Antipsychotics induced Movement disorders in nowadays clinical practice

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Antipsychotics induced Movement disorders

- Types:

  -Akatesia

  -Acute Dystonia

  -Psuedoparkinsonism

  -Tardive Dyskinesia

Movement Disorders

- Lithium
- SSRIs
- Valproate
- Metoclopramide
- Promethazine

Indications

- Schizophrenia
- Bipolar disorder
- Depression
- others

Diverse adverse effect

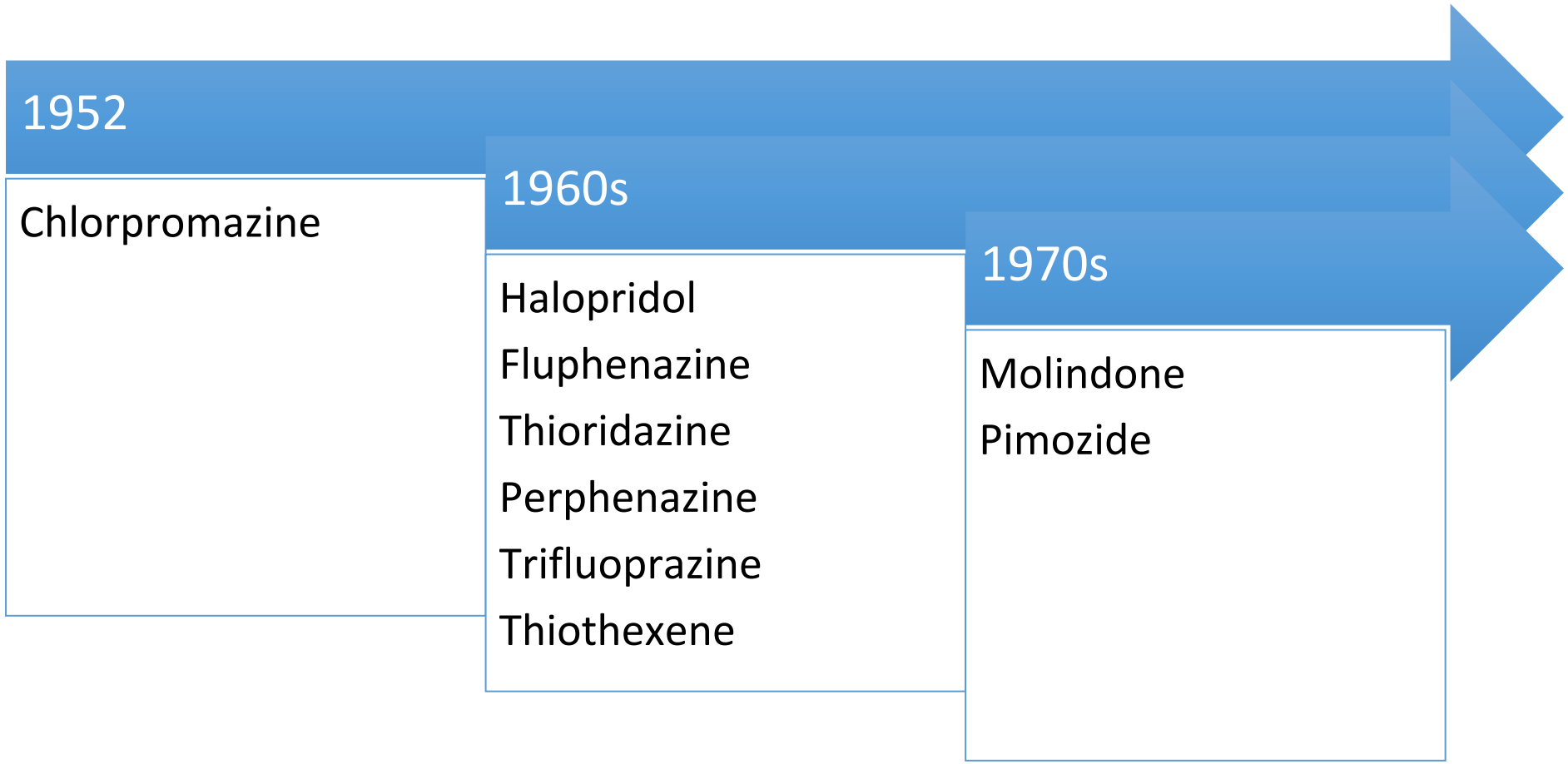
- Weight gain
- Metabolic side effects
- Sedation
- Prolactin
- QTc prolongation

Movement disorder

- Decreased quality of life
- Decreased adherence to medication
- Increase use of health care recourses

- Neglect in second generations

First generation Antipsychotics



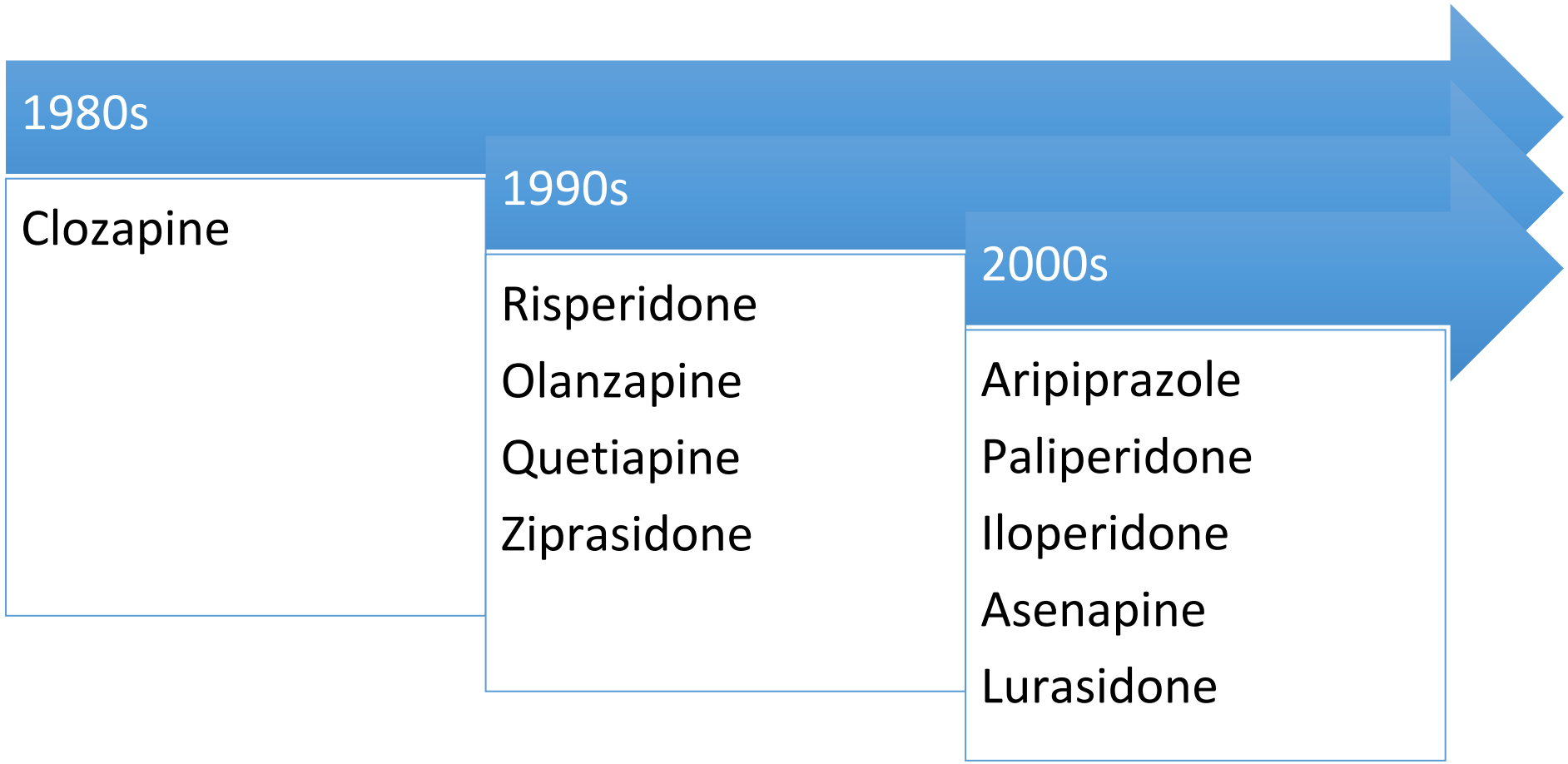
Tardon R.J Clin Psychiatry 2011;72(supp1):4-8

FGAs:Efficacy and EPS

Dopamine D2 receptore blockade

60% for antipsychotic effect &80% leads to EPS

Second Generation Antipsychotics



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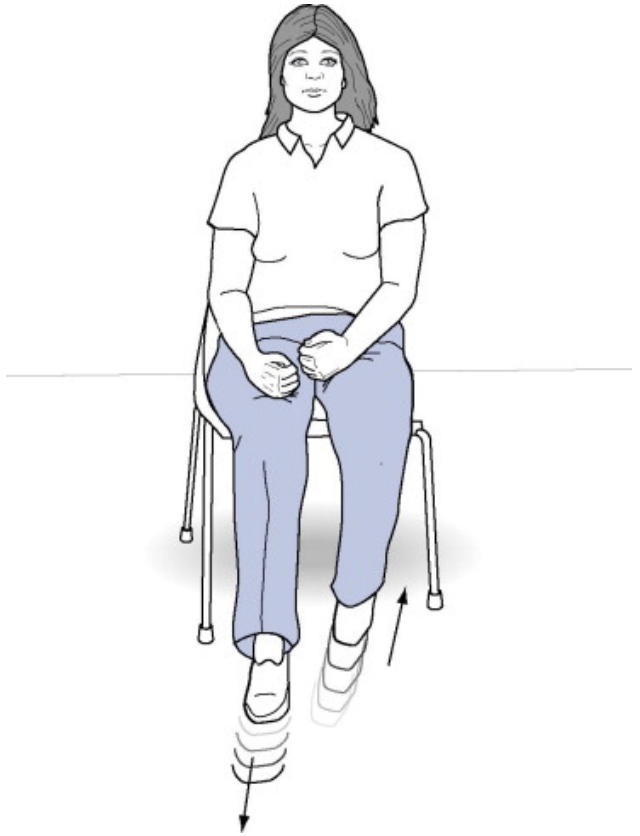
D2 Antagonism

D2 Antagonistim	FGA	SGA
LOW	Chlorpromazine Thioridazine	Clozapine Quetiapine
INTERMEDIATE	Trifluoprazine Perphenazine	Olanzapine
HIGH	Halopridol Fluphenazine	Risperidone Ziprasidone Aripiprazole

FGA	EPS risk
Chlorpromazine	Moderately high
Halopridol	High
Perphenazine	High
Thioridazine	Moderately High
Thiothixene	High
SGA	
Aripiprazol	Low
Clozapine	Low
Olanzapine	Moderate
Quetiapine	Low
Risperidone	Moderate
Ziprasidone	Moderate

Akathitic Movements

- “Unable to sit still”
- Feeling of inner, general restlessness that is reduced or relieved by moving about
- Complex and usually stereotyped movements
- Can be both generalized and focal
- Can usually be briefly suppressed
- Most common cause is iatrogenic



Akatesia

- Symptoms:

  "An inability to sit still"

  Shuffling, pacing, tapping feet

  Feeling of inner restlessness

- Onset:

  Usually occurs within first three months of starting antipsychotic

Similar Conditions

- Agitation due to psychotic symptoms or affective disorder

Anxiety

Delirium

Head injury

Parkinson's disease

Huntington's disease

Restless legs syndrome

Kane JM, et al. J Clin Psychiatry 2009; 70 (5): 627-643.

- Monitoring:

Barnes Akathisia Rating Scale (BARS)

Barnes TRE. Br J Psychiatry 1989:154:672-6.

Barens rating Scale

Name:_____ **Date:**_____

Barnes Akathisia Rating Scale (BARS)

Instructions: Patient should be observed while they are seated, and then standing while engaged in neutral conversation (for a minimum of two minutes in each position). Symptoms observed in other situations, for example while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

Objective

0 Normal, occasional fidgety movements of the limbs
1 Presence of characteristic restless movements: shuffling or tramping movements of the legs/feet, or swinging of one leg while sitting, *and/or* rocking from foot to foot or "walking on the spot" when standing, but movements present for less than half the time observed
2 Observed phenomena, as described in (1) above, which are present for at least half the observation period
3 Patient is constantly engaged in characteristic restless movements, *and/or* has the inability to remain seated or standing without walking or pacing, during the time observed

Subjective

Awareness of restlessness
0 Absence of inner restlessness
1 Non-specific sense of inner restlessness
2 The patient is aware of an inability to keep the legs still, or a desire to move the legs, *and/or* complains of inner restlessness aggravated specifically by being required to stand still
3 Awareness of intense compulsion to move most of the time *and/or* reports strong desire to walk or pace most of the time

Distress related to restlessness
0 No distress
1 Mild
2 Moderate
3 Severe

Global Clinical Assessment of Akathisia

0 *Absent.* No evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia
1 *Questionable.* Non-specific inner tension and fidgety movements
2 *Mild akathisia.* Awareness of restlessness in the legs *and/or* inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress.
3 *Moderate akathisia.* Awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing
4 *Marked akathisia.* Subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least five minutes. The condition is obviously distressing.
5 *Severe akathisia.* The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia.

Akatesia managment

- Discontinue or reduce dose
- Switch to a second-generation antipsychotic
- Quetiapine and clozapine – least likely to cause akathisia

Beta blockers

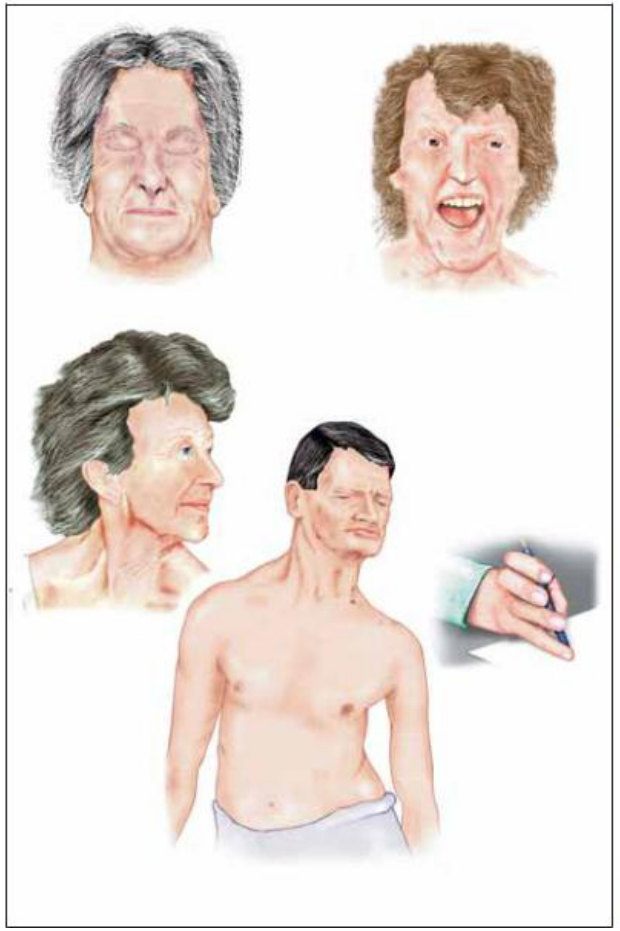
- Beta-blocker (off-label) (Cochrane??)
- First choice of treatment
- Examples: propranolol, metoprolol
- Side effects: bradycardia, hypotension, depression, dizziness, drowsiness

- Benzodiazepines (off-label)
- Example: Lorazepam
- Used with caution due to high prevalence of substance abuse
- Side effects: drowsiness, confusion, dizziness
- Cyproheptadine,clonidine,Mirtazapine,or clozapine.

- Anticholingergics
- Examples: benztropine
- Diphenhydramine
- Generally not helpful

Acute Dystonia

- Symptoms:
- Sustained muscle contractions or spasms
- Abnormal postures, twisting, repetitive movements
- Involuntary
- May affect neck, extremities, larynx, trunk, jaw
- Potentially life-threatening



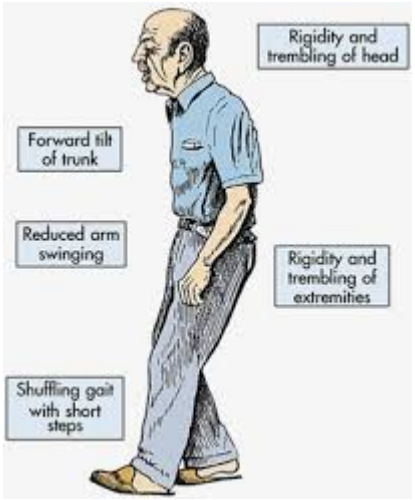
- Onset: Rapid (within 2-5 days of initiation/dose increase) Risk Factors: Younger men Use of first-generation antipsychotics Especially high-potency

- Anticholinergics
- Benztropine
- Diphenhydramine
- Benzodiazepines (off-label)
- Lorazepam
- Local injection of botulinium

Antipsychotics induced parkinsonism

- Imbalance of dopamine and acetylcholine
- Resembles Parkinson's disease
- Triad Tremor,rigidity,and brady kinesia

- Symptoms: Akinesia, bradykinesia, or decreased motor activity
- difficulty initiating movement, slowed speech, masklike facial expression, micrographia, decreased arm swing
- Tremor
- Cogwheel rigidity
- Postural abnormalities



Clinical Staging of PH According to Hoehn-Yahr Scale

0- Asymptomatic

1- Unilateral involvement

2- Bilateral involvement

3- Involvement of postural reflexes, imbalance and falls
Mild-moderate morbidity

4- Needs continious support

5- Bedridden

- Onset: 1-2 weeks after initiation or dose increase
- Risk factors:
- Elderly
- Monitoring: Simpson-Angus Scale

Simpson G, Angus J. Acta Psychiatr Scand 1970:212 (Suppl 44):11-9

Patient Name:_____ Date: _____

SIMPSON-ANGUS EXTRAPYRAMIDAL SIDE EFFECTS SCALE

The exam should be conducted in a room where the subject can walk a sufficient distance to allow him/her to get into a natural rhythm (e.g. 15 paces). Each side of the body should be examined. If one side shows more pronounced pathology than the other, this score should be noted and this taken. Cogwheel rigidity may be palpated when the examination is carried out for items 3, 4, 5, and 6. It is not rated separately and is merely another way to detect rigidity. It would indicate that a minimum score of 1 would be mandatory.

1. **Gait**: The patient is examined as he walks into the examining room, his gait, the swing of his arms, his general posture, all form the basis for an overall score for this item. This is rated as follows:
   - 0 Normal
   - 1 Diminution in swing while the patient is walking
   - 2 Marked diminution in swing with obvious rigidity in the arm
   - 3 Stiff gait with arms held rigidly before the abdomen
   - 4 Stooped shuffling gait with propulsion and retropulsion

2. **Arm Dropping:** The patient and the examiner both raise their arms to shoulder height and let them fall to their sides. In a normal subject, a stout slap is heard as the arms hit the sides. In the patient with extreme Parkinson's syndrome, the arms fall very slowly:
   - 0 Normal, free fall with loud slap and rebound
   - 1 Fall slowed slightly with less audible contact and little rebound
   - 2 Fall slowed, no rebound
   - 3 Marked slowing, no slap at all
   - 4 Arms fall as though against resistance; as though through glue

3. **Shoulder Shaking:** The subject's arms are bent at a right angle at the elbow and are taken one at a time by the examiner who grasps one hand and also clasps the other around the patient's elbow. The subject's upper arm is pushed to and fro and the humerus is externally rotated. The degree of resistance from normal to extreme rigidity is scored as follows:
   - 0 Normal
   - 1 Slight stiffness and resistance
   - 2 Moderate stiffness and resistance
   - 3 Marked rigidity with difficulty in passive movement
   - 4 Extreme stiffness and rigidity with almost a frozen shoulder

4. **Elbow Rigidity:** The elbow joints are separately bent at right angles and passively extended and flexed, with the subject's biceps observed and simultaneously palpated. The resistance to this procedure is rated. (The presence of cogwheel rigidity is noted separately.)
   - 0 Normal
   - 1 Slight stiffness and resistance
   - 2 Moderate stiffness and resistance
   - 3 Marked rigidity with difficulty in passive movement
   - 4 Extreme stiffness and rigidity with almost a frozen elbow

5. **Wrist Rigidity or Fixation of Position:** The wrist is held in one hand and the fingers held by the examiner's other hand, with the wrist moved to extension, flexion and ulnar and radial deviation:
   - 0 Normal
   - 1 Slight stiffness and resistance
   - 2 Moderate stiffness and resistance
   - 3 Marked rigidity with difficulty in passive movement
   - 4 Extreme stiffness and rigidity with almost frozen wrist

6. **Leg Pendulousness:** The patient sits on a table with his legs hanging down and swinging free. The ankle is grasped by the examiner and raised until the knee is partially extended. It is then allowed to fall. The resistance to falling and the lack of swinging form the basis for the score on this item:
   - 0 The legs swing freely
   - 1 Slight diminution in the swing of the legs
   - 2 Moderate resistance to swing
   - 3 Marked resistance and damping of swing
   - 4 Complete absence of swing

7. **Head Dropping:** The patient lies on a well-padded examining table and his head is raised by the examiner's hand. The hand is then withdrawn and the head allowed to drop. In the normal subject the head will fall upon the table. The movement is delayed in extrapyramidal system disorder, and in extreme parkinsonism it is absent. The neck muscles are rigid and the head does not reach the examining table. Scoring is as follows:
   - 0 The head falls completely with a good thump as it hits the table
   - 1 Slight slowing in fall, mainly noted by lack of slap as head meets the table
   - 2 Moderate slowing in the fall quite noticeable to the eye
   - 3 Head falls stiffly and slowly
   - 4 Head does not reach the examining table

8. **Glabella Tap**: Subject is told to open eyes wide and not to blink. The glabella region is tapped at a steady, rapid speed. The number of times patient blinks in succession is noted:
   - 0 0-5 blinks
   - 1 6-10 blinks
   - 2 11-15 blinks
   - 3 16-20 blinks
   - 4 21 and more blinks

9. **Tremor:** Patient is observed walking into examining room and is then reexamined for this item:
   - 0 Normal
   - 1 Mild finger tremor, obvious to sight and touch
   - 2 Tremor of hand or arm occurring spasmodically
   - 3 Persistent tremor of one or more limbs
   - 4 Whole body tremor

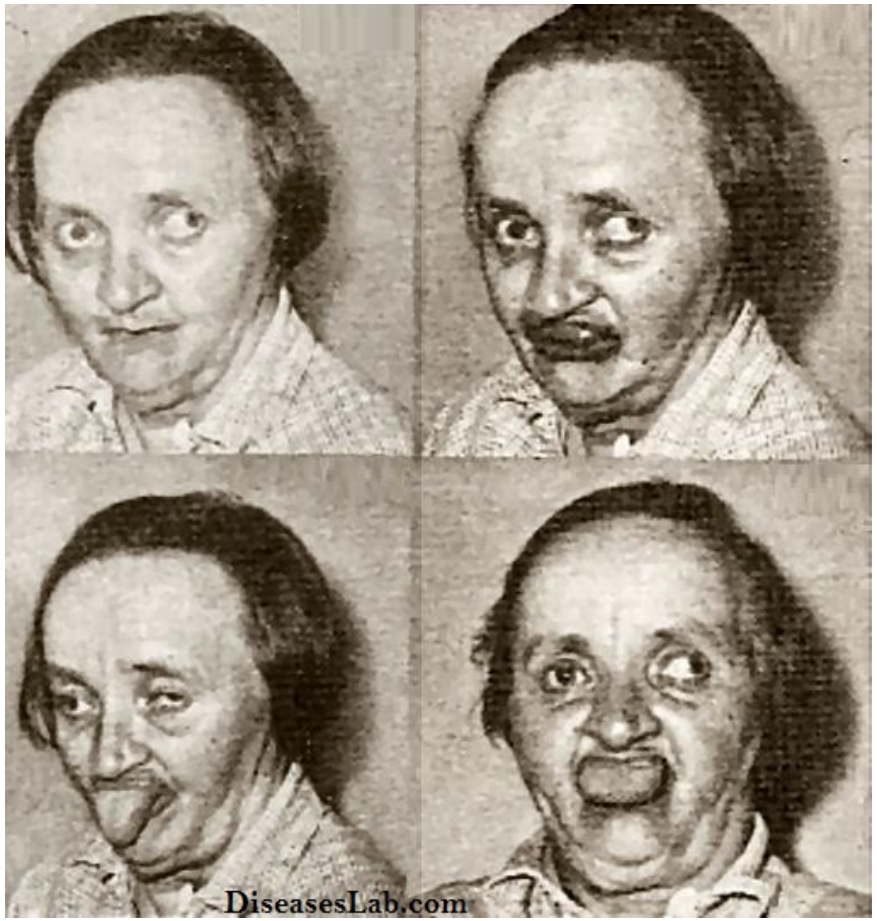
10. **Salivation:** Patient is observed while talking and then asked to open his mouth and elevate his tongue. The following ratings are given:
    - 0 Normal
    - 1 Excess salivation to the extent that pooling takes place if the mouth is open and the tongue raised
    - 2 When excess salivation is present and might occasionally result in difficulty speaking
    - 3 Speaking with difficulty because of excess salivation
    - 4 Frank drooling

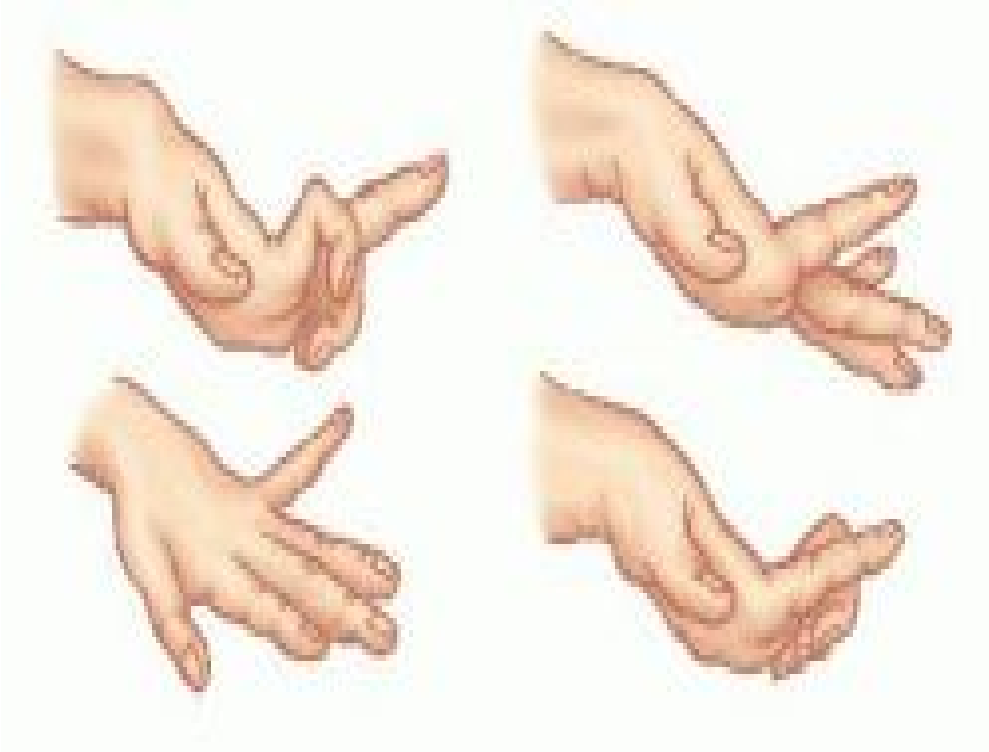
- Benztropine
- Trihexyphenidyl
- Diphenhydramine
- Amantadine
- Side effects: dizziness, anxiety, impaired concentration, insomnia
- Night dose#review regualrly,prophylactic use?,

Tardive Dyskinesia

- Symptoms:
- Involuntary movements of face, neck, back, trunk, extremities
- Orofacial movements
- Typically first detectable sign : Tongue thrusting, rolling
- Interferes with chewing, swallowing, speaking

Chorea: quick,irregular,semipurposive and predominantly distal involuntary movement.


DiseasesLab.com



- Sometimes irreversible
- Not painful, but cause embarrassment and disability
- Disappear during sleep

- Onset:
- Late in onset in relation to initiation of therapy (after at least one month)
- Within the first 5 years of treatment Complications:
- Oral ulcerations
- Inability to wear dentures
- Eating difficulties
- Weight loss
- Respiratory difficulties

- Chen J. Ment Health Clin 2012;1(7):17.

- Risk Factors:
- Increased age
- Elderly 5 times more likely to develop
- Long treatment duration Screening & Monitoring
- Abnormal Involuntary Movement Scale (AIMS)
- Dyskinesia Identification System Condensed User Scale (DISCUS)

Jeste D. J Clin Psychiatry 2004;65 (Suppl 9):21-4. Guy W. AIMS ECDUE Assessment Manual for Psychopharmaco

AIMS

- Uses a 5-point rating scale
- Facial and oral movements
- Muscles of facial expression
- Lips and Perioral area (Jaw,Tongue)

- Extremity Movements (Upper , Lower)

Guy W. AIMS ECDUE Assessment Manual for Psychopharmacology. 1976:534-7.

- Trunk Movements
- Severity of Movements
- Patient's awareness
- Dental Status

Guy W. AIMS ECDUE Assessment Manual for Psychopharmacology. 1976:534-7

Abnormal Involuntary Movement Scale (AIMS)

Patient Name _____ Date of Visit _____

Code: 0 = None 1 = Minimal 2 = Mild 3 = Moderate 4 = Severe

Movement Ratings:
- Rate highest severity observed in category I, II, III.
- Rate movements that occur upon activation one point less than those observed spontaneously.
- Circle movements as well as code number that applies.

		RATER / DATE	RATER / DATE	RATER / DATE	RATER / DATE
I FACIAL & ORAL MOVEMENTS	1. **Muscles of Facial Expression** e.g. movements of forehead, eyebrows, periorbital area, cheeks, including frowning, blinking, smiling, grimacing	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	2. **Lips and Perioral Area** e.g. puckering, pouting, smacking	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	3. **Jaw** Biting, clenching, chewing, mouth opening , lateral movement	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	4. **Tongue** Rate only increases in movement both in and out of mouth. NOT inability to sustain movement. Darting in and out of mouth	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
II EXTREMITY MOVEMENTS	5. **Upper (arms, wrists, hands, fingers)** Include choreic movements (i.e. rapid objectively purposeless, irregular, spontaneous) athetoid movements. DO NOT INCLUDE TREMOR (i.e. repetitive, regular, rhythmic)	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	6. **Lower (legs, knees, ankles, toes)** Lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
III TRUNK MOVEMENTS	7. **Neck, shoulders and hips** Rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
IV GLOBAL JUDGEMENT	8. **Severity of abnormal movements overall**	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	9. **Incapacitation due to abnormal movements**	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	10. **Patient's awareness of abnormal movements. Rate only patients report:** No Awareness = 0 Aware, no distress = 1 Aware, mild distress = 2 Aware, moderate distress = 3 Aware, severe distress = 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
V DENTAL STATUS	11. **Current problems with teeth and/or dentures**	YES NO	YES NO	YES NO	YES NO
	12. **Are dentures usually worn**	YES NO	YES NO	YES NO	YES NO
	13. **Endentia?**	YES NO	YES NO	YES NO	YES NO
	14. **Do movements disappear with sleep?**	YES NO	YES NO	YES NO	YES NO

Available for use in the public domain.

- Early detection is key because the longer the duration of TD, the less likely that remission will occur.
- Occasionally TD may occur when an antipsychotic is withdrawn. This usually improves within 3 months.

- Discontinuing or reducing dose(chocrane review)
- May consider a switch to a second-generation antipsychotic
- Discontinuing anticholinergic medications
- Treatment has limited efficacy, clonazepam,tetrabenazne,ondansetrone,baclofene,pallidotomy.
- Vitamin E (off-label),ginko biloba
- Others

- Worse negative symptoms
- Worse cognition
- Worse depression/suicidality
- Increased risk of tardive dyskinesia

FGAs versus SGAs

- Most studies comparing FGAs and SGAs focused on efficacy
- EPS is less frequent than several decades ago

- 7 randomized controlled trials showed that haloperidol increased rates of EPS compared to a second-generation antipsychotics
- In 2009, meta-analysis also showed that haloperidol had increased rates of EPS

Pakpoor J et al. Psychiatr Danub 2014; 26 (Suppl 1):273-84. Leucht S et al. Lancet 2009;373: 31-41.

CATIE study

- 3-phase, 18-month, randomized controlled trial
- 2 FGAs (perphenazine and fluphenazine)
- 5 SGAs (clozapine, olanzapine, quetiapine, risperidone, ziprasidone)

Lieberman J et al. N Engl J Med 2005:353:1209-23

CATIE outcomes

Outcome Measure	Perphenazine	Olanzapine	Quetiapine	Risperidone	Ziprasidone
AIMS Global>=2	17%	14%	13%	16%	14%
Barens Akatesia>=3	7%	5%	5%	7%	9%
Simpson Angus EPS Scale>=1	6%	8%	4%	8%	4%

Lieberman J et al. N Engl J Med 2005:353:1209-23.

CUtLASS

- Cost Utility of the Latest Antipsychotics in Schizophrenia Study

Randomized controlled trial

No difference in Parkinsonism between FGAs and SGAs

Peluso MJ et al. Br J Psychiatry 2012;200:387-92.

2009 Meta analysis

- Meta-analysis of randomized controlled trials to compare SGAs and FGAs
- Multiple outcomes including EPS
- SGAs fewer EPS than haloperidol
- SGAs (except clozapine, olanzapine, and risperidone) not better than low potency FGAs

Leucht S et al. Lancet 2009;373: 31-41

2013 Meta analysis

- Meta-analysis of randomized controlled trials
- 15 antipsychotics (only 2 FGAs)
- Multiple secondary outcomes including EPS
- Clozapine fewer EPS than all others
- Haloperidol more EPS except for chlorpromazine and zotepine

Leucht S, et al. Lancet 2013;382:951-62.

Tardive Dyskinesia

- Objective: Incidence of TD with SGAs compared to FGAs
- Prospective Cohort of 350 outpatients
- Rate-ratio=0.68 (95%CI 0.29-1.64)

Woods S, et al. J Clin Psychiatry 2010;71(4):463-74

Discrepancies

- In earlier studies, difference between FGA and SGAs may have been exaggerated
- high-dose haloperidol
- CATIE minimized difference by selecting a study population at unusually low risk of EPS

- Tandon R. Curr Psychiatry 2006;5(11):35-45

Tip for Use

- GOAL – minimize EPS
- Focus on antipsychotic dosing to achieve an antipsychotic effect without EPS
- Select an antipsychotic and dosage with consideration of the individual's vulnerabilities

Tandon R. Curr Psychiatry 2006;5(11):35-45.

- Avoiding EPS without anticholinergics is key
- Better cognition
- Less negative symptoms
- Less dysphoria
- Lower risk of tardive dyskinesia

- EPS can greatly impact quality of life
- Importance of screening for both FGAs and SGAs
- Individualize treatment with consideration of patient's goals