Antipsychotic Drugs, Dose Equivalents, and Recommended Daily Dose Ranges

<table>
<thead>
<tr>
<th>Drug</th>
<th>Relative Therapeutic Potency</th>
<th>Recommended Daily Dose Range (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>100</td>
<td>25-800</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>2-3</td>
<td>1-60</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>6-10</td>
<td>16-40</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>3-5</td>
<td>4-60</td>
</tr>
<tr>
<td>Thoridazine</td>
<td>100</td>
<td>50-900</td>
</tr>
<tr>
<td>Mesocondine</td>
<td>50</td>
<td>24-400</td>
</tr>
<tr>
<td>Piperoxazine</td>
<td>10</td>
<td>10-160</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>1.5-2</td>
<td>1-100</td>
</tr>
<tr>
<td>Thioridinone</td>
<td>2-4</td>
<td>5-120</td>
</tr>
<tr>
<td>Butaperazine</td>
<td>10-15</td>
<td>15-100</td>
</tr>
<tr>
<td>Loxapine</td>
<td>10-16</td>
<td>20-150</td>
</tr>
<tr>
<td>Molindone</td>
<td>7.5-12</td>
<td>15-200</td>
</tr>
<tr>
<td>Sulpiride</td>
<td>100</td>
<td>100-1000</td>
</tr>
<tr>
<td>Pinolide</td>
<td>1-2</td>
<td>2-20</td>
</tr>
</tbody>
</table>

Binding Affinities of Antipsychotics

- Haloperidol
- Clozapine
- Quetiapine
- Risperidone
- Olanzapine
- D1
- D2
- Musc
- 5-HT
- a1
- a2
- H1
### Atypical Antipsychotics

- Risperidone (Risperdal (M-tab) + Consta)
- Clozapine (Clozaril)
- Olanzapine (Zyprexa (Zydis))
- Quetiapine (Seroquel)
- Ziprasidone (Zeldox / Geodon)
- Paliperidone (Invega + Sustenna)
- Asenapine (Saphris → S/L)
- Aripiprazole (Abilify)

* (form. dissoudre rapide)  
• + IM LA  
• 3ieme génération

### Unique Properties

- Potent dopamine (D₂) and Serotonin (5-HT₂) antagonism
- Less occurrence of extrapyramidal adverse effects
- Decreased theoretical risk of Tardive Dyskinesia
- Greater impact on negative symptoms of schizophrenia

### Indications in Individuals with Developmental Disabilities

- Schizophrenia and related psychotic disorders
- Adjunctive mood stabilizers in Bipolar Disorder
- Adjunctive treatment in Obsessive-Compulsive Disorder
- Tic Suppression in Tourette's Syndrome
- Symptomatic treatment in Pervasive Developmental Disorders
- Conversion strategy to reduce risk of Tardive Dyskinesia
Estimated Weight Gain After 10 Weeks

Allison DB et al. (1999). American Journal of Psychiatry, 156, 1686-1696

Weight Gain by Individual Atypical Antipsychotic Drug

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight gain (kg/month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine*</td>
<td>2,3</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>1,8</td>
</tr>
<tr>
<td>Clozapine*</td>
<td>1,7</td>
</tr>
<tr>
<td>Risperidone</td>
<td>1,0</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>0,8</td>
</tr>
</tbody>
</table>

*Risk of dyslipidemia & diabetes also elevated, 2004

“I must be losing weight! I can see the tips of my toes.”
Medical Hazards of Obesity

- Hypertension
- Blood Lipid abnormalities
- Coronary Heart Disease
- Diabetes Mellitus
- Gallbladder Disease
- Respiratory Disease
- Cancer
- Gout
- Arthritis
- (Low Self Esteem)
- (Birth Defects)

Monitoring

<table>
<thead>
<tr>
<th>Table 3 - American Diabetes Association (ADA) and American Psychiatric Association (APA) consensus guidelines for baseline assessment and monitoring of patients receiving typical antipsychotic medications [71].</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Personal/family history</td>
</tr>
<tr>
<td>Weight/height/Lean</td>
</tr>
<tr>
<td>Waist circumference</td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
</tr>
<tr>
<td>Fasting lipid profile</td>
</tr>
</tbody>
</table>

* More frequent assessments may be warranted based on clinical status.
* Personal and family history of obesity, diabetes, dyslipidemia, hypertension, or cardiovascular disease.

SE Clozaril

- Agranulocytosis...FATAL!
- Regular bloodwork:
  - CBC & diff weekly X 26 weeks
  - Every 2 weeks thereafter
  - If stable after one year, every 4 weeks
- Important to check if person has a fever (symptom of infection)
- Constipation!
Considerations

- Ziprasidone WITH food
- Asenapine WITHOUT food, under the tongue & DO NOT SWALLOW!
- Avoid grapefruit juice
- Zydis -> aspartame

Typical Antipsychotics

- Haldol (haloperidol)
- Loxapac (loxapine)
- Largactil (chlorpromazine)
- Nozinan (methotrimeprazine)
- Clopixol (zuclopenthixol)

Abnormal Involuntary Movement Scale (AIMS)

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>Minimal</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>Moderate</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Conditions:
- Consider the patient’s medical history and current medications.
- Ask the patient about any past experiences with involuntary movements.
- Observe the patient’s behavior and make note of any unusual movements.
- Evaluate the patient’s pain and discomfort levels.
- Assess the patient’s overall physical and mental health status.
- Collaborate with healthcare professionals to manage the patient’s condition.

Intravenous medications:
- Haldol
- Loxapac
- Largactil
- Nozinan
- Clopixol
Videos

- http://www.youtube.com/watch?v=_dnK578aZdo
- http://www.youtube.com/watch?v=W_3bbpFjl68
- http://www.youtube.com/watch?v=FUr8ltXh1Pc

EPS Assessment

- Monitored on a regular basis means every person receiving drug therapy must be assessed at least once:
  - Every 3 to 6 months
  - After the initiation of a new psychotropic medication or a dose increase

Examination & Checklist for EPS
Acute Dystonia

Clinical Signs/Symptoms

<table>
<thead>
<tr>
<th>Motor Symptoms</th>
<th>Psychological Symptoms</th>
<th>Differential Diagnosis</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Briefly sustained or fixed abnormal movement</td>
<td>• fear</td>
<td>• malingering</td>
<td>• high potency first-generation antipsychotics (FGAP)</td>
</tr>
<tr>
<td>e.g., torticollis (30%)</td>
<td>• anxiety</td>
<td>• seizure</td>
<td>• young males</td>
</tr>
<tr>
<td>tongue (25%)</td>
<td></td>
<td>• catatonia</td>
<td>• first exposure to FGAP</td>
</tr>
<tr>
<td>trismus (14.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>oculogyric crisis (6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>laryngospasm</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatments

- Lorazepam S/L
- Benztropine IM
- Diphenhydramine IM
- Rx antiparkinsonian as prophylaxis
- Decrease the dose
- Change Rx
Akathisia

Clinical Signs/Symptoms

<table>
<thead>
<tr>
<th>Motor Symptoms</th>
<th>Psychological Symptoms</th>
<th>Differential Diagnosis</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot shifting</td>
<td>Agitation</td>
<td>Psychotic exacerbation</td>
<td></td>
</tr>
<tr>
<td>Pacing</td>
<td>Restlessness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocking</td>
<td>Decreased concentration</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- High potency first-generation antipsychotics (FGAP)
- Elderly
- Female
- Anemia
- SSRIs

Treatments

- Antiparkinsonians NOT EFFECTIVE
- Diazepam, clonazepam, lorazepam
- β-blocker
- Decrease the dose
- Change Rx

Parkinsonism

Clinical Signs/Symptoms

<table>
<thead>
<tr>
<th>Motor Symptoms</th>
<th>Psychological Symptoms</th>
<th>Differential Diagnosis</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor</td>
<td>Poor concentration attention</td>
<td>Depression</td>
<td>High potency first-generation antipsychotics (FGAP)</td>
</tr>
<tr>
<td>Bradykinesia</td>
<td></td>
<td>Negative symptoms of psychosis</td>
<td>Elderly</td>
</tr>
<tr>
<td>Rigidity</td>
<td></td>
<td></td>
<td>Female</td>
</tr>
<tr>
<td>Akinesia</td>
<td>(masked facies, decreased arm swing)</td>
<td></td>
<td>Neurological disorders</td>
</tr>
<tr>
<td>Pill rolling movements</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treatments

- Decrease the dose
- Change Rx
- Antiparkinsonian
  - Caution side effects: anticholinergic symptoms, exacerbation of psychosis, decrease cognition, unmask / ↑ TD
  - Less use of anticholinergic medication w/ Olanzapine, Seroquel

Classification of Movement Disorders

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical Tardive Dyskinesia</td>
<td>Lip smacking and pursing&lt;br&gt;Tongue side to side movement (bon-bon)&lt;br&gt;Tongue protrusion (Fly-catcher)&lt;br&gt;Chewing movements&lt;br&gt;Respiratory Dyskinesia&lt;br&gt;Pelvic thrusting&lt;br&gt;Choreoathetoid limb movements&lt;br&gt;Tapping, side to side foot movements&lt;br&gt;Marching in place</td>
</tr>
<tr>
<td>Tardive Dystonia</td>
<td>Similar to Idiopathic Torsion Dystonia&lt;br&gt;Generalized or Focal/Segmental</td>
</tr>
<tr>
<td>Tardive Tic</td>
<td>Motor and Vocal Tics</td>
</tr>
<tr>
<td>Tardive Akathisia</td>
<td>Subjective restlessness or need to move</td>
</tr>
<tr>
<td>Withdrawal Emergent Syndrome</td>
<td>Transient, 6-12 weeks duration&lt;br&gt;Begin immediately following abrupt discontinuation of neuroleptics&lt;br&gt;Children &gt; Adults&lt;br&gt;Generalized Chorea</td>
</tr>
</tbody>
</table>

Tardive Dyskinesia (TD)

Diagnostic Criteria:

- History of three months total cumulative neuroleptic use
- Dyskinesia of lingual-facial-buccal muscle (most common), upper face, limb, trunk
- Movements which are repetitive, stereotyped in appearance and distribution
- Most common is choreoathetoid movements (classical TD)
- Motor impersistence is NOT a feature
- Gait is usually not affected
### Tardive Dyskinesia Risk Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Factor</th>
<th>Determinant of Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Characteristics</td>
<td>• Age</td>
<td>• Increased risk with age (&gt;55 years)</td>
</tr>
<tr>
<td></td>
<td>• Gender</td>
<td>• Female (slightly higher)</td>
</tr>
<tr>
<td></td>
<td>• Diagnosis</td>
<td>• Affective disorder</td>
</tr>
<tr>
<td></td>
<td>• Previous EPS</td>
<td>• Risk 2 to 3 times higher</td>
</tr>
<tr>
<td></td>
<td>• Diabetes Mellitus (NIDDM)</td>
<td>• Risk 50-100% higher</td>
</tr>
<tr>
<td>Drug Characteristics</td>
<td>• Type of neuroleptic</td>
<td>• Typical neuroleptics have similar liability</td>
</tr>
<tr>
<td></td>
<td>• Dose/Duration</td>
<td>• Positive correlation with total drug exposure</td>
</tr>
<tr>
<td></td>
<td>• Continuous vs. intermittent</td>
<td>• Higher with intermittent treatment</td>
</tr>
</tbody>
</table>

### Epidemiology (TD)

<table>
<thead>
<tr>
<th></th>
<th>AP-1G</th>
<th>AP-2G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (per year)</td>
<td>5 %</td>
<td>0 - 2 %</td>
</tr>
<tr>
<td>Prevalence</td>
<td>25 % (elderly:50-60 %)</td>
<td>0 - 3 % (elderly: 0 - 5 %)</td>
</tr>
</tbody>
</table>

### Treatment for TD

- Change to 2nd /3rd generation AP
- Pyridoxine up to 400 mg/jr
- Clonazepam 0.5 - 6 mg/jr
- Tetrabenazine 25 - 75 mg/jr
- Clonidine 0.05 - 0.2 mg/jr
Tardive Dystonia

Clinical Signs/Symptoms

Motor
- Sustained muscle contractions
- Blepharospasm
- Sustained jaw opening (83%)
- Torticollis (50-65%)
- Arm hyperextension (42%)
- Back arching/extension/leaning (35%)
- Hand flexion/grasp-like

Psychological
- Distress
- Mobility dysfunction
- Embarrassment

Risks
- Abnormal birth
- Abnormal development
- Neurological disorders
- Mental retardation
- Male, younger age
- Earlier onset

NMS : F-E-V-E-R

(d/t blockage of dopamine receptors)

- Fever: hyperthermia & diaphoresis
- Encephalopathy: abrupt onset confusion, stupor
- Vital sign instability: BP unstable, tachycardia
- Enzyme elevation: CPK (creatine phosphokinase, hepatic enzymes)
- Rigidity: “lead pipe” rigidity (generalized)

Anticholinergic Side Effects

- Blurry vision
- Nasal congestion
- Dry mouth
- Urinary retention
- Constipation*

(*deaths with Clozapine)

Rx : tricyclic antidepressants, antipsychotics
Other Side Effects (SE)

- Sedation
- Orthostatic Hypotension
- Prolongation of QTc interval (dizziness, fainting, palpitations, N & V)
- Galactorrhea / increased prolactin
- Sexual dysfunction
- Sun hypersensitivity

Withdrawal Symptoms

- N & V, diaphoresis, myalgia, insomnia, anxiety, confusion (rebound cholinergic effects) (within days after D/C)
- Psychosis (2-3 weeks after D/C)
- Dyskinesia (2-4 weeks after D/C)
- Dystonia, parkinsonism, akathesia (within days after D/C)
Spectrum of Depression and Anxiety Disorders

- Posttraumatic Stress Disorder
- Social Anxiety Disorder
- Panic Disorder
- Obsessive-Compulsive Disorder
- Generalized Anxiety Disorder

ANXIOLYTICS (*benzodiazepines)

- Valium*
- Ativan*
- Rivotril*
- Serax*
- Xanax*
- Lectopam*
- Dalmane*
- Restoril*
- Librium*
- Buspar
- Buspirone

Indications for use of benzodiazepines

<table>
<thead>
<tr>
<th>Clear Indications</th>
<th>Probable Indications</th>
<th>Possible Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panic</td>
<td>Coping difficulties with anxiety</td>
<td>Akathisia</td>
</tr>
<tr>
<td>Generalized anxiety</td>
<td>Acute insomnia related to stress</td>
<td>Tourette Syndrome</td>
</tr>
<tr>
<td>Social Phobia</td>
<td>Sleep-wake cycle disturbance</td>
<td>Severe agitation (emergency/crisis)</td>
</tr>
<tr>
<td>Mania/agitated schizophrenia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Use of Benzodiazepines

- Useful by NOT recommended as first-line
- For short periods (less than 4 months)
- Side effect profile
  - Sedation
  - Reduced coordination
  - Impaired cognition
- Risk of dependency/tolerance
- Withdrawal symptoms/rebound anxiety

**((decrease gradually: 10 - 25% every 1 - 4 weeks.))**

---

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication</th>
</tr>
</thead>
</table>
| 1. Long half-life
  (>13hrs) & high potency | Clonazepam (Rivotril)
Clobazam (Frisium) (*AED) |
| 2. Long half-life
  (>13hrs) & low potency | **Chlordiazepoxide (Librium)**
**Diazepam (Valium)**
**Flurazepam (Dalmane)**
Nitrazepam (Mogadon)
(**active metabolites**) |
| 3. Short half-life
  (<13hrs) & high potency | Lorazepam (Ativan)
Alprazolam (Xanax) |
| 4. Short half-life
  (<13hrs) & low potency | Oxazepam (Serax)
Temazepam (Restoril) |

---

Risks and Side Effects Associated with Anxiolytics

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS Depressant</td>
<td>Antikolinergics</td>
</tr>
<tr>
<td>\textalk{Anxiolation}</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>CoM/Depression</td>
<td>Amphetamine</td>
</tr>
<tr>
<td>Aggression</td>
<td>Benzodiazepine</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>Dextramet</td>
</tr>
<tr>
<td>Depression</td>
<td>Delirium</td>
</tr>
<tr>
<td>Dependence</td>
<td>Depressant</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>Delirium</td>
</tr>
<tr>
<td>Somnolence</td>
<td>Nausea</td>
</tr>
</tbody>
</table>

---
Benzodiazepines

Persons with IDD are at an increased risk of exhibiting behavioral side effects, possibly due to:

- Decreased tolerance threshold to frustration
- More stressful living environments (group homes lacking privacy, with rigid structure, & limited trained staff) in combination with their own limited social skills & coping strategies
- **These side effects can appear from the 2nd to the 7th day or up to 55 days after starting/increasing the Rx (average = 23 days)**

---

Buspirone

**Pharmacology**
- 5HT1A partial agonist

**Adverse Effects**
- Little sedation
- Headaches, dizziness, GI upset
- No tolerance to date
- May precipitate hypomania in the elderly

**Interactions**
- Increased neuroleptic serum levels (+ risk EPS)
- Increased benzodiazepine levels
- Case reports of serotonin syndrome with SSRIs & trazodone.

---

Surprising Drug Interactions
Grapefruit & Grapefruit Juice

- Fresh or frozen, it can increase or less frequently, decrease the effects of certain drugs by interfering with their metabolism & elimination, resulting in serious adverse reactions.
- As little as 250 ml (1 cup) can cause significant increased blood levels of certain drugs.
- These effects can last up to 3 days or longer!

Medications to avoid with GRAPEFRUIT

- Amiodarone p.o. (Cordarone)
- Aripiprazole (Abilify)
- Atorvastatin (Lipitor)
- Buspirone (Buspar)
- Carbamazepine (Tegretol)
- Clomipramine (Anafranil)
- Dextromethorphan (DM)
- Diazepam p.o. (Valium)
- Erythromycin p.o.
- Estrogens
- Fluvoxamine (Luvox)
- Fluoxetine (Prozac)
- Itraconazole (Sporanox)
- Lovastatin (Mevaco)
*if given IV, no interaction noted

Effects of Tobacco on Rx

- Increased metabolism of fluvoxamine by 25% (via CYP182)
- Increased clearance of cyclic anti-depressant (induction via CYP182)
- Decreased plasma levels of chlorpromazine, haloperidol, fluphenazine, thiothixene, clozapine & olanzapine by 20-100% (induction)
- Increased clearance of diazepam & chlordiazepoxide (induction)
Effects of Caffeine on Psychotropics (coffee, tea, cola)

With SSRIs:
• Increased jitteriness & insomnia
• Increased caffeine levels with fluvoxamine, half-life increased from 5hr to 31hr!

With antipsychotics:
• Increased akathisia & agitation
• Increased levels of clozapine (competition for metabolism via CYP1A2)

Effects of Caffeine on Psychotropics (coffee, tea, cola)

With drugs that treat EPS:
• May offset benefits of Rx by increasing tremor & akathisia

With anxiolytics & sedatives:
• May counteract sedation & increase insomnia

With lithium:
• Increased renal excretion of lithium resulting in decreased plasma levels
• May increase lithium tremor