PENYAKIT PARKINSON

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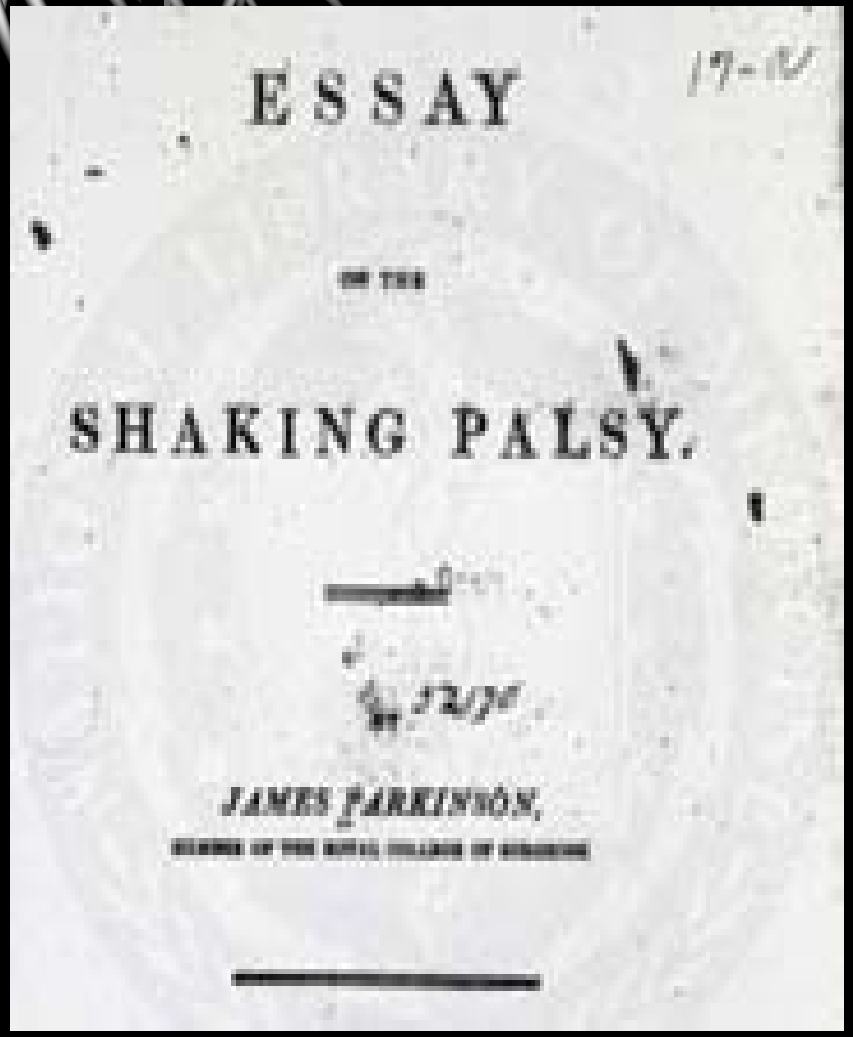
Pendahuluan

- Th 1817 → Dr. James Parkinson mempublikasikan kasus pasien yang mengalami "shaking palsy" (shake = gemetar, palsy = kelumpuhan)
- Sejak saat itu → muncul istilah Parkinsonism → menggambarkan gejala klinik yang ditandai dg : gemetar, kekakuan, bradikinesia, dan instabilitas postural.


James C Parkinson



ESSAY

ON THE

SHAKING PALSY.

JAMES PARKINSON,

AN

ESSAY

ON THE

SHAKING PALSY.

CHAPTER I.

DEFINITION–HISTORY–ILLUSTRATIVE CASES.

SHAKING PALSY. *(Paralysis Agitans.)*

Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured.

Definisi

- Penyakit Parkinson:

  Penyakit gangguan syaraf kronis dan progresif yang ditandai dengan gemetar, kekakuan, berkurangnya kecepatan gerakan, dan ekspresi wajah kosong seperti topeng dg salivasi berlebihan.

Epidemiologi

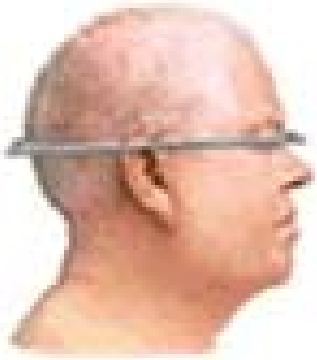
- Kejadian meningkat dengan meningkatnya usia (angka harapan hidup)
- Onsetnya terjadi pada sekitar usia 60 th
- Faktor lingkungan tidak begitu berpengaruh
- Pada penyakit Parkinson yang terjadi di bawah 50 th, mungkin ada faktor genetik

Etiologi

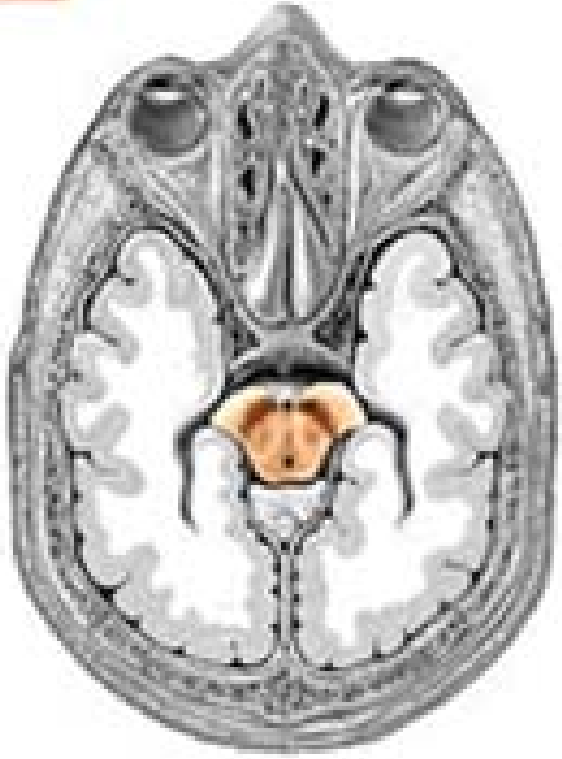
- faktor resiko tidak diketahui, tapi sebagian besar pasien yang etiologinya dapat diidentifikasi adalah pasien yang menerima antagonis dopamine
- selain itu, beberapa hal yang dapat menyebabkan gejala Parkinson antara lain:
  - obat, spt: fenotiazin, benzamid, metildopa, dan reserpin, metoklopramid, SSRI, Amiodarone, Diltiazem, asam Valproat
  - keracunan logam berat (Mn)
  - anoksia (keracunan CO)
  - pasca trauma, dll.

Patofisiologi

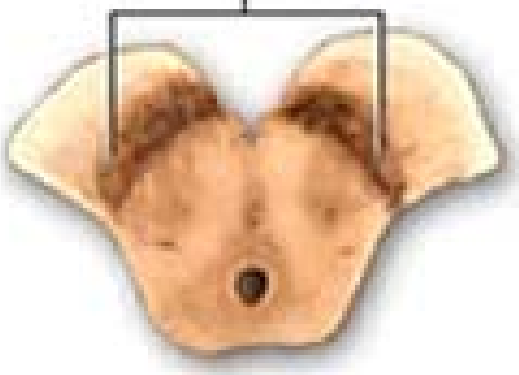
- Abnormalitas patologis yang utama: degenerasi sel dengan hilangnya neuron dopaminergik yang terpigmentasi di pars compacta substansia nigra di otak dan ketidakseimbangan sirkuit motor ekstrapiramidal (pengatur gerakan di otak).
- Pd orang normal: berkurangnya dopamin: 5% per dekade
- Pd penderita Parkinson → 45% selama dekade pertama setelah diagnosis
- Biasanya gejala baru muncul ketika dopamin di striatal sudah berkurang sampai 80%
- Degenerasi saraf dopamin pada nigrostriatal menyebabkan peningkatan aktivitas kolinergik striatal → efek tremor



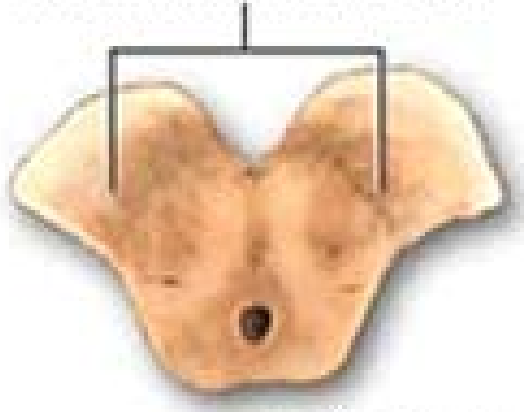
Cut section of the midbrain where a portion of the substantia nigra is visible



Substantia nigra



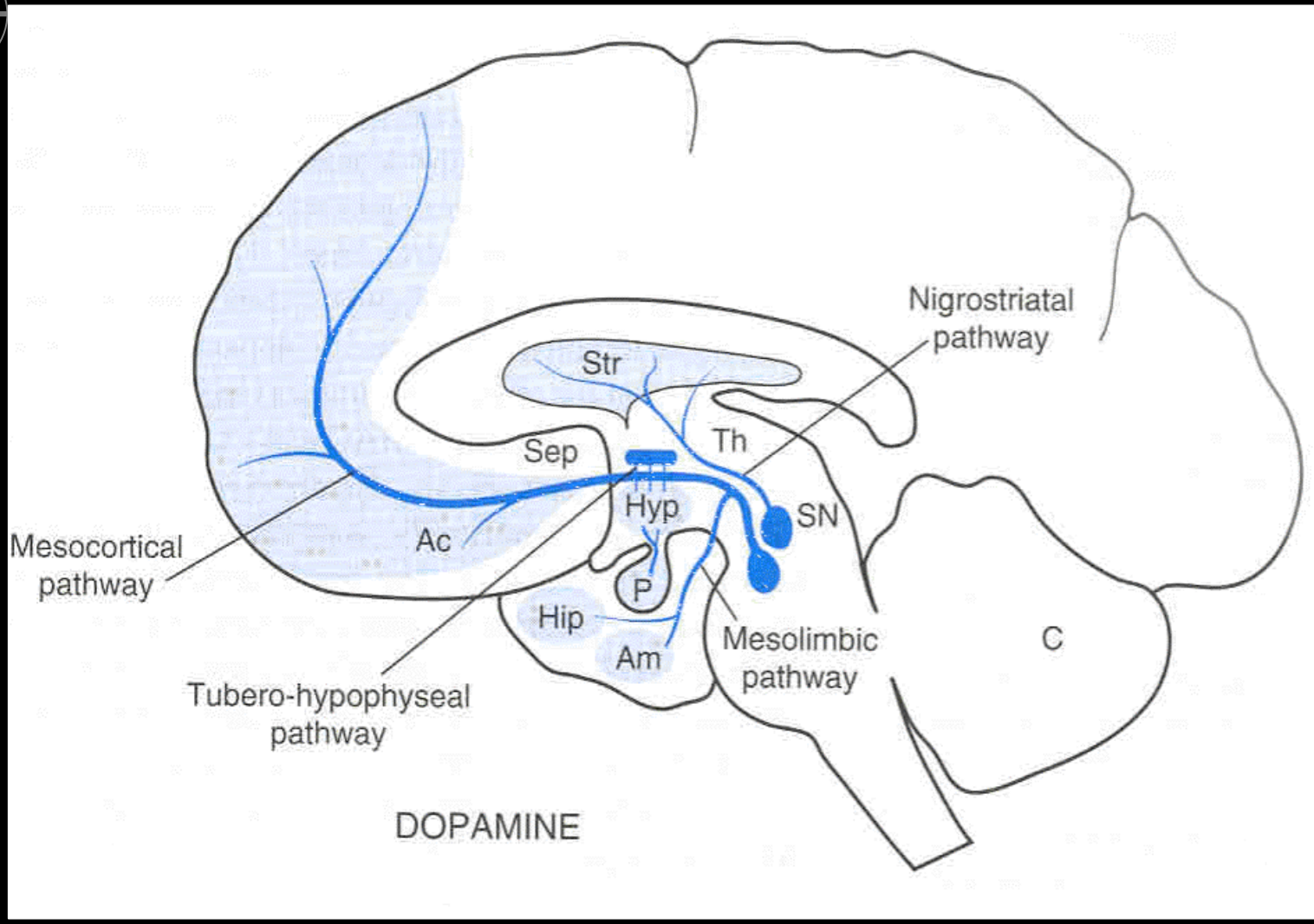
Diminished substantia nigra as seen in Parkinson's disease

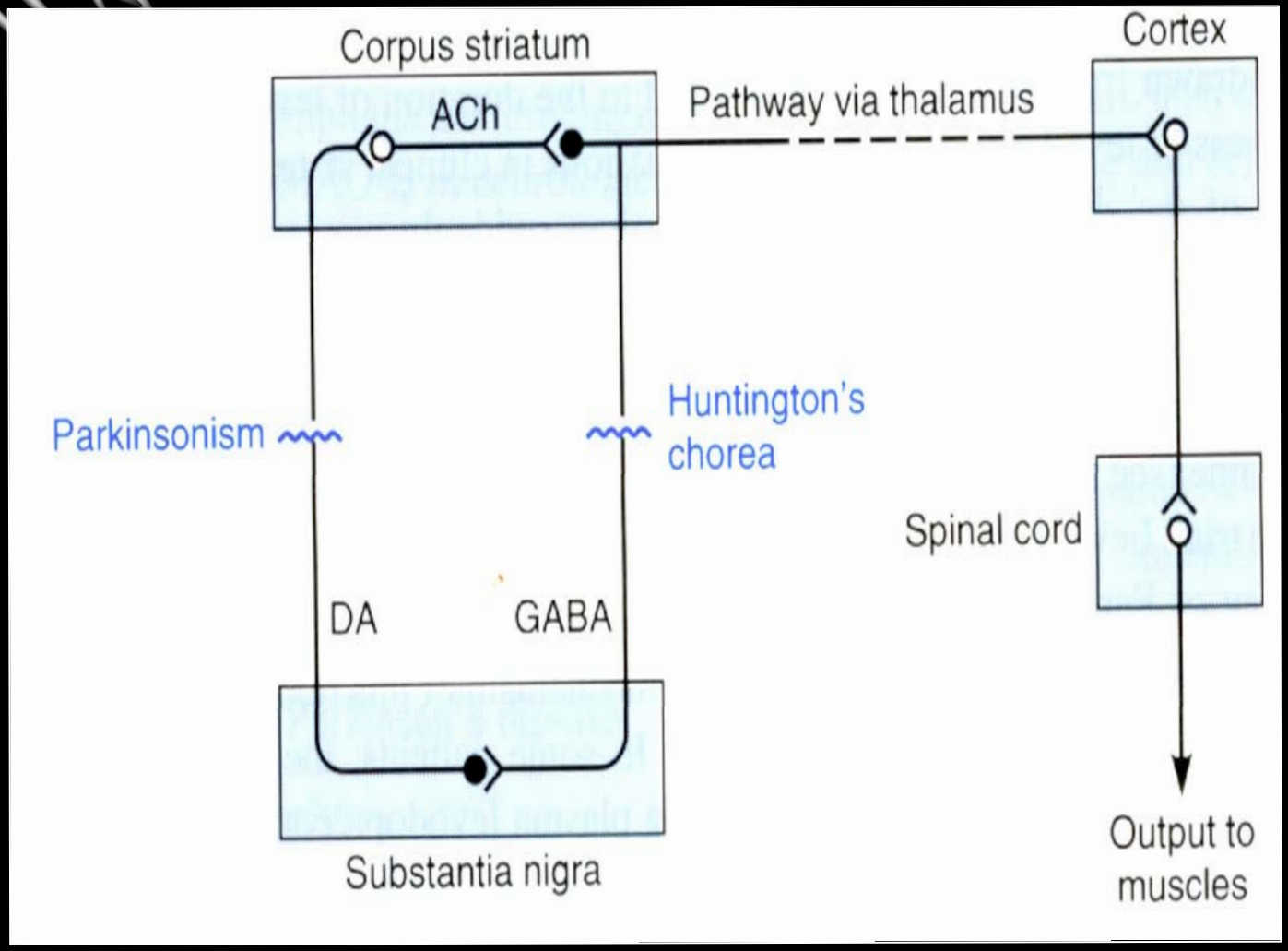


ADAM.

Medline Plus

Dopaminergic neurons



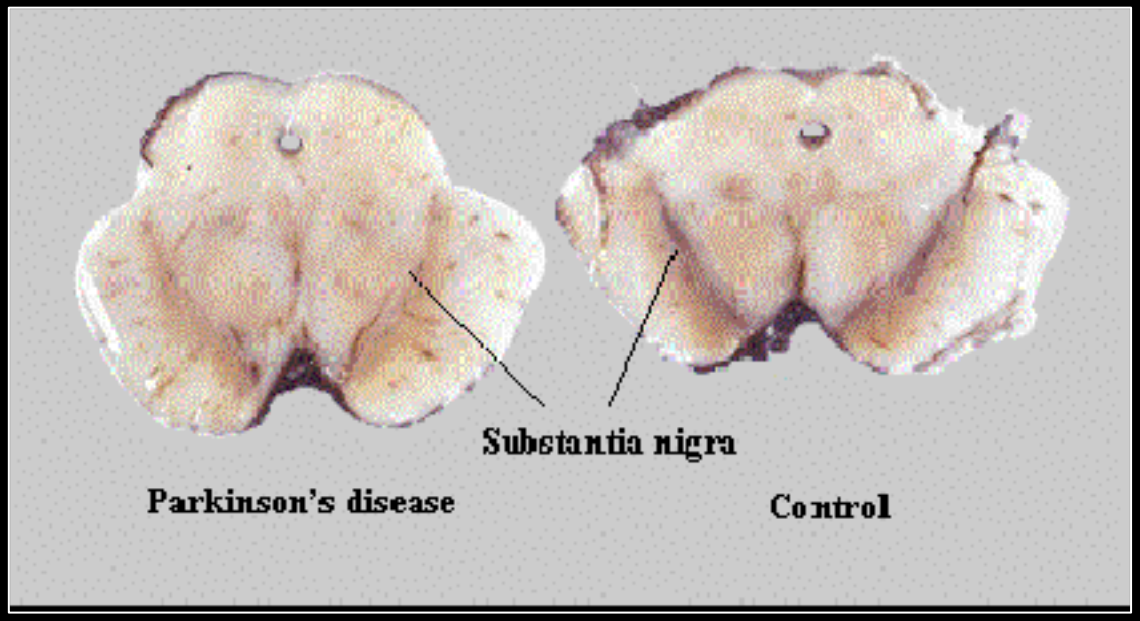


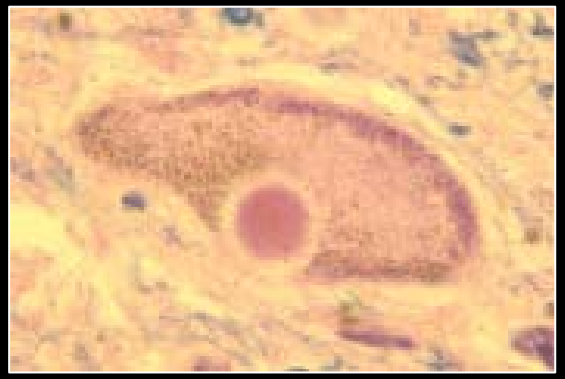
Dopamin di corpus striatum meregulasi aktivitas kolinergik

Degenerasi dopamin di striatal → aktivitas kolinergik meningkat

Lanjutan patofisiologi

- Dr. Lewy (1912) menemukan bahwa pada PD:
  - Terjadi kerusakan pada substantia nigra
  - Terdapat Lewy bodies (eosinofil yang terkurung) di substansia nigra → tanda utama penderita Parkinson

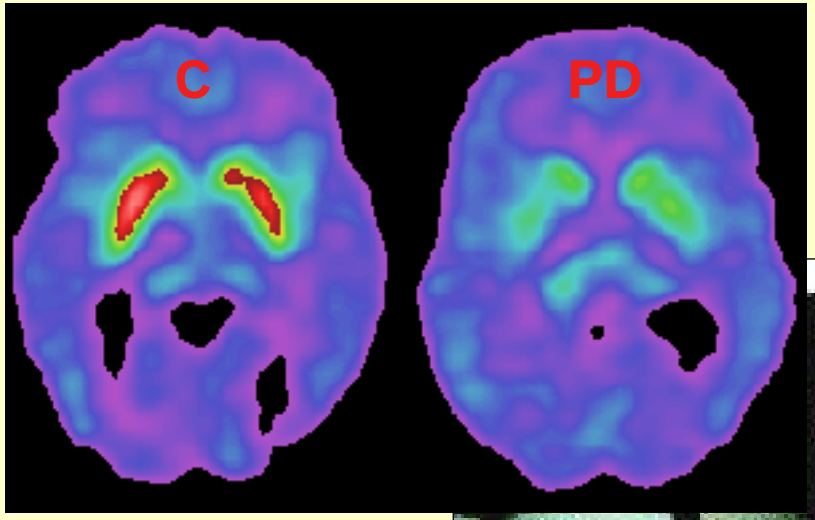


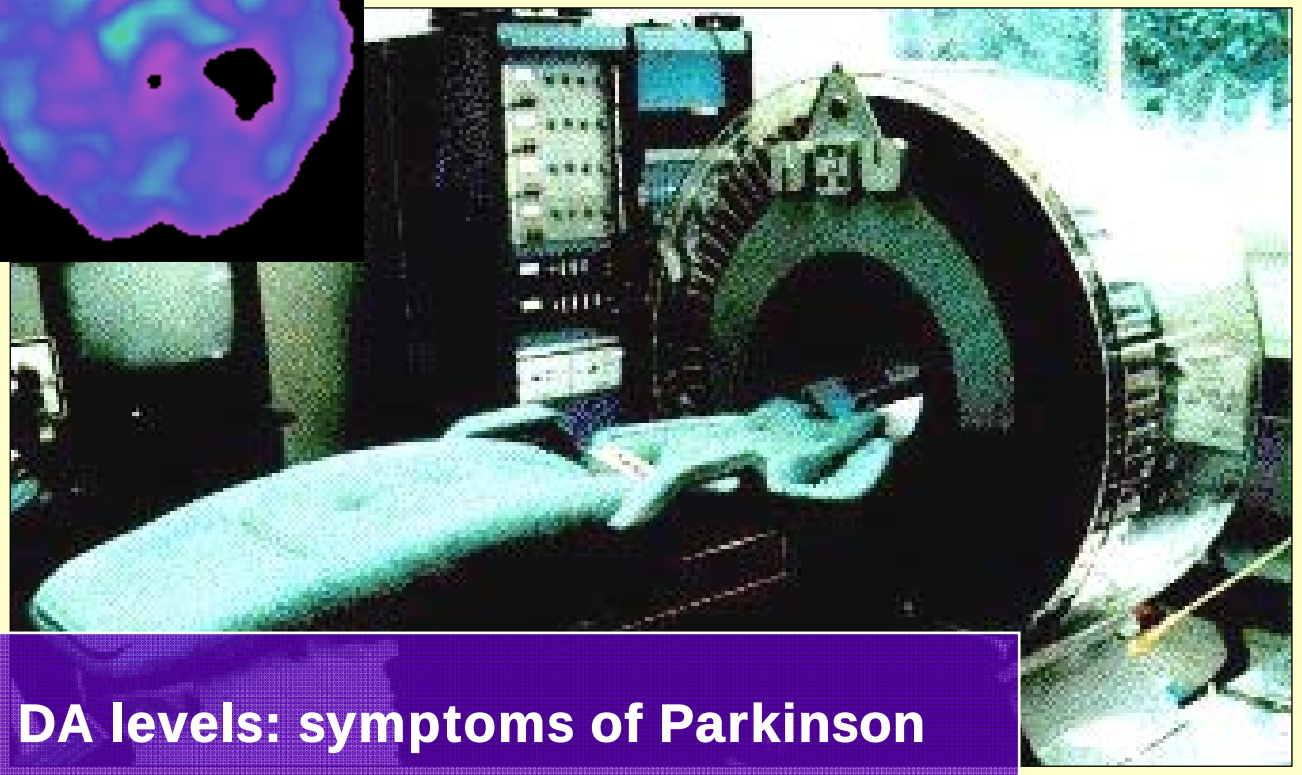


Lewy bodies

^{18}F-DOPA in human brain

positron emission tomography





- only at 20-40 % DA levels: symptoms of Parkinson

Gejala dan tanda

Tanda utama:

- tremor → pada saat istirahat, tingkat keparahan relatif stabil
- kekakuan → gerakan putar siku dan pergelangan tangan berkurang, ekspresi wajah kaku
- melemahnya gerakan → akinesia atau bradikinesia → langkah pendek-pendek, lambaian tangan berkurang
- ketidakseimbangan tubuh → sering jatuh

Tanda non-motorik

- inkontinensia
- dementia
- depresi
- dysphagia
- gangguan tidur
- konstipasi
- berkeringat,
- dll.

Diagnosis

- Perlu dilihat ada info sejarah penggunaan obat → *drug-induced Parkinsonisme*
- Kemungkinan diagnosis tepat jika pasien menunjukkan bradikinesia, tremor, kekakuan
- Tanda-tanda motorik biasanya berawal secara unilateral
- Sekali didiagnosis, dapat dievaluasi perkembangan penyakitnya dengan skala Hoehn dan Yahr

Skala Hoehn dan Yahr

Stage 0	Tidak ada tanda-tanda penyakit
Stage 1	Tanda-tanda unilateral
Stage 1,5	Tanda-tanda unilateral dan axial
Stage 2	Tanda-tanda bilateral tanpa gangguan keseimbangan
Stage 2,5	penyakit bilateral ringan
Stage 3	Penyakit bilateral ringan – sedang, tjd ketidak-seimbangan tubuh, secara fisik masih mandiri
Stage 4	Penyakit parah, tidak mampu hidup sendiri
Stage 5	Tidak bisa berjalan atau berdiri tanpa bantuan

Tujuan terapi

- Meminimalkan kecacatan (disability) dan efek samping, serta meningkatkan kualitas hidup semaksimal mungkin

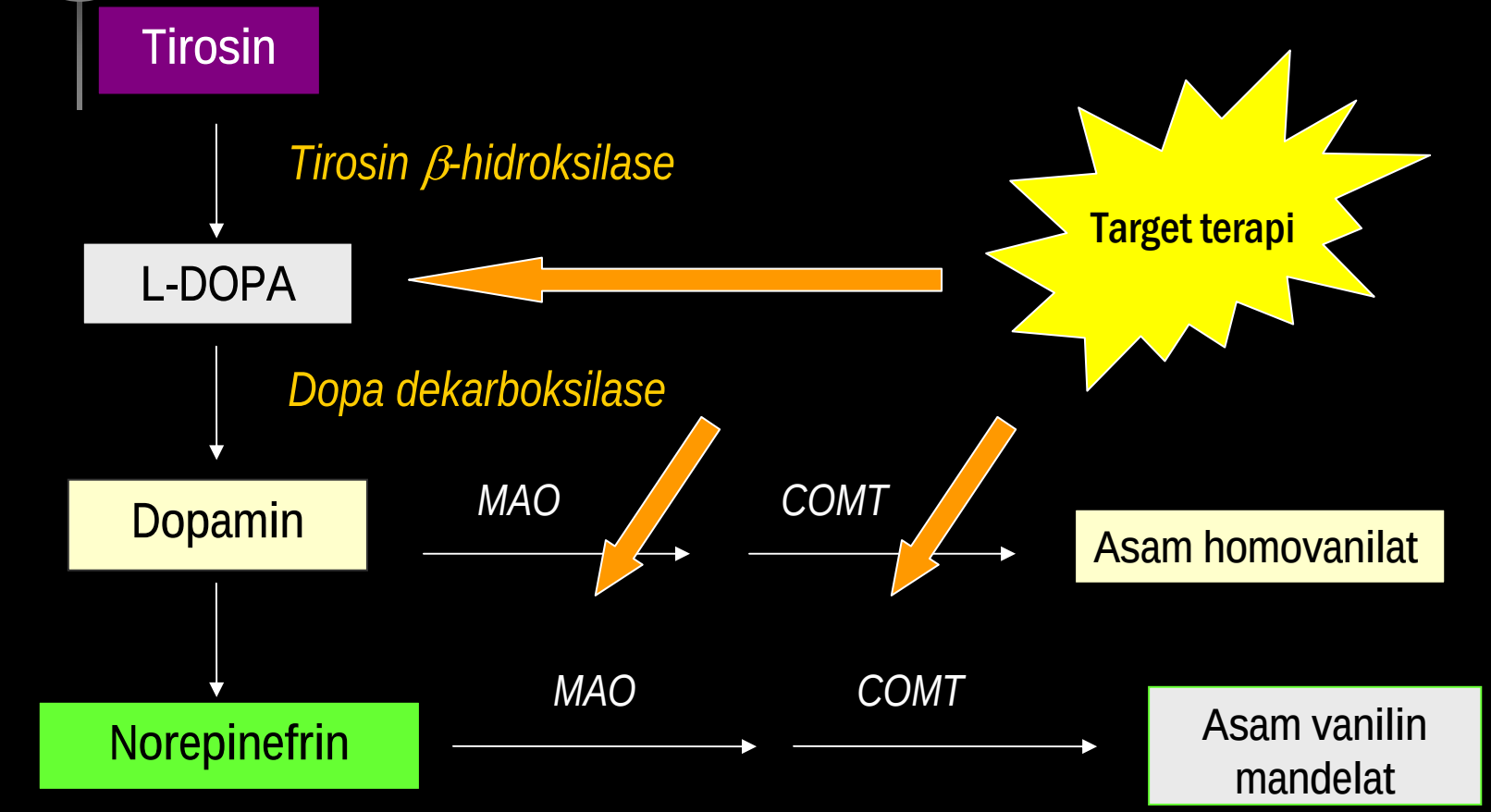
Strategi terapi

- Non-farmakologi :
  - Latihan
  - Edukasi
  - Nutrisi
  - Pembedahan
- Farmakologi :
  - Meningkatkan kadar dopamin endogen
  - Mengaktifkan reseptor dopamin dengan agonis
  - Menekan aktivitas kolinergik dgn obat-obat antikolinergik

Obat-obat yang digunakan dan mekanismenya

- Meningkatkan kadar dopamin endogen
  - L-Dopa → prekursor Dopa
  - Carbidopa, Benserazid → menghambat metabolisme perifer oleh dopa dekarboksilase
  - Entacapon, tolcapon → menghambat degradasi Dopa oleh O-metiltransferase
  - Selegilin → menghambat degradasi Dopa oleh MAO B
  - Amantadin → meningkatkan sintesis dan pelepasan dopamin, menghambat re-uptake
- Mengaktifkan reseptor dopamin dengan agonis
  - Bromokriptin, lisurid → agonis D2
  - Pramipeksol, ropinirol → agonis D2 dan D3
  - Pergolid, apomorfin → agonis D1 dan D2
- Menekan aktivitas kolinergik dgn obat-obat antikolinergik
  - Benztropin, triheksifenidil

Biosintesis dan degradasi katekolamin



Algoritma tatalaksana terapi Parkinson tahap awal

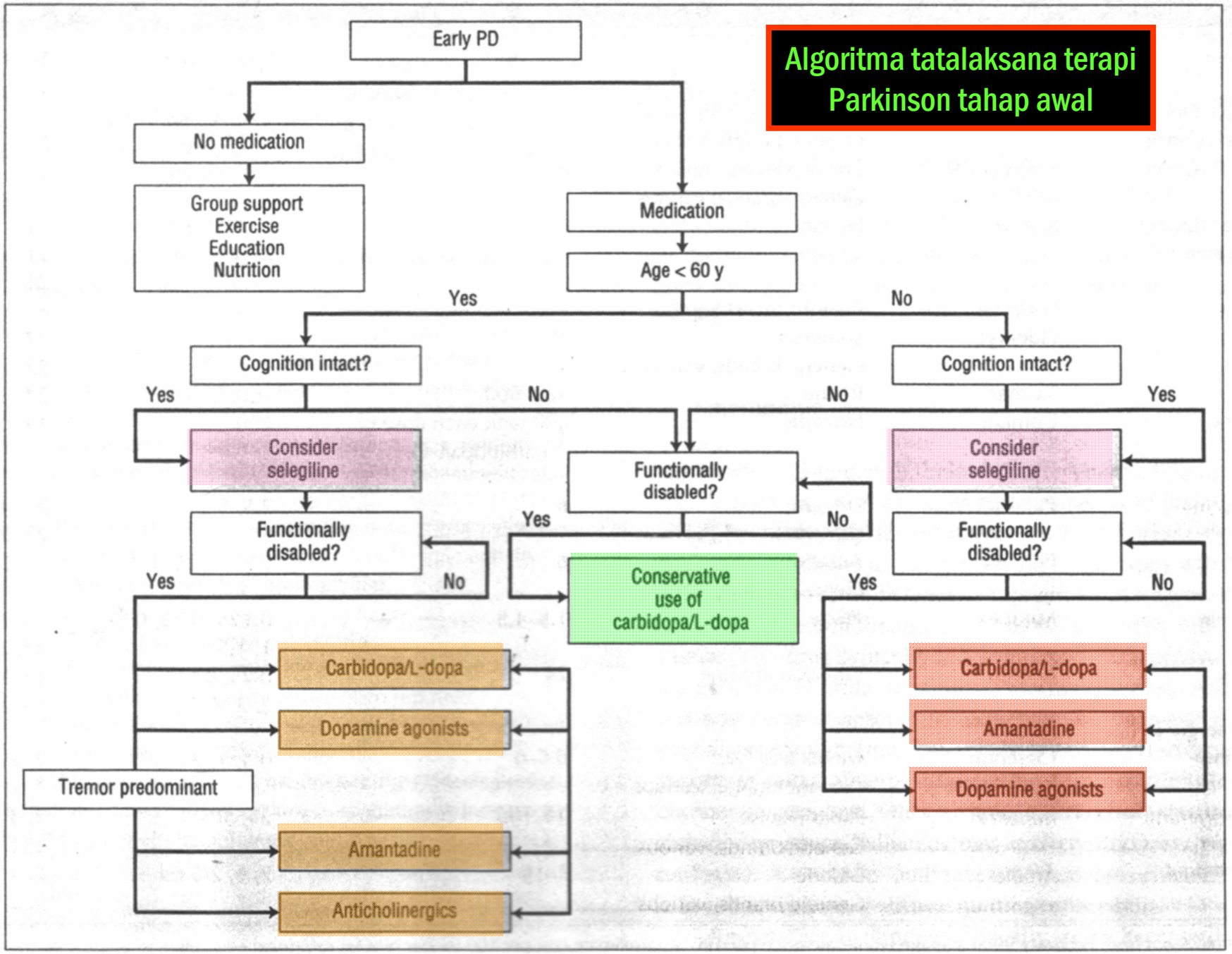
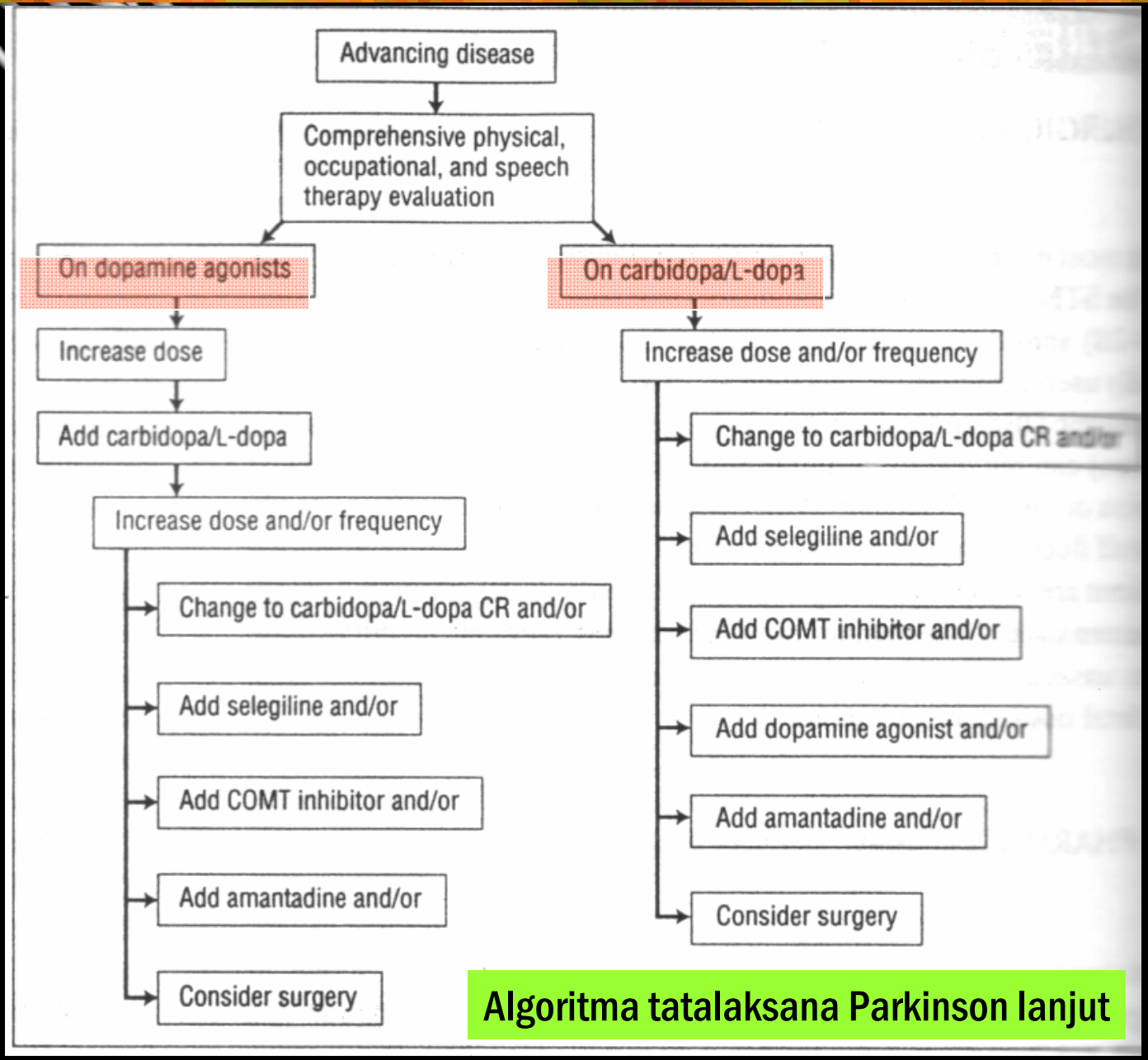


FIGURE 57–4. General algorithm for treating early IPD.



Algoritma tatalaksana Parkinson lanjut

TABLE 57–4. Drugs Used in Parkinson's Disease

Generic Name	Trade Name	Manufacturer	Dosage Range (mg/day)	Dosage Forms (mg)
Amantadine	Symmetrel	Endo Labs Generic brands, various	200–300	100, 50/5 mL
Carbidopa/L-Dopa	Sinemet	Bristol-Meyers Squibb Generic brands, various	*b*	10/100, 25/100, 25/250
Carbidopa/L-Dopa Controlled-release	Sinemet CR	Bristol-Meyers Squibb Generic brands, various	*b*	25/100, 50/200
Carbidopa/L-Dopa/ entacapone	Stalevo	Novartis	*b*	12.5/50/200 25/100/200 37.5/150/200
Carbidopa	Lodosyn	Bristol-Meyers Squibb	*b*	25
Selegiline	Eldepryl	Somerset Generic brands, various	10	5
Tolcapone	Tasmar	Roche	300–600	100, 200
Entacapone	Comtan	Novartis	200 with each dose of carbidopa/L-Dopa	200
Agonists				
Bromocriptine	Parlodel	Novartis Generic brands, various	*b*	2.5, 5
Pergolide	Permax	Amarin Generic brands, various	*b*	0.05, 0.25, 1
Pramipexole	Mirapex	Pfizer	1.5–4.5	0.125, 0.25, 0.5 1, 1.5
Ropinirole	Requip	GlaxoSmithKline	24	0.25, 0.5; 1 2, 3, 4, 5
Anticholinergic Drugs				
Benztropine	Cogentin	Merck and Co. Generic brands, various	0.5–6	0.5, 1, 2
Diphenhydramine	Benadryl	Parke-Davis Generic brands, various	25–100	25, 50
Trihexyphenidyl	Artane	Lederle Generic brands, various	1–15	2, 5, 2/5 mL

Contoh Evidence-based Medicine pada pengobatan Parkinson

What is the role of selegiline in the treatment of early PD?

- Selegiline has mild symptomatic benefit (class II). There is no convincing clinical evidence for neuroprotective benefit with selegiline (class II). There is no convincing evidence for increased mortality with selegiline whether it is given in combination with levodopa or as monotherapy (class II).

Recommendations for patients with PD who require symptomatic treatment.

- Initial symptomatic treatment of patients with PD with selegiline in order to confer mild, symptomatic benefit prior to the institution of dopaminergic therapy may be considered (level A, class II evidence).
- There is insufficient evidence to recommend the use of selegiline to confer neuroprotection in patients with PD (level U).

- *When symptomatic therapy is required does levodopa or a dopamine agonist offer best control of motor symptoms?*
- Conclusions: Levodopa, cabergoline, ropinirole, and pramipexole are effective in ameliorating motor and ADL (activities of daily living) disability in patients with PD who require dopaminergic therapy.
- Levodopa is more effective than cabergoline, ropinirole,
- and pramipexole in treating the motor and ADL features of PD.

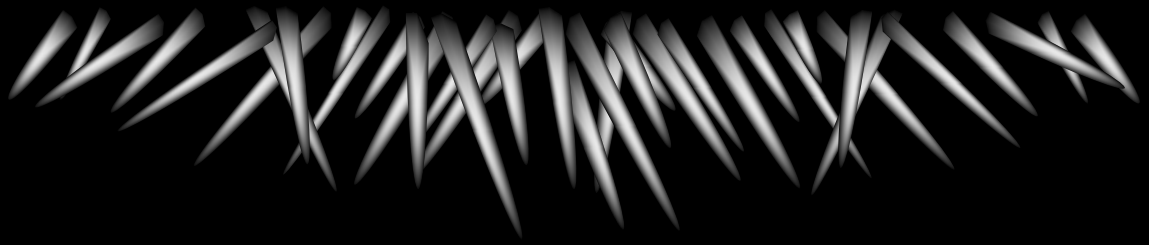
When symptomatic therapy is required, does levodopa or a dopamine agonist offer the most favorable long-term complication profile?

- **Conclusions :** Cabergoline, ropinirole, and pramipexole treatment of PD patients requiring dopaminergic therapy results in fewer motor complications than levodopa treatment after 2.5 years of follow-up.
- Cabergoline, ropinirole, and pramipexole treatment of PD patients requiring dopaminergic therapy is associated with more frequent adverse events including hallucinations, somnolence, and edema than levodopa therapy.
- **Recommendations:** In patients with PD who require the initiation of dopaminergic treatment, either levodopa or a dopamine agonist may be used. The choice depends on the relative impact of improving motor disability (better with levodopa) compared with the lessening of motor complications (better with dopamine agonists) for each individual patient with PD (level A, class I and class II evidence).

Sustained-release versus immediate release levodopa: When initiating levodopa therapy, which formulation should be used—immediate-release or sustained-release levodopa?

- Conclusions : When initiating therapy with levodopa, there is no difference in the rate of motor complications between immediate-release levodopa and sustained-release levodopa.
- Recommendations. For patients with PD in whom levodopa treatment is being instituted, either an immediate-release or sustained-release preparation may be considered (level B, class II evidence).

selesai



See you next week