CPD May 2024

Levodopa

**[Dr Sharon Rees](https://twitter.com/reesprescribe)**

Day 1: Still the mainstay of Parkinson’s disease (PD) treatment, [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) was extracted from faba bean seedlings in the early 20C. Deployed in the 1960s with dramatic ‘wakening’ effects on immobile people with PD. Side-effects were also dramatic! The era of catecholamine pathway discovery followed & it was realised that dopamine couldn’t cross the BBB, but prodrug L-dopa could with decarboxylation to dopamine in the brain; also rapidly converted in the gut (side-effects)

[](https://twitter.com/reesprescribe)

Day 2: [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) is always combined with a dopa decarboxylase inhibitor such as [#carbidopa](https://twitter.com/hashtag/carbidopa?src=hashtag_click) to inhibit the peripheral metabolism of [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click); this allows a lower dose & fewer side-effects, while more drug reaches the brain. I.r or m.r tablets in various combination strengths. Duodopa is an intestinal gel (levo+carbidopa) for advanced disease/tx for ‘on/off’ issues. Continuous jejunal delivery via percutaneous tube. Bypasses stomach/stabilises concentration/improves motor symptoms. Daily cassette £77/day. USA have inhaled L-dopa;not available UK

Day 3: [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) undergoes rapid enzymatic breakdown in blood which means a short t½. Breakdown is prevented by drugs like carbidopa & entacapone. Metabolised in blood & peripheral tissues into metabolites including epinephrine with predominantly renal excretion. Combined t½ 1-2 hrs

Day 4:[#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) replaces lost endogenous dopamine in basal ganglia & stimulates dopamine receptors reducing symptoms e.g slowness, stiffness, tremor. Long-term use ltd by dyskinesias, ‘on/off’ syndrome & loss of efficacy. Avoid abrupt withdrawal. [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) loss of efficacy over time is poorly understood. Mooted to be from loss of neurons & ability for dopamine ‘storage/buffering’. Unpredictable gastric emptying may contribute.

Day 5: [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) adverse drug effects mostly 'frequency not known'. Includes dyskinesias, on/off syndrome, GI disorders; dark urine, sexual dysfunction, psychosis, blood disorders, dementia; eye disorders. Sudden onset of sleep can mean risk assessment/counselling needed. NOT exhaustive

Day 6: [#levodopa](https://twitter.com/hashtag/levodopa?src=hashtag_click) DDIs: Severe; D2 receptor antagonists e.g clozapine or aripiprazole could reduce effects. Avoid with MAOIs (hypertensive crisis). Baclofen could increase risk of ADEs. Iron salts or high protein diet could impair absorption. NOT exhaustive

**Day 7:** Impulse control disorder is a feature of ‘dopamine dysregulation syndrome’ & #levodopa tx is associated with issues such as pathological gambling, compulsive shopping & sex addiction. Ensure safety netting systems in place

CPD. In addition to the tweets, read the BNF treatment summary on Parkinson’s disease, as well as the BNF monographs on the levodopa combination drugs. The SPC for a common levodopa-carbidopa combination is also useful

<https://bnf.nice.org.uk/treatment-summaries/parkinsons-disease/>

<https://bnf.nice.org.uk/drugs/co-careldopa/>

<https://bnf.nice.org.uk/drugs/co-beneldopa/>

<https://www.medicines.org.uk/emc/product/1654/smpc#gref>

1. **Levodopa was first extracted from the cocoa bean**

**True or False**

1. **Levodopa is a prodrug**

**True or False**

1. **Dopamine can cross the blood brain barrier but is slow to do so**

**True or False**

1. **It is standard practice to choose to give levodopa either on its own or in combination with other drugs**

**True or False**

1. **Which of the following is TRUE?**
2. **Levodopa is a dopamine antagonist**
3. **Levodopa has a long half-life**
4. **Levodopa is broken down exclusively in the liver**
5. **Levodopa has multiple metabolites**
6. **Which of the following is known to be managed by levodopa?**
7. **Tremor**
8. **Dementia**
9. **Poor sense of smell**
10. **Disease progression**
11. **Levodopa maintains its ability for good symptom control throughout the course of the disease**

**True or False**

1. **Which of the following is NOT a side-effect of levodopa combined with carbidopa?**
2. **Sudden onset of sleep**
3. **Psychotic disorder**
4. **Ankle oedema**
5. **Haemolytic anaemia**
6. **Why is there a mission to find alternative ways to administer levodopa while by-passing the gut?**
7. **Because concordance is difficult from daily doses**
8. **Because of the gut’s rapid breakdown requiring enzyme inhibitors to improve efficacy and prevent side-effects**
9. **Because the combination drugs are so expensive**
10. **Because of ongoing drug supply shortages**
11. **A dopamine imbalance in the brain, such as caused by levodopa, can cause dysregulation in the ‘reward’ pathway, leading to addictions and compulsive behaviours**

**True or False**