a starting point


Learning is like
rowing upstream;
not to advance
is to fall back.
- Chinese Proverb