PARKINSON'S SCHOOL

An Online Course for Patients and Providers

2. Dopamine Repletion
In Search of a Smoother Ride

Laurie K Mischley, ND PhD MPH

28 Jan 2021

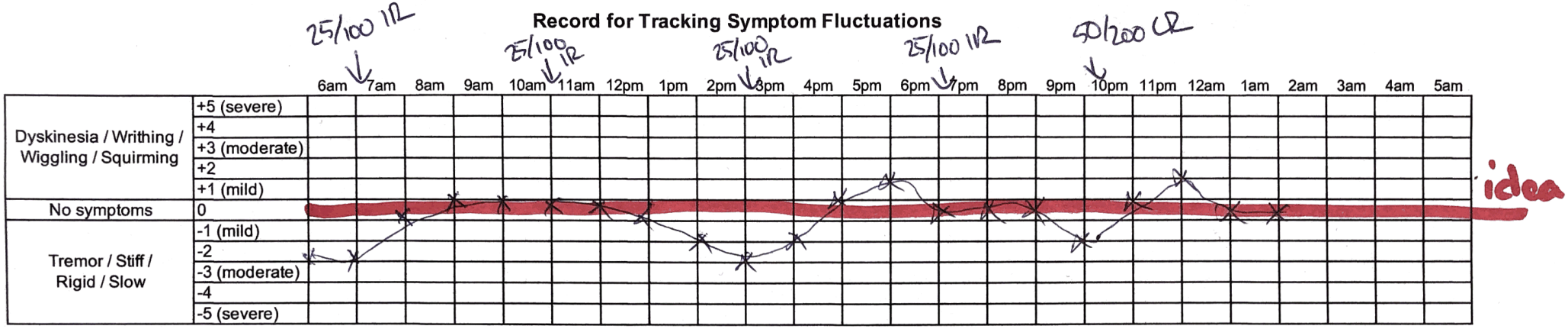
Goals

- Make meds last longer
- Make meds kick in faster
- Optimize how well they can work
- Understand the role of mind in dosing and delivery
- Ensure medication maintains effectiveness long-term
- Minimize unwanted side effects



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Record for Tracking Symptom Fluctuations



		6am	7am	8am	9am	10am	11am	12pm	1pm	2pm	3pm	4pm	5pm	6pm	7pm	8pm	9pm	10pm	11pm	12am	1am	2am	3am	4am	5am
Dyskinesia / Writhing / Wiggling / Squirming	+5 (severe)																								
	+4																								
	+3 (moderate)																								
	+2																								
	+1 (mild)																								
No symptoms	0																								
Tremor / Stiff / Rigid / Slow	-1 (mild)																								
	-2																								
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Name:

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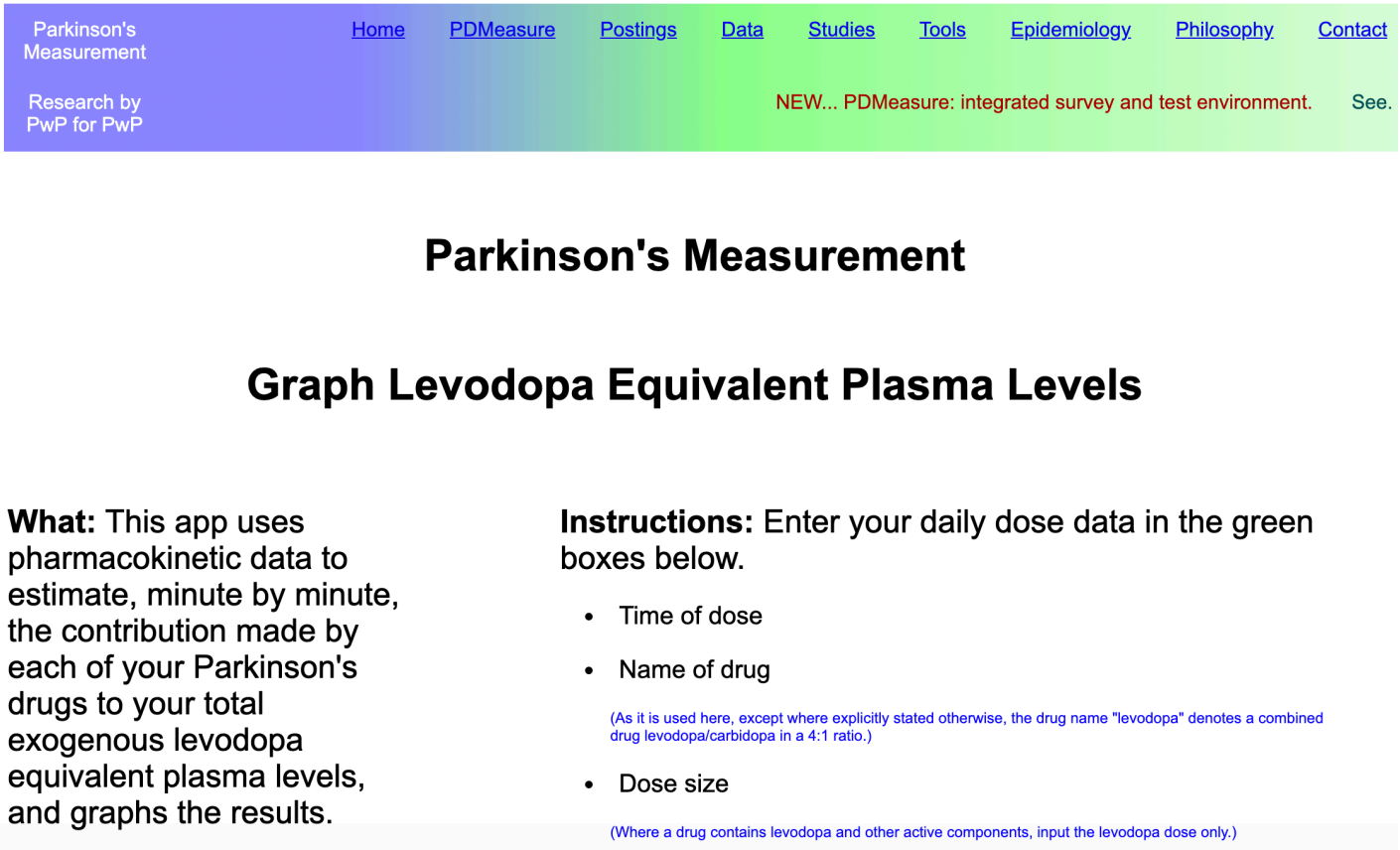
Too much dopamine		6am	7am	8am	9am	10am	11am	12pm	1pm	2pm	3pm	4pm	5pm	6pm	7pm	8pm	9pm	10pm	11pm	12am	1am	2am	3am	4am	5am
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ParkinsonsMeasurement.org

- https://www.parkinsonsmeasurement.org/index.htm





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Pharmacokinetics

LED conversion factors and pharmacokinetic parameters

The conversion factors used are shown in the table below. Where the literature shows large variations in what is thought to be the correct conversion factor to use, a tuple is shown meaning (lowest estimate/highest estimate/average estimate)

Drug	Conv Factor	CMAX (rel levodopa)	TMAX (min)	THALF (min)	Sources and Notes
Amantadine	1	0.169	126	847	+[14] Choose CMAX to equate AUC. Maximum daily dose is 400mg.
Apomorphine (intranasal)	7.5	19.59	23	31	+[12] bioavailability of intranasal cf subcutaneous = 45%
Apomorphine (subcutaneous)	10	30.62	18	27	+[12]
Levodopa	1	1	60	81	[1]*[5]
Levodopa CR	0.7	0.4	120	137	* [13] bioavailability 70%, CMAX 60% lower than IR, TMAX approximately 2 hours, THALF chosen to equate AUC
Madopar	1	1	60	81	*[10] Brand name of levodopa with benserazide
Mirapexin	100	19.92	120	600	+[11] Max concentrations "between 1 and 3 hours",
Neupro Patch	30	3.215	0	10000	[15] Brand name of rotigotine patch. Assumed constant levels. CMAX adjusted to equate AUC.
Pramipexole	100	19.92	120	600	+[11] Max concentrations "between 1 and 3 hours", elimination half life varies from 8 to 12 hours
Rasagiline	100	10.72	0	10000	[1] Maximum effect found with 1mg. Estimate based on AUC argument and constant effect.
Requip	20	5.59	90	360	Brand name of ropinirole
RequipXL	20	4.34	480	360	Inferred from [3]. Brand name of ropinirole CR
Ropinirole	20	5.59	90	360	[1][2] (16.67,33.3,21.3)[6]+
RopiniroleCR	20	4.34	480	360	See RequipXL.[7]+
Rotigotine Patch	30	3.215	0	10000	+[15] Constant in steady state.
Sinemet	1	1	60	81	Brand name of levodopa with carbidopa.*
Sinemet CR	0.7	0.4	120	137	* [13] brand name Levodopa CR
Stalevo	1.33	1.08	90	117	[1][2] (1.2,1.33,1.25)*[5] The THALF estimate is derived from [5]. Go to the heading THALF "after the last dose in PD patients". The average of Group I and II is 1.95 hours or 117 minutes as shown.

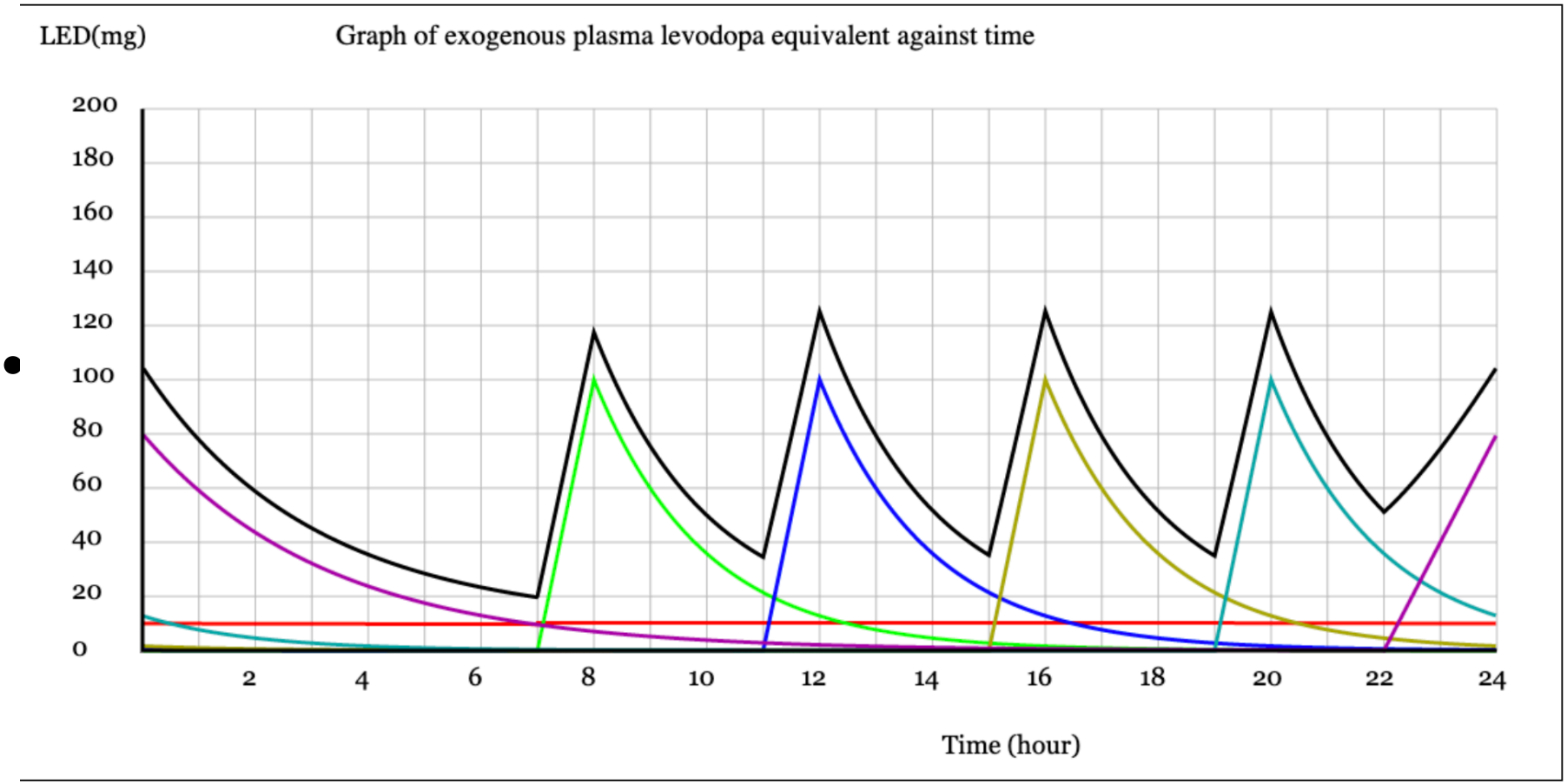
- https://www.parkinsonsmeasurement.org/index.htm

My most frequent recommended dosing schedule:

- 7 am: 1 mg rasagiline + 25/100 IR carbidopa/ levodopa
- 11 am: 25/100 IR carbidopa/ levodopa
- 3 pm: 25/100 IR carbidopa/ levodopa
- 7 pm: 25/100 IR carbidopa/ levodopa
- 9:30/10 pm (bedtime): 50/200 CR

Time hh	Time mm	Drug	Dose mg	Conversion Factor	LED mg	CMAX 1mg this rel 1mg LD	TMAX min	THALF min	AUC mg.min	Colour
7		Rasagiline	1	100	100	10.715	0	10000	14502	
7		Levodopa	100	1	100	1	60	81	14686	
11		Levodopa	100	1	100	1	60	81	14686	
15		Levodopa	100	1	100	1	60	81	14686	
19		Levodopa	100	1	100	1	60	81	14686	
22		Levodopa CR	200	0.7	140	0.4	120	137	20592	

Time hh	Time mm	Drug	Dose mg	Conversion Factor	LED mg	CMAX 1mg this rel 1mg LD	TMAX min	THALF min	AUC mg.min	Colour
7		Rasagiline	1	100	100	10.715	0	10000	14502	
7		Levodopa	100	1	100	1	60	81	14686	
11		Levodopa	100	1	100	1	60	81	14686	
15		Levodopa	100	1	100	1	60	81	14686	
19		Levodopa	100	1	100	1	60	81	14686	
22		Levodopa CR	200	0.7	140	0.4	120	137	20592	



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Bedtime Meds

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I’m not taking any levodopa at bedtime. Do I need to?

- Early in the disease, usually not.
- A couple years in, people will usually begin to complain the they are waking up stiff in the morning, maybe with curling toes, having trouble turning over in bed, or stiffness and pain (or anxiety) are interfering with their sleep.
    - *Then* I’ll add 50/200 CR at bedtime.



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A student in the class said they take 2 25/100 IR at bedtime. Is that the same as a 50/200 CR?

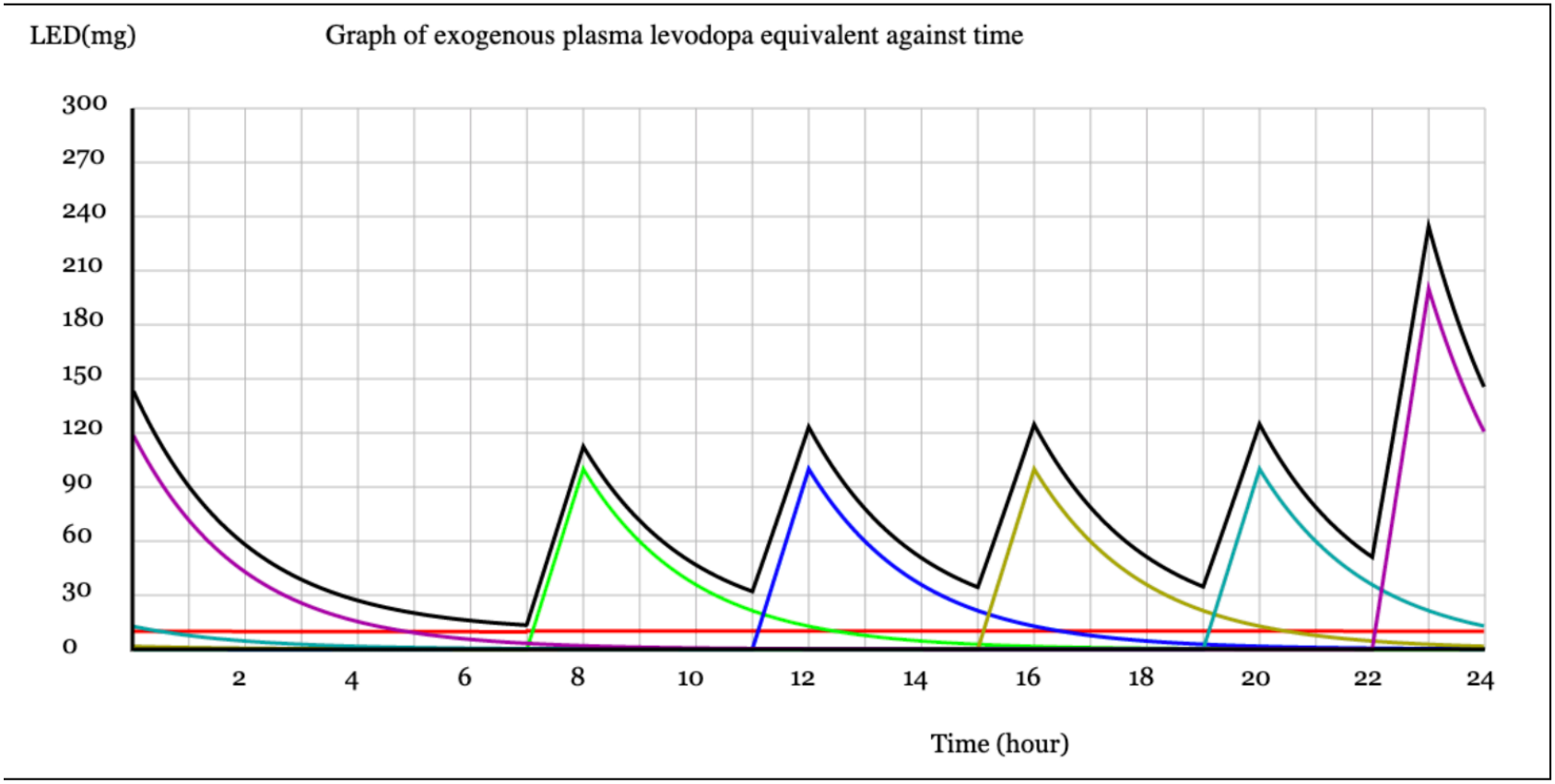
Time hh	Time mm	Drug	Dose mg
7		Rasagiline	1
7		Levodopa	100
11		Levodopa	100
15		Levodopa	100
19		Levodopa	100
22		Levodopa	200

- https://www.parkinsonsmeasurement.org/index.htm



2-25/100 IR

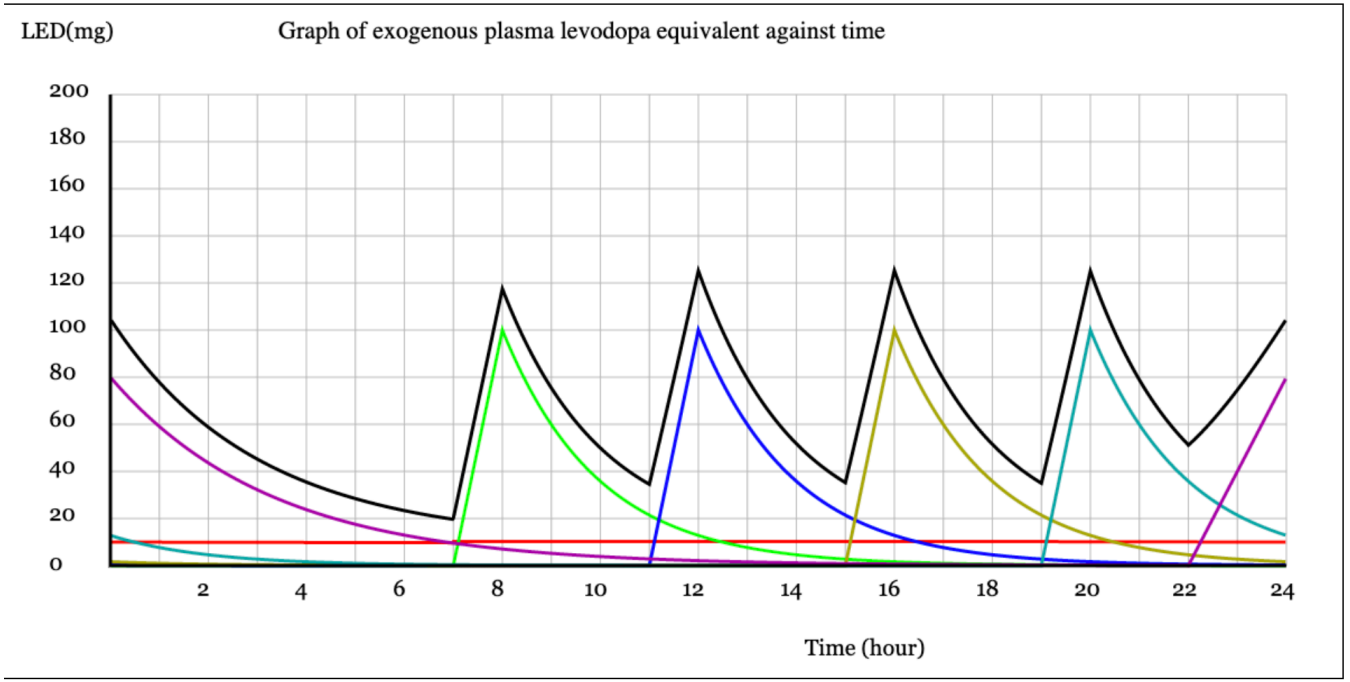
Time hh	Time mm	Drug	Dose mg
7		Rasagiline	1
7		Levodopa	100
11		Levodopa	100
15		Levodopa	100
19		Levodopa	100
22		Levodopa	200



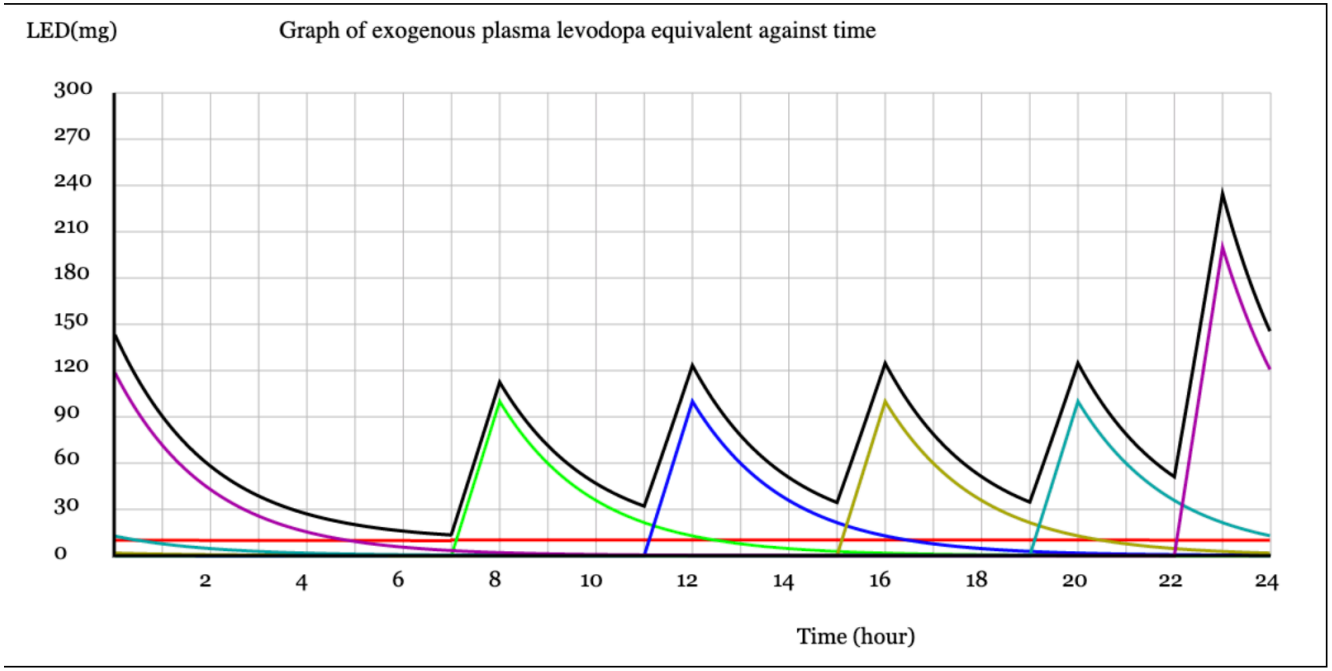
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50/200
CR at
bedtime



2 25/100
IR at
bedtime



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Should my dad take cur turmeric and quercitin to strengthen his immune system and protect against Covid?

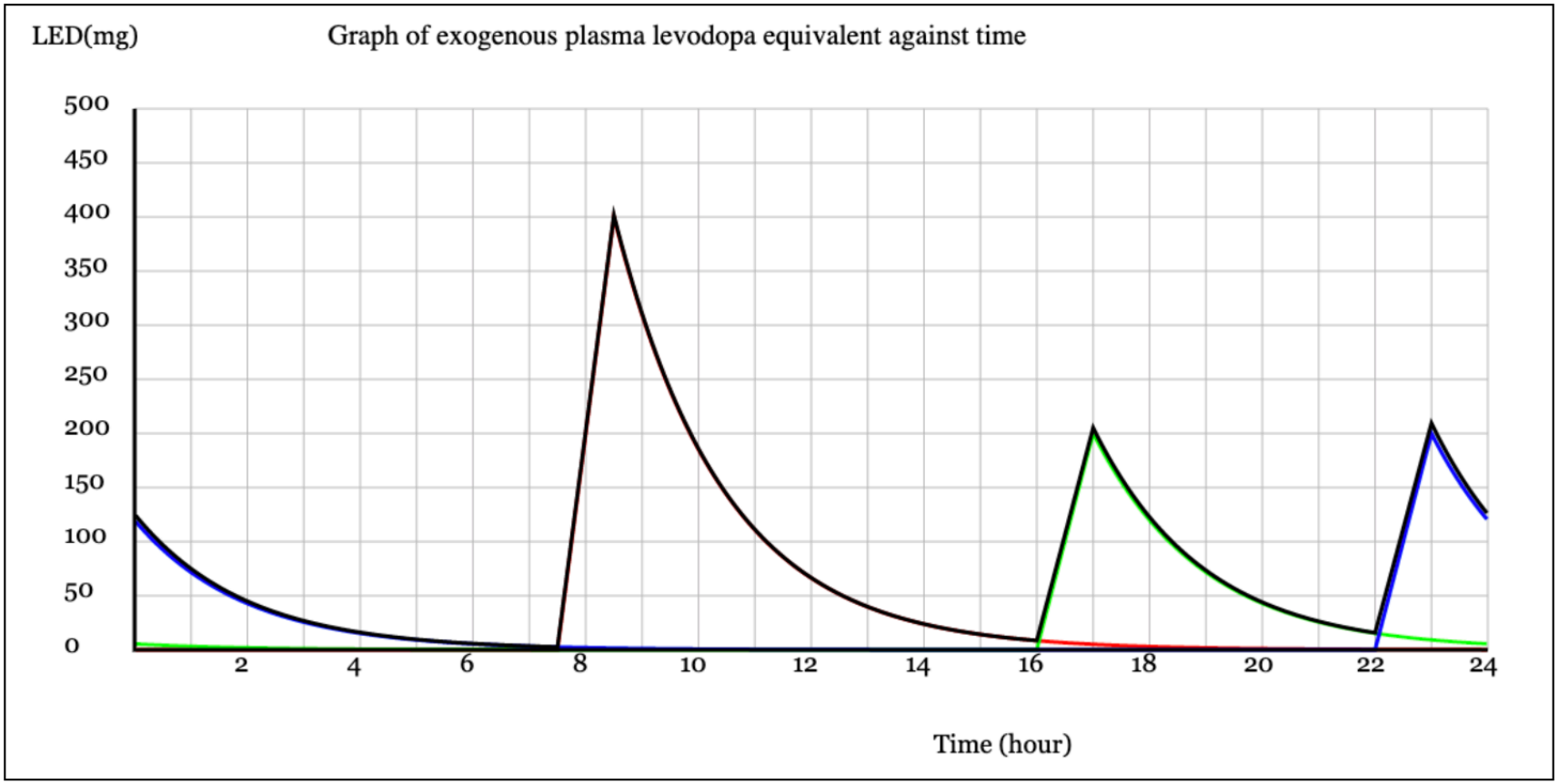
- Med review:

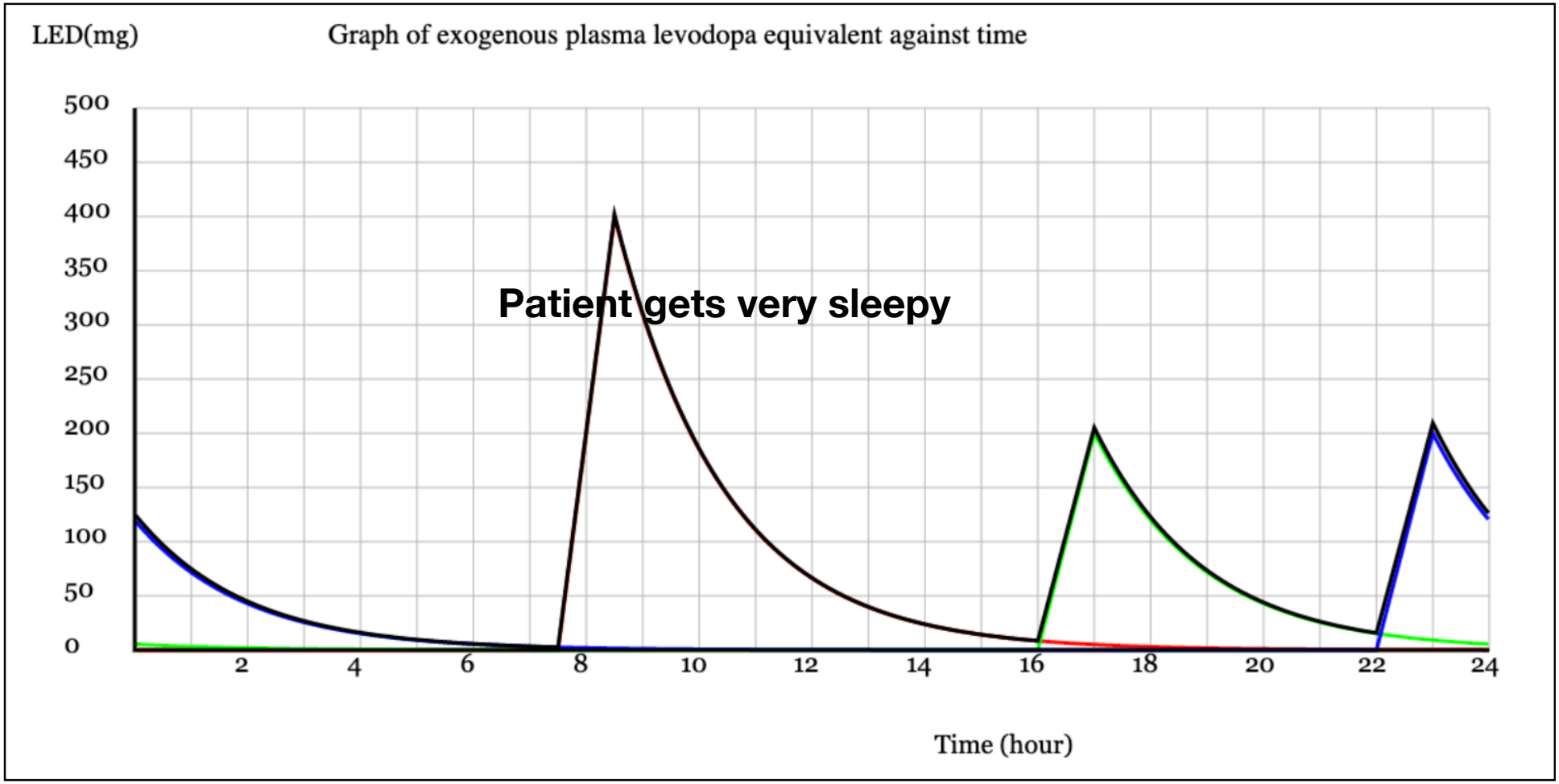
Time hh	Time mm	Drug	Dose mg
7	30	Levodopa	400
16		Levodopa	200
22		Levodopa	200

  - 7 am: 4 - 2
  - 4 pm: 2 25/100 IR
  - 10 pm: 2 25/100 IR



Patient from New York





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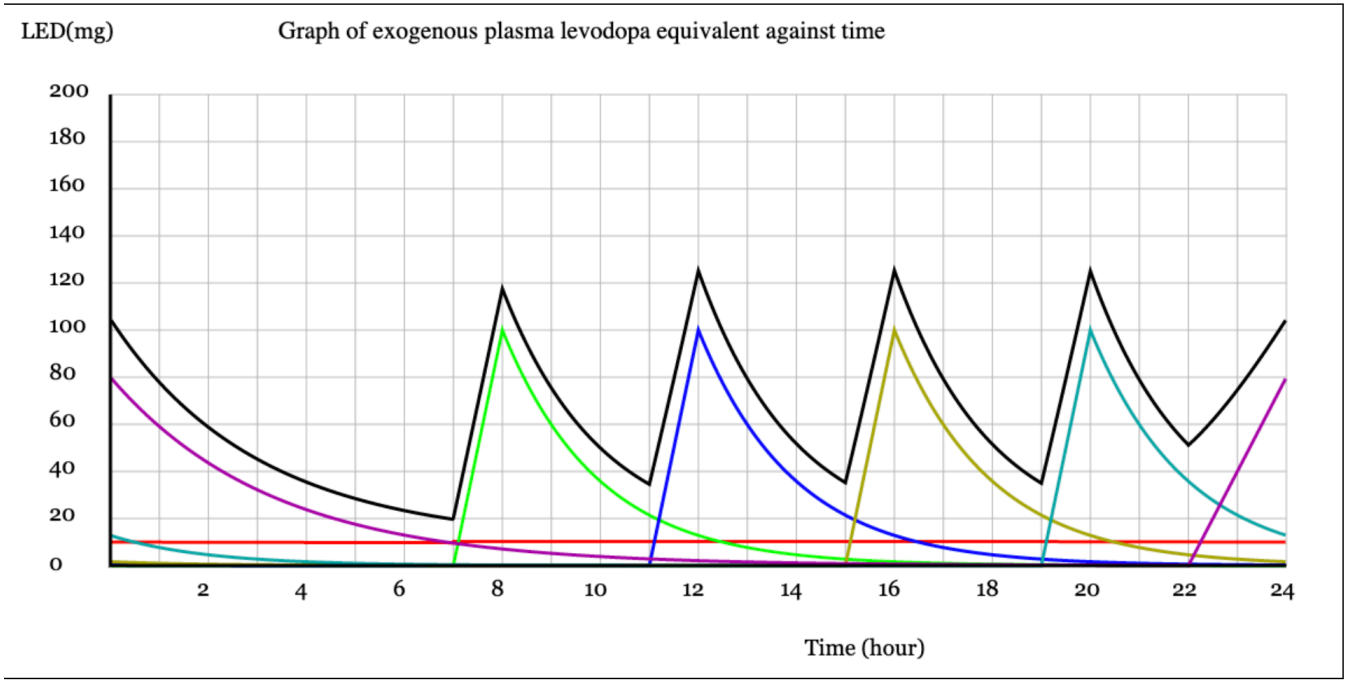
Levodopa Equivalent

- Why you should know your LEq
  - Over time, just as I have you track your PRO-PD, so should be able to track change over time. Doctors should be tracking it. (I haven't been, but intend to start)
    - A person that doubles in a year should be managed very differently than someone that doubles every 10 years.

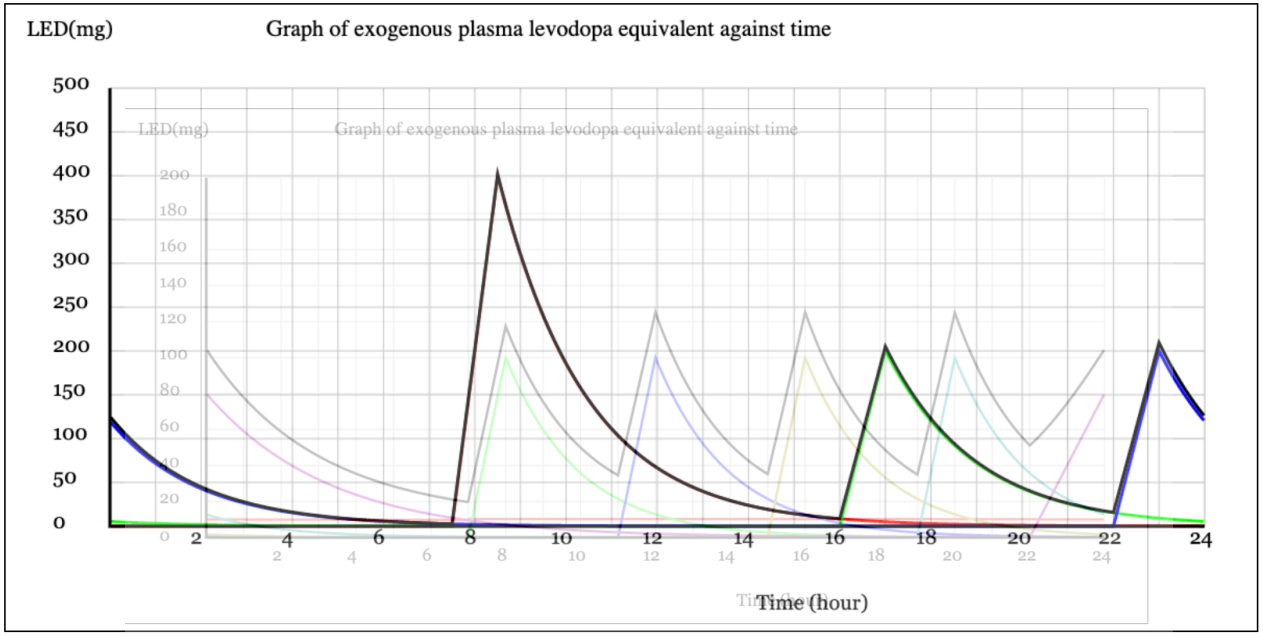


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LD 550

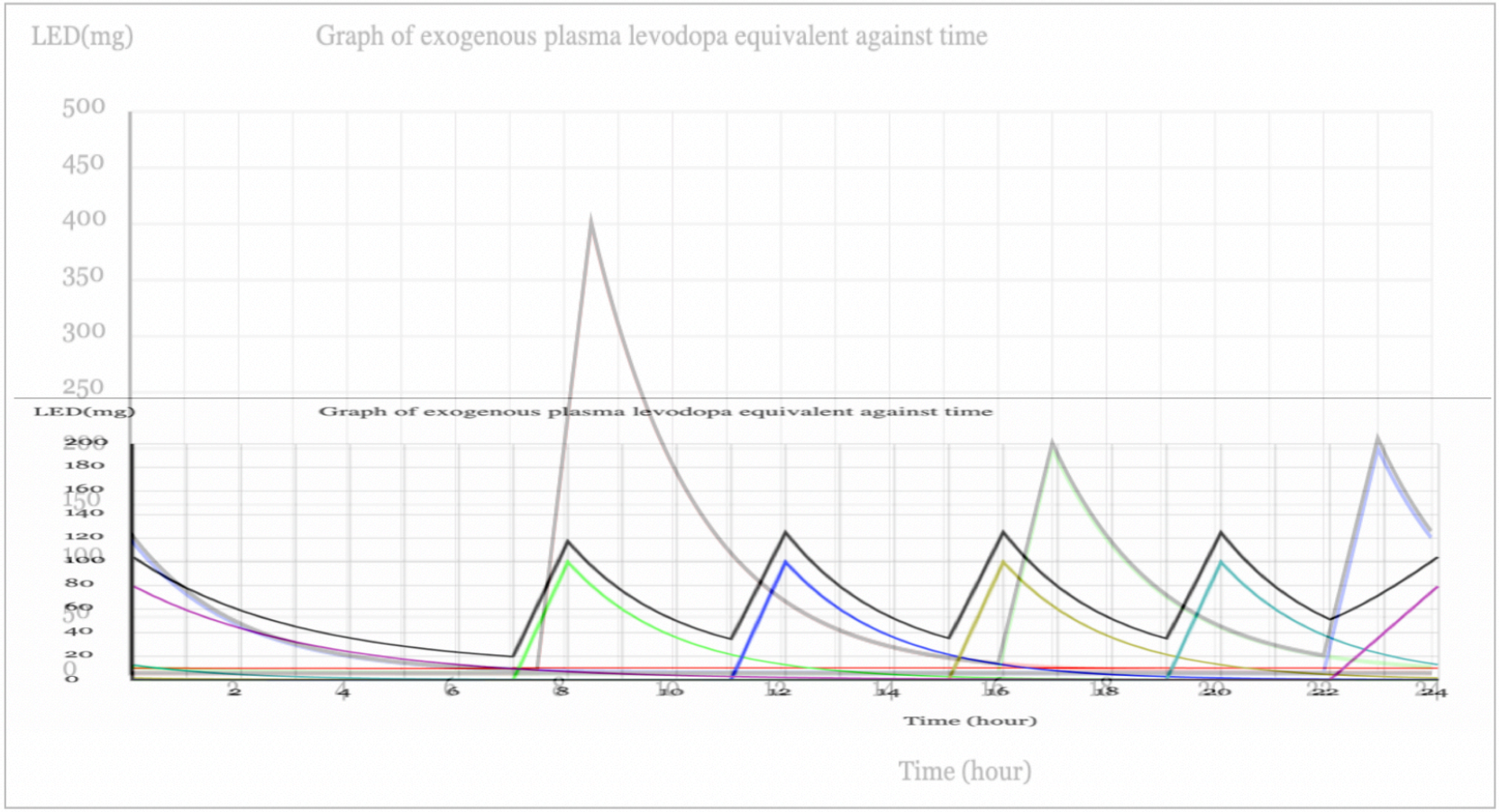


LD 800



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Dosing Diversity



Levodopa - Compulsive Behavior

- Too much of ANY dopamine medication can lead to poor judgment and impulse control issues.
- Agonists are definitely the most common offender
- It can happen with levodopa too, although less common
  - Gambling, Shopping, Sex/ Porn, Driving fast
  - Tinkering, Hobbies, Punding

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Wearing On/Wearing Off Dyskinesia

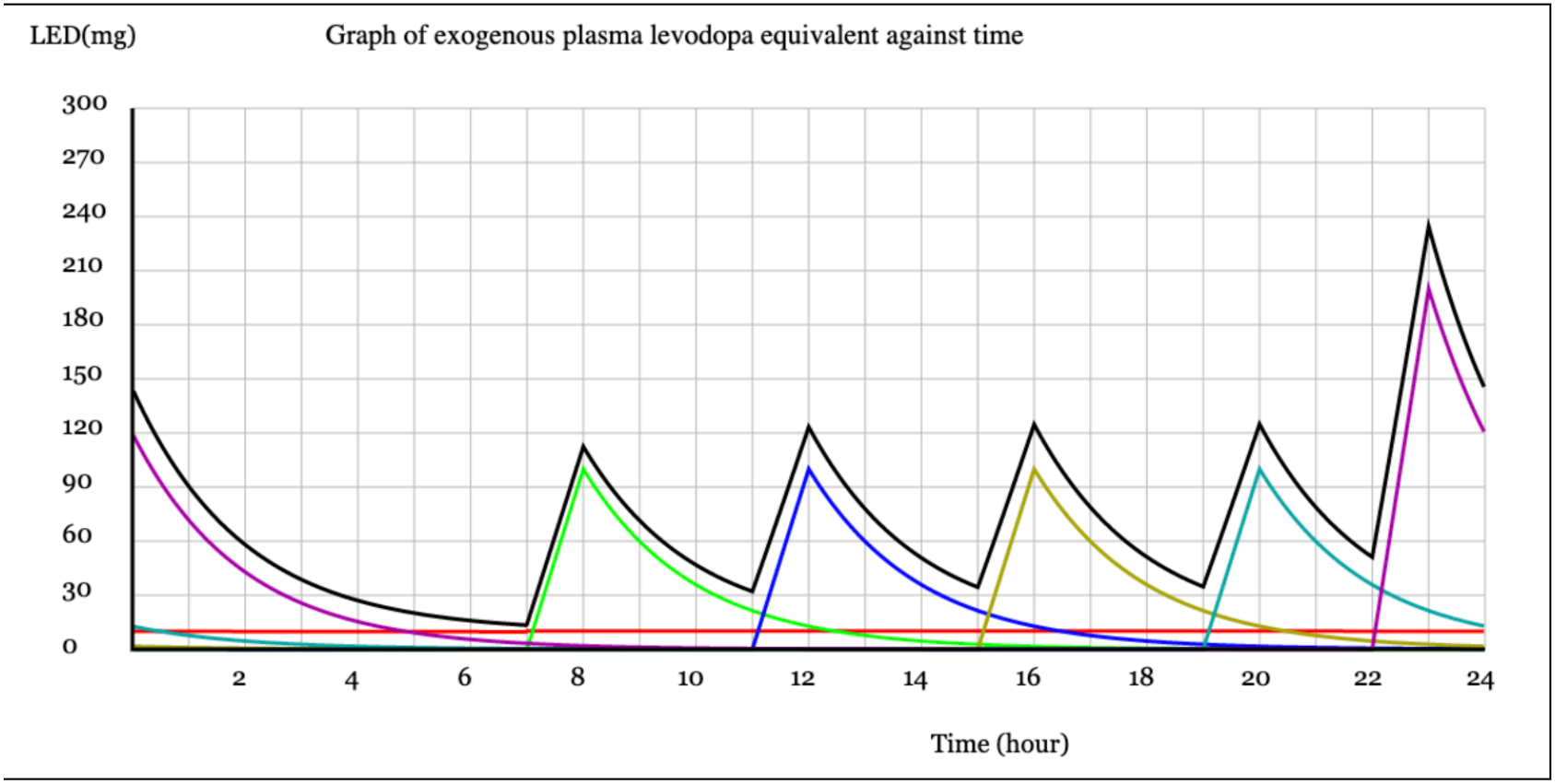
- Trouble shifting gears
- Can often be prevented by changing the timing of meds
  - Usually happens 30-60 min before next dose is due, or in the 30 min or so after taking a pill.
  - Moving next dose 30-60 min sooner may help.
  - The Levodopa Equivalent calculator can be helpful.



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2-25/100 IR

Time hh	Time mm	Drug	Dose mg
7		Rasagiline	1
7		Levodopa	100
11		Levodopa	100
15		Levodopa	100
19		Levodopa	100
22		Levodopa	200



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Training Your Response

- Fabrizio Benedetti in Italy
- Apomorphine subcutaneous injections
  - The more days you have exposure to the medication, the stronger the placebo response (body gets trained)
  - Effect wears off after 24 h

“Priming”

- a.k.a. the placebo response.
- The effect of any medicine is only, in part, due to the biological substance being swallowed. Expectation, both conscious and subconscious, plays a role.

  —> Take your medicine with an alarm,

  e.g. chirping bird, bell, favorite song, etc.

  - **Do NOT turn off the sound until you’ve swallowed your pill.**
- Teach your body how to budget. Train your brain to trust that it will get what it needs, reliably.



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Avoiding Protein Works

- Dozens of you have personally told me this year that reducing the intake of dietary protein has reduced your off times and led to an overall smother ride.
- HUMANS REQUIRE PROTEIN
    - How to ensure adequacy?

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Preventing Protein Deficiency

TO MAINTAIN

- 0.8 - 1 mg / kg body weight for healthy adults
  - 150 lb person/ 2.2 lb/kg = 68 kg —> ~ 68 mg protein/day

TO BUILD & REPAIR

- 1-1.5 mg/kg if elderly, losing weight, senescence, repair
  - 150 lb/ 2.2 lb/kg = 68 kg x 1.5 mg/kg= ~102 mg protein/day



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Easily Digested High-Protein Foods (sneak these in between c/l doses)

- Sushi, Poached fish, Pickled herring, Lox, Smoked fish (19 g/ 3 oz fish)
- Beans- lentils (18 g/c), **fava beans (13 g/cup)**
- Nuts and seeds: e.g. sunflower seeds, cashew butter on apple, edamame, chia seeds (5g/oz), almonds (6 g/oz)
    - Peanut butter smoothie, e.g. oat milk (4g/c), peanut butter (8 g/ 2 Tablespoons), bananas (1.3 g), chocolate (1g/Tbsp)
- Blended nuts & seeds + beans: E.g. Hummus (sesame butter + garbanzo beans (15 g/c))
- Vegetables- brussels sprouts (6 g/c), yellow corn (5 g/ear), potatoes (5g/potato)
- Grain— quinoa (8g/c), wild rice (6 g/c)
- Fruit: avocado (4 g/ avocado)

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Who are we?

Dr. Pamela Hutchison BSc, ND



- Naturopathic Doctor
- 20 years - Neurological and Mental Health focused practice
- World PD Congress 2016, 2019, hopefully 2022!
- Volunteer with Dr. Laurie Mischley PhD, ND for PD School. - 2019
- Exercise enthusiast - run, swim, bike, repeat!

Tiffany Rusch BSc, MAN, RD



- Registered Dietitian
- Wide range of dietetic experience
  - Community health, sport nutrition, workplace wellness, diabetes ed, long term care, and more
- New to Victoria & Acacia
- Also a big fan of running and biking, but the swim is holding me back from a triathlon!

Typical Food Examples

• 3 oz meat	25g
• ¾ cup Greek yogurt	18g
• ¼ cup pumpkin seeds	17g
• ½ cup cottage cheese	15g
• 2 Lg eggs	13g
• ½ cup tofu	10g
• ½ cup beans/lentils	10g
• 2 T Peanut butter	8g
• 1 cup cow's milk	9g
• 1 cup soy milk	7g



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Foods that are low in protein



Breads, rice, pasta - 2 grams per serving
1 serving: 1 slice of bread, 1/2 cup rice,1/2 cup pasta



Cereal - 2 grams/serving
1 serving: 1/2-1 cup



Vegetables - 1 gram/serving (1/2 cup)



Oils, vinegars, herbs, & spices



Fruits - trace amount/serving (1/2 cup)

Live Well With Parkinson's

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However....

Not all vegetables are “Free”



Nutrition Facts

Serving Size 1 Avocado	201 g
Amount Per Serving	
Calories 322	Calories from fat 245
	% Daily Value
Total Fat 29g	45%
Saturated Fat 4g	21%
Trans Fat 0G	
Cholesterol 0g	0%
Sodium 12mg	1%
Total Carbohydrate 17g	6%
Dietary Fiber 13g	54%
Sugars 1g	
Protein 4g	
Vitamin a	6%
Vitamin C	33%
Calcium	2%
Iron	6%

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.

1 Lima Beans



23% DV (11.6g) protein **per cup cooked**

209 Calories

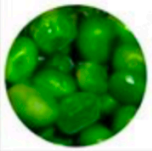
2 Soybean Sprouts



18% DV (9.2g) protein **1 cup**

85 Calories

3 Green Peas



17% DV (8.6g) protein **1 cup**

134 Calories

4 Spinach



11% DV (5.3g) protein **per cup cooked**

41 Calories

5 Sweet Corn



9% DV (4.7g) protein **per cup cooked**

125 Calories

6 Asparagus



9% DV (4.3g) protein **per cup cooked**

40 Calories

7 Artichokes (Globe or French)



8% DV (4.2g) protein **in a medium artichoke**

60 Calories

8 Brussels Sprouts



8% DV (4g) protein **per cup cooked**

56 Calories

9 Mushrooms (Button)



8% DV (3.9g) protein **1 cup**

28 Calories

10 Broccoli



7% DV (3.7g) protein **per cup cooked**

55 Calories

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Inbrija (inhaled levodopa)

- I love the idea of patients and doctors getting used to the idea that not all medications come in the form of a pill.
- This is the perfect “get out of jail free card” for times when you’ve had dietary protein, etc.
- Inhaling it completely bypasses the gut.

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Inbrija®
(levodopa inhalation powder)
42 mg capsules

US Healthcare Professionals Website | Patient Information | 1-833-INBRIJA | Información en español

For US Residents Only

OFF PERIODS | ABOUT INBRIJA | HOW TO USE INBRIJA | INBRIJA SUPPORT | RESOURCES | SIGN UP | MEET WITH A DOCTOR ONLINE

HOW TO USE INBRIJA®



Watch the demonstration video now.



Please see Patient Information Leaflet and Instructions For Use

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Does the lemon juice need to be straight, or can it be added to a glass of water?

- Water will not make the lemon juice less effective.
- 1 lemon ~ 3 Tbsp
- Trader Joe's



What about entacapone / Stalevo?

- Entacapone is a COMT inhibitor that makes each dose of levodopa last a little bit longer. When people experience ‘wearing off,’ sometimes it is given to extend the life of the levodopa dose a bit.

- Stalevo is a “pre-packaged” combination pill with carbidopa+ levodopa + entacapone

CDP-Choline

- 250 mg caps
- The study I reference most often used 2 caps in the morning, 2 caps at night
- Most of my patients prefer to take 1 cap 4x/ day (with their levodopa)
- 30-50% ‘boost’ for dopamine. Takes ~ 30 days to get the full effect.
- *** If you quit, you will have a 30-50% worsening in dopamine-responsive symptoms.



Should everyone on levodopa take CDP-choline?

- No! Take as little as you need of all this stuff. If your medications are working well and you're on a reasonably low dose… enjoy.
- Whatever dose you're on, 4 CDP-choline caps will give it a ~ 40% boost. ($35/ mo)
  - 3 pills / day —> behaves like 4/ 4.5 pills/day
  - **12 pills/ day —> behaves like 16 pills/day**



Where can I find the High DHA oil?



- 2-2.5 tsp of this will get your 4000-5000 mg (4-5 g) DHA
- You should notice a 40-50% reduction in dyskinesia by the end of the month. 2 months is even better.
- Even after stopping, the benefit usually persists. (But don't stop entirely- switch to a cheaper formulation/ lower dose!)

This is another product they offer with even more DHA: Ultra DHA



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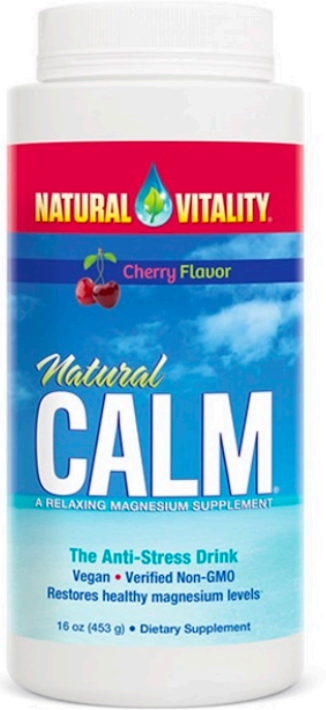
Is krill oil as effective as fish oil?

- Probably.
- General PD— As long as you get your 3000-4000 mg / d EPA +DHA, I don't really care whether it comes from cod liver oil, fish oil (fat under the skin), krill, or algae (vegan-preferred)
- Dyskinesia reduction — must be 4-5 g DHA



Instead of orange juice…

- No, orange juice, grapefruit juice, and vinegar are not acidic enough to mimic stomach acid.
- The things that *are* equally acidic
  - Lime juice
  - Ascorbic acid (vit C powder)
  - CALM magnesium powder



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Sample Acid Fortification

- 7 am- meds + water with fresh lemon
- 11 am - meds + powdered vit C
- 3 pm - meds + powdered vit C
- 7 pm - meds + CALM magnesium powder
- 10 pm- meds alone

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What about homeopathic mucuna?

- Homeopathy is this belief system, an ‘energetic vaccine’. (my words, not theirs). Energized (diluted and succussed) sugar pills. e.g. “sulfur” for people that wear mismatched socks. Intake in long, intimate, patients feel heard…

- I do not use homeopathy and I do not believe there is any logical or scientific evidence to support its efficacy, save perhaps the therapeutic intake and [possibly very real] placebo.

- For people that believe it works for them- great! If it is cheap and effective with minimal risk, use whatever works.

Is mucuna a good way to “dip my toes” in the l-dopa repletion quest?

- Exactly what it is best for!

Is there a preferred brand of mucuna? I've heard Japanese green tea works similarly to carbidopa- true?

LK Mischley 2021