Maintenance Treatment of Schizophrenia

Stephen R. Marder, M.D
UCLA
James Halper, M.D.
Lenox Hill Hospital

Pre-Lecture Exam Question 1

1. **Antipsychotics can be effective for which of the following indications?**

A. Major depression with psychotic features
B. Psychotic disorders secondary to medical conditions
C. Mania
D. Tourette's syndrome
E. All of the above

Question 2

2. **Which of the following statements about the pharmacokinetics of antipsychotics is incorrect?**

A. Patients receiving an oral antipsychotic reach a peak plasma level more rapidly than those receiving an intramuscular preparation.

B. Patients reach a peak plasma concentration 1-4 hours after receiving an oral dose.

C. Patients receiving an oral antipsychotic reach steady state in 3-5 days.

D. Antipsychotics are well-absorbed when administered orally.

Question 3

3. **Which of the following statements about the time course of antipsychotic response is correct?**

A. Patients usually improve in agitation and excitement after psychosis improves.

B. Delusions commonly improve before thought disorder.

C. Psychosis will commonly improve three to five weeks after starting an antipsychotic.

D. If patients fail to demonstrate improvement in psychotic symptoms three days after starting an antipsychotic, they should be switched to another drug.

Question 4

4. Most antipsychotics are effective when they occupy what proportion of D_2 receptors?

A. 10%
B. 30%
C. 70%
D. 95%

Question 5

5. Which of the following dopamine pathways is related to the neurological side effects of antipsychotics?

A. Nigrostriatal
B. Tuberoinfundibular
C. Mesolimbic
D. Mesocortical

Question 6

6. **Which of the following is recommended by the Texas Medication Algorithm Project for refractory schizophrenia?**

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C. First generation (typical) antipsychotics as first line agents

Stabilization phase: Management

- If a patient responds to a medication they should continue on a therapeutic dose for at least 6 months
- Psychotherapeutic interventions should be supportive
- This phase may be a good time for educating patients and families

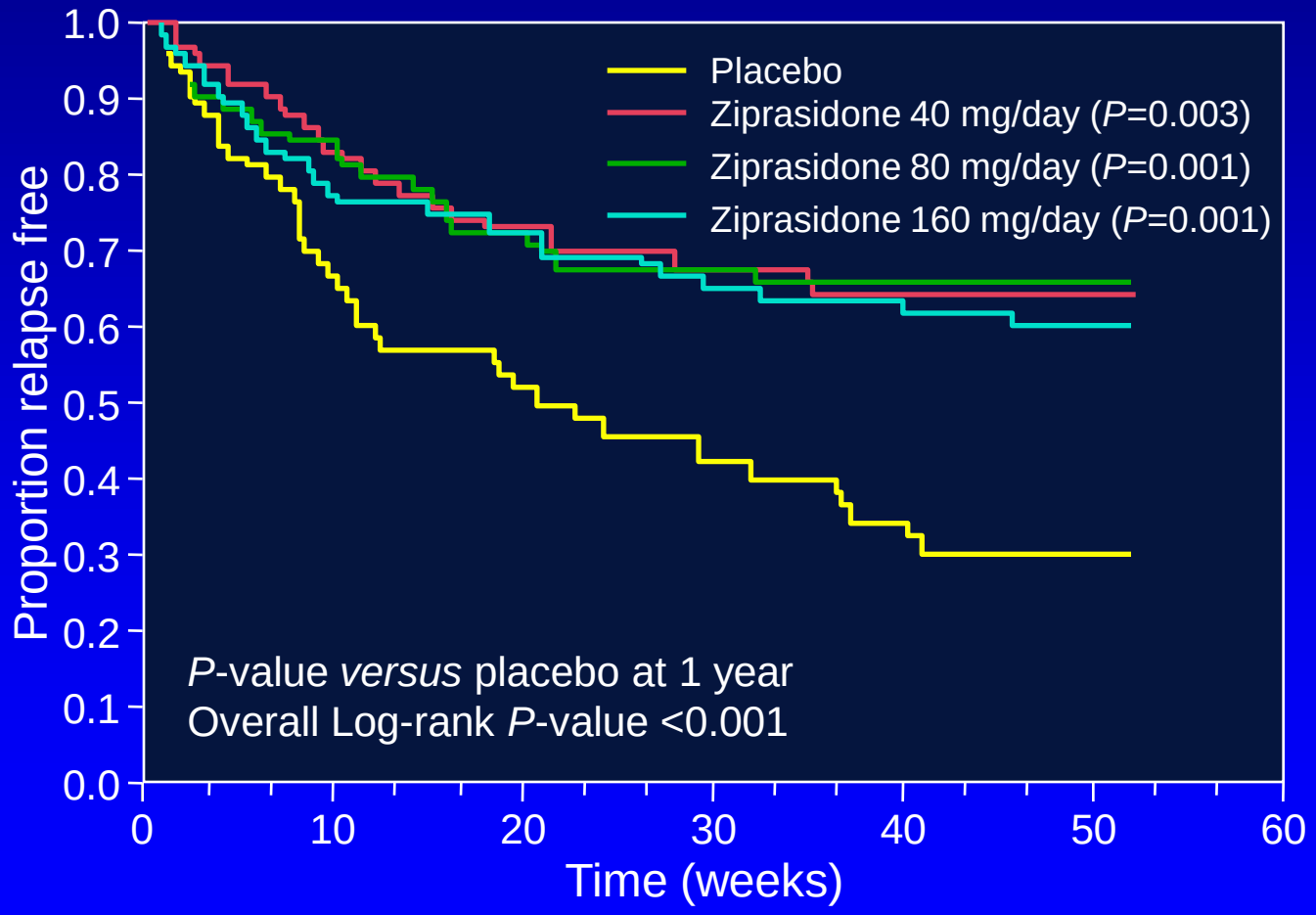
Stable phase: Assessment

- Consider positive, negative, cognitive, and mood symptoms as well as side effects
- Evaluate level of compliance
- Examine for tardive dyskinesia
- Regular assessment of prodromal symptoms

Stable phase: Antipsychotic medications

- Antipsychotic drugs reduce relapse risk
- Long-acting depot medications are more effective for many patients
- Patients without positive symptoms may be candidates for dose reduction

ZEUS: Results Time to Impending Relapse



Maintenance Treatment Of Schizophrenia

- Antipsychotics reduce relapse risk
- Patients who relapse when they are receiving antipsychotic medications have episodes that are less severe than those in patients who discontinue their drugs
- Patients may require as long as 6 months to fully recover from a psychotic episode

First-episode Schizophrenia

- The risk of relapse for first-episode patients who do not receive maintenance therapy is 40 to 60% during the year following an initial episode and 60 to 90% during the first 3 years
- The most severe disruption and deterioration of social function may occur early in the course of schizophrenia

Recommendations For First Episode Patients

- At least 1-2 years of maintenance neuroleptic treatment
- If and when medications are discontinued, these patients should be carefully monitored for evidence of impending relapse
  - from the International Consensus Conference (Bruge, Belgium)

Multiepisode Patients

- Risk of relapse is approximately 75% during the year following an episode and 80 to 90% during the second year
- Even when patients have been free of symptoms for at least 5 years, relapse rates are high when antipsychotic medications are discontinued

Recommendations For Multiepisode Patients

- Multiepisode patients should receive maintenance neuroleptic treatment for at least five years
- Under routine treatment conditions, depot medication ensures better compliance and, as a result, lower relapse rates

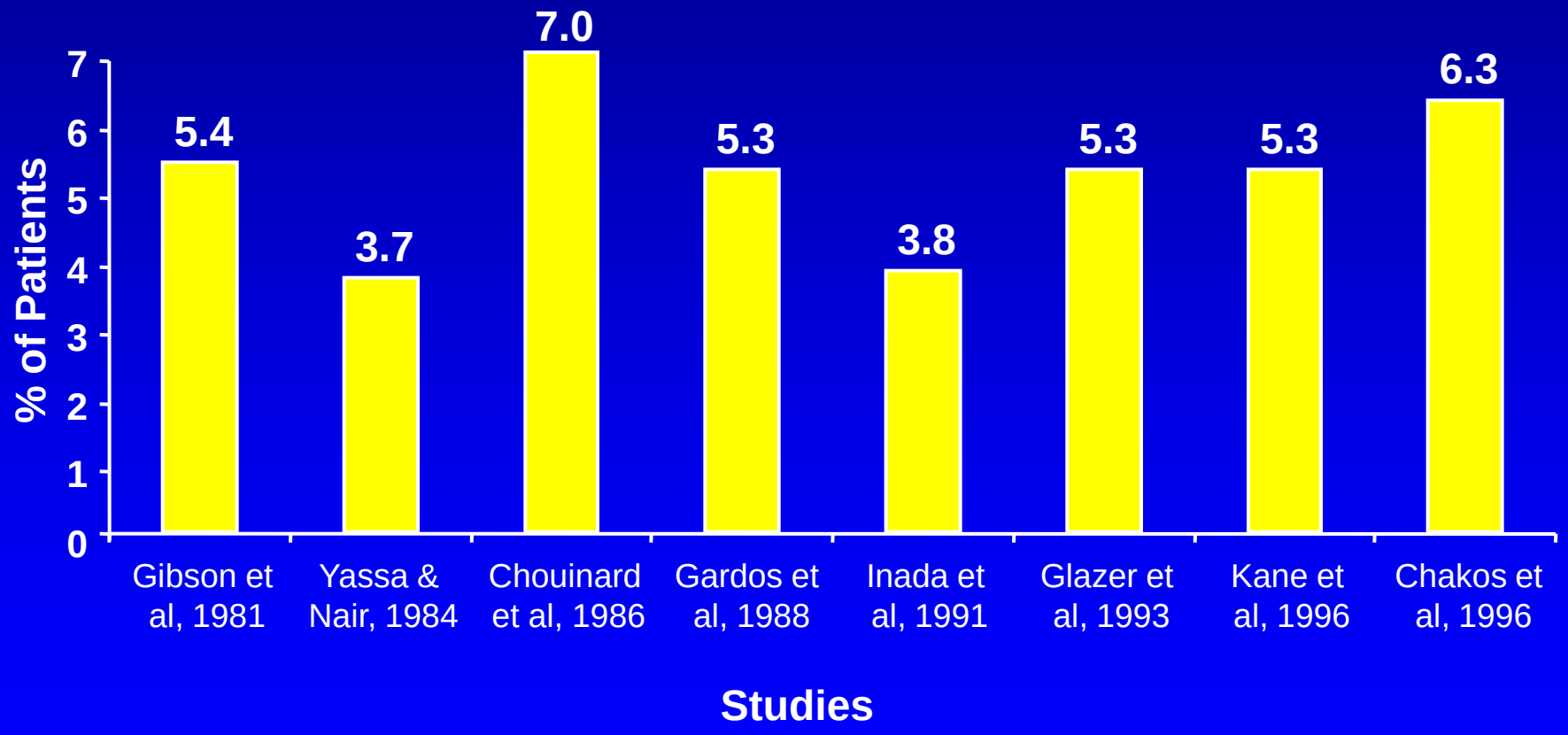
Tardive dyskinesia

- Mouth and tongue movements such as puckering, lip smacking, sucking, grimacing
- Choreoathetoid-like movements of the limbs, fingers and toes, slow writhing movements of the trunk

Tardive dyskinesia (continued)

- Movements of TD tend to increase with arousal and decrease with relaxation
- Incidence is about 5% each year
- Risk factors include increasing age, affective disorders, history of EPS, organic mental illness
- Other possible risk factors are high dose treatment and the duration of drug treatment

% of Patients on Conventional Antipsychotics with Tardive Dyskinesia in 1 Year



Tardive Dyskinesia (TD) with Novel Antipsychotics

- Crude TD incidences in the long-term, double-blind comparison of risperidone (2-8 mg /day) vs. haloperidol (5-20 mg/day)[1]
  - risperidone group: 0.6%
  - haloperidol group: 2.7%

- Newly reported TD (final 2 AIMS assessments) in the pooled data from three blind, responder long-term studies of olanzapine (max 20 mg/day) vs. haloperidol (max 20 mg/day)[2]
  - olanzapine: 1.0%
  - haloperidol: 4.6% (p-value: 0.003)

- TD virtually absent in clozapine-treated patients[3]

[1]Csernansky *et al*. (1999); [2]Tollefson *et al*. (1997); [3]Marder (1999)

Neurocognitive deficits in schizophrenia

- Attention
- Executive functioning
- Working memory
- Learning and memory
- Visuospatial analysis
- Verbal fluency
- Digit symbol substitution
- Fine motor function

Adapted from Keefe et al., 1999

Effects of conventional neuroleptics on cognition

- Acute treatment
  - can impair sustained attention
- Chronic administration may
  - improve measures of
    - » sustained attention/information processing
    - » abstract thinking
  - impair measures of
    - » motor speed and dexterity

Novel antipsychotic effects on cognitive function

	Risperidone	Clozapine	Olanzapine	Quetiapine
Working memory	↑	↓	↑	
Learning and recall	↑	↓		
Executive functioning	↑	↓		
Attention	↑	↑	↑	↑
Verbal fluency	↑	↑		
Reaction time		↓		
Motor speed	↑	↑		
Motor learning				
Trails B	↑			

Differential diagnosis of depression in schizophrenia

- Depression in psychosis
- Antipsychotic-induced akinesia
- Dysphoria from akathisia
- Demoralization syndrome
- Negative symptoms

Management of depression in schizophrenia (Siris)

- Assure that depression is not part of a psychotic decompensation
- Rule out EPS, particularly akinesia; change to an SDA
- Add an antidepressant

Effective Psychosocial Treatments: Schizophrenia PORT

- Supportive, reality-based individual and group therapies
- Family interventions that provide education and support
- Vocational rehabilitation
- Assertive Community Treatment

Drug-psychosocial interactions in schizophrenia

- Psychosocial treatments are more effective when psychotic symptoms are controlled with drugs (May et al, 1968)
- Psychosocial treatments can be toxic when patients are not adequately treated with drugs (Hogarty et al, 1974)
- Psychosocial treatments are more effective when compliance is assured (Hogarty et al, 1979

Drug-psychosocial interactions in schizophrenia (cont)

- Drugs may be more effective when compliance is enhanced by psychosocial treatment (Marder et al, 1996)
- Drugs and Psychosocial treatments may affect different outcome domains (ie, drugs control symptoms and psychosocial treatments affect social adjustment) (Marder et al, 1996).

Trials Combining Medication (MED) With Psychosocial Treatments (PST) (Both Controlled)

Author	N	Medication	Psychosocial Treatment	Outcome	Result
Hogarty et al. (1973, 1974)	360	Chlorpromazine	Major role therapy	Relapse	> 1 year: MED + PST ↑
Hogarty et al. (1979)	105	Fluphenazine	Social therapy	Relapse	> 1 year: MED + PST ↑
Hogarty et al. (1986, 1991)	90	Fluphenazine	Family treatment, social skills training	Relapse EE	1 year + 2 years: MED ⇟ PST
Schooler et al. (1997)	313	Fluphenazine	Psychoeducation vs family therapy	Rehospitalization symptoms	No difference between 2 PSTs
Marder et al. (1996)	80	Fluphenazine	Behavioral skills training, supportive group	Relapse, social adjustment	MED + PST adjustment ↑

Program For Assertive Community Treatment (PACT)

- Developed in Madison, Wisconsin by Leonard Stein and Mary Ann Test and now widely disseminated.
- PACT = A comprehensive, community-based service delivery model to treat those persons with severe and persistent mental illness who cannot be effectively treated through less intensive approaches.

Components of PACT

- A multidisciplinary team to organize and deliver comprehensive services to pts in a timely and integrated fashion.
- Team is mobile and provides most services in the community.
- High staff:patient ratio, eg. 1:10 or 1:12
- 24 hrs, 7 days

Components of PACT (cont)

- Social services that are frequently brokered such as housing, benefits, etc are provided by the team.
- Focus on high utilizers of services

Research on the PACT Model

- All studies document a reduction in hospital days.
- Some studies suggest PACT is cost effective
- PACT improves likelihood of independent living and may reduce symptomatology
- Effects last as long as PACT management continues

Post Lecture Exam Question 1

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Answers to Pre & Post Competency Exams

1. E
2. A
3. C
4. C
5. A
6. A