

**Panic Disorder**  
"I feel that I'm going to Die"

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**Panic Disorder**

- Angere-Latin root word for "To choke or strangle"
- Symptoms described by Freud in 1885
- Fear & anxiety symptoms of other diseases
- One of 9 types of anxiety disorder
- Unique diagnosis since 1980 with DSM-III
- Symptoms rarely occur alone

**Pathogenesis**

"We don't know yet how these parts work" Tomb 1995

**Biologic - Nervous System**

- Biochemical - amygdala
- Genetics - Chromosome 16
- Neurochemical** - norepinephrine (locus ceruleus )
- Serotonic (dorsal raphe nucleus)
- GABA (couples with benzodiazepine receptor)
- Limbic system - hippocampus, amygdala

**Psychodynamic -**

- Stressors
- Biological vulnerability
- Hereditary - 20-25% in families with history
- **Behavioral** - - Unresolved dependence vs. independence
- Threat to ego
- **Anatomically**  
Thalamus  
Frontal Cortex

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## Definitions

- Generalized Anxiety Disorder (GAD) - constant state of tension and anxiety over various situations, this state lasts more than six months despite the lack of an obvious or specific stressor.
- Panic Disorder - the presence of recurring, unexpected panic attacks.
- Panic Attack - discrete periods of intense fear or discomfort; was not triggered by situations in which the person was the focus of others' attention.

## Defining Panic Disorder

- Unexpected occurrence - did not occur immediately before or on exposure to a situation
- Residual effect - one or more attacks have been followed by a period of at least a month of persistent fear of having another attack
- Agoraphobia - fear of being in places or situations from which escape might be difficult or embarrassing in event of panic symptoms

## Panic Disorder Subtypes per DSM-IV

- Panic Disorder
- Panic Disorder with Agoraphobia
- Panic Disorder without Agoraphobia
- Agoraphobia without history of panic disorder

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### DSM-IV Criteria for Diagnosis of Panic Disorder

- One or more panic attack have occurred that were unexpected and not triggered by a known situation where person was focus of others' attention.
- Four attacks within a four-week period or at least one attack followed by at least of a month of persistent fear of another attack.
- Development of at least four (4) of the defined symptoms in at least one of the attacks.
- Symptoms developed suddenly and increased in intensity within ten minutes.
- Organic factors have been eliminated as causes.

### 5 Levels of Severity of Panic Attacks - DSM-IV

- 1. Mild - all attacks have limited number of symptoms (fewer than four), or there has been no more than one attack in the past month.
- 2. Moderate - attacks for the past month have been between "mild" and "severe", more than one attack and fewer than 8, less than four symptoms per attack.
- 3. Severe - at least eight panic attacks in past month.
- 4. Partial remission the condition is between "full remission" and "mild" attacks.
- 5. Full remission - no panic or limited symptom attacks during the past six months

### Categories of Anxiety in Primary Care Settings

- Anxiety in response to psychosocial or physical stressors-adjustment disorder with anxious mood.
- Anxiety due to general medical conditions - directly linked physiologically to medical condition.
- Substance-induced anxiety disorder.
- Anxiety associated with another psychiatric condition.

Uphold & Graham, 1999

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### Panic Disorder - Physiological Symptoms

- shortness of breath (dyspnea) or smothering sensations
- dizziness, unsteady feelings, or faintness
- palpitations or accelerated heart rate (tachycardia )
- trembling or shaking
- sweating
- choking
- nausea or abdominal distress
- depersonalization or derealization
- numbness or tingling sensations (paresthesias)
- flushes (hot flashes) or chills
- chest pain or discomfort
- fear of dying
- fear of going crazy or of doing something uncontrolled

DSM-IV

### Medical Conditions With Common Anxiety Components

- **Cardiovascular**
  - Arrhythmia
  - Cardiomyopathies
  - CAD
  - CHF
  - Mitral Valve Prolapse
  - Myocardial Infarction
- **Endocrine**
  - Hyperadrenalism
  - Hypocalcemia
  - Hypothyroidism
  - Cushing's Syndrome
- **Neurologic**
  - Akathisia
  - Encephalopathy
  - Essential tremor
  - Multiple Sclerosis
  - Restless leg Syndrome
  - Temporal lobe epilepsy
- **Immunologic**
  - Anaphylaxis
  - Systemic lupus
  - HIV

### Medical Conditions With Common Anxiety Components

- **Metabolic**
  - Anemia
  - Hypoglycemia
  - Hyponatremia
  - Hypokalemia
  - Hyperthermia
- **Respiratory**
  - Asthma
  - COPD
  - Pulmonary Embolism
- **Secreting Tumors**
  - Carcinoid
  - Pheochromocytoma
- **Other**
  - Peptic Ulcer Disease

Valente, 1996

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### Drugs and Medications with Common Anxiety Components

**Prescription**

- Aminophylline
- Anticholinergics
- Antihypertensives
- Antituberculous agents
- Cycloserine
- Digitalis (toxicity)
- Dopamine
- Epinephrine
- Lidocaine
- Levodopa
- Methylphenidate
- Neuroleptics (akathisia)
- Phenylephrine
- Phenylpropanolamine
- Procainazine
- Sedative-hypnotics (use/withdrawal)
- SSRIs
- Steroids/prednisone
- Theophylline

**Non-prescription**

- Pseudoephedrine
- Salicylates
- Ephedrine
- NSAIDs

**Non-medications**

- Alcohol
- Amphetamines
- Caffeine
- Cocaine
- Hallucinogens
- Marijuana
- Monosodium glutamate
- Nicotine/Nicotinic Acid

### Objectives of Case Study

- Identify target symptoms of Panic Disorder
- Recommend appropriate pharmacotherapy for a patient with Panic Disorder
- Counsel a patient concerning use of alprazolam (Xanax)
- Understand the usefulness of several non-pharmacotherapeutic approaches to the treatment of panic disorder
- Distinguish between diagnosis of Panic Disorder and Panic Disorder with Agoraphobia
- Review efficacy of Imipramine (TCA) and Phenelzine (MAOI)
- Acknowledge cost of therapies for Panic Disorder: Pharmacologic, CBT, and Combination

### Patient Presentation

CC: "Sometimes I feel like I have lost control of myself and that I am going to die."

HPI: 25 yo, single, female  
Presents to cardiologist with CC  
3- ED visits in past 8 months  
"feared was having a heart attack";

Negative for medical causes (labs, ECG, PE)

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### HPI - Description of Episodes

- Episodes are “extremely frightening and paralyzing; attacks appear to involve heart”, awakens in middle of night with “feeling of doom”, “difficult to describe feeling”, “not like any dream or nightmare she has ever experienced”
- First attack 8 months ago - had moved out of parents home for first time
- Attacks are more frequent - two times a week; sometimes occur during the day
- Symptoms - wet with sweat and her heart is racing
- Precipitating factor - She feels the attacks are precipitated by being around large groups of people; such as when she has to meet with clients at work
- Consideration for relief - she has thought of skipping work but she is concerned she could lose her job if she misses too many days.

### Patient’s History

- **PMH** - *Gastroesophageal Reflux*- started on meds 8-10 months prior to first attack. *Irritable bowel syndrome* suspected at time (c/o diarrhea) but has not had symptoms in recent months. No other known illnesses
- **FH** - Mother - has *major depressive disorders* with medications.  
Father - *alcoholic*; atrial arrhythmia controlled with medications.  
Maternal grandmother had *major depressive disorder*; *committed suicide*.  
No other family medical problems.  
*No siblings*.
- **SH** - Single, *engaged* to be married in coming year; college graduate; *works in advertising sales* at radio station. Non-smoker, physically fit; no coffee or caffeinated drinks they make her “feel too nervous”.  
Admits that when *she does have a drink, she feels calmer* and less threatened by a panic attack.

(Italics indicate possible risk factors for Panic Disorder)

### Patient’s History/Physical

- Meds - Cimetidine 300 mg po QD for “chronic indigestion”
- Allergies - NKA
- ROS - *Episodic* periods of “*pounding heart*” and *shortness of breath*, no other complaints except those in HPI.
- PE - All WNL except Heart Rate
  - Gen - alert, cooperative woman in NAD, oriented to all spheres
  - VS - B/P 125/70; **P 120**; RR 21, T 36.8 C
  - HEENT - PERRLA, EOMI, Fundusnormal, TM clear, Nares clear; pharynx WNL
  - Neck - Supple, thyroid normal size without nodules
  - Cardiac - Tachycardia, no murmurs
  - Resp - Breath sounds clear throughout
  - Abd - BS+, non-tender, no guarding
  - Ext - Negative cyanosis, edema, clubbing; ROM normal

## Pertinent Findings

- **Positives**
  - Family MHx.
  - Personal hx. GERD, Sp. bowel
  - ED visits x 3
  - Increase freq. of attacks x 8 months
  - Stressors
    - Job
    - Engagement
    - Left home
    - Only child
- **Negatives**
  - Works
  - Does not have agoraphobia
  - No diagnosis of MH problem
  - Seeking help
  - No positive physical findings

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## Patient Lab/ECG/Holter Monitor Results

- **Lab Results Chemistry (Normal)**
  - K+ 4.1 mEq/L (3.5-5.0)
  - Na+ 138mEq/L (135-145)
  - Cl- 108 mEq/L (98-106)
  - CO2 25 mEq/L (10-40)
  - BUN 13 mg/dl (7-18)
  - Creat. .08 mg/dl(0.4-1.5)
  - Glucose 78 mg/dl(70-110)
  - AST 24 IU/L (5-40)
  - ALT 29 IU/L (7-56)
  - ALP 48 IU/L(17-142)
  - Tot. bil. 1.0 mg/dl(2-1.1)
  - Chol. 185 (140-199)
- **Hematology**
  - Hgb 14.5
  - Hct 41.2
  - Platelets 340,000 /mm3
  - WBC 10.3 with normal diff.
- **UA - WNL**
- **Thyroid profile:**
  - T3 Resin Uptake 42%(26-39)
  - T4 Total 11.9 (5-11.5)
  - TSH 0.6IU/ml (5-5.0) 24 hr
- **Pregnancy test - Neg.**
- **Holter Monitor** - one 30 min. episode of tachycardia with rates of 120-130
- **ECG - NSR**

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## Case Study Questions :Problem Identification

### 1. What information in this patient's case is consistent with the diagnosis of panic disorder?

- “extremely frightening and paralyzing attacks that appear to involve the heart” (recurrent, discrete periods of intense fear or discomfort).
- Frequency 2 attacks per week (4 attacks in 4 week period).
- Feel like losing control or going to die; considering skipping work on days when she thinks she might have an attack but is concerned she could lose her job if she misses work (fear/worry about the consequences of the attacks)

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### Case Study Questions :Problem Identification

- Pounding and racing heart, shortness of breath, awoken with feeling of doom, wet with sweat (Four or more symptoms).
- Recent psychosocial stressors - moved into own apartment for first time; engaged to be married within year, doing presentations to groups.
- Family history of psychiatric disorder (major depression) mother and grandmother, father alcoholic.

DSM-IV Criteria

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### Differential Diagnosis:

- Anxiety as a primary psychiatric disorder.
- Anxiety as a response to psychological or physical stressors.
- Anxiety due to a medical condition.
- Substance induced anxiety.
- Anxiety associated with other psychiatric disorders

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### Diagnostic Test:

- Laboratory (hematology, chemistry)
  - Routine Screening laboratory of : CBC with differential (hematologic function), Full chemistry (adrenal, renal, liver function), Thyroid Function, Lipid Profile,
  - Drug screen or levels for substance associated panic. Stimulants, anticholinergics, insulin, corticosteroids, alcohol, cannabis, cocaine, hallucinogens, inhalants carbon monoxide
- Cardiac testing
  - Electrocardiogram
  - Holter Monitor
  - CPK-isoenzymes, troponin
- Pulmonary function
  - Arterial blood gases
  - Chest radiography
  - Pulmonary function
- Neurologic (if there is suspicion of metastatic disease or neurological involvement)
  - CAT scan of head, spine as indicated.
- Common Psychological Screening Tools
  - Zung Anxiety Self Assessment Scale
  - Hamilton Anxiety and Depression Scale
  - Beck Depression Inventory

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**Problem Identification:**

**In making the diagnosis, why did the psychiatrist not refer to the disorder as panic disorder with agoraphobia?**

- Diagnosis of Agoraphobia by DSM-IV includes:
  - Meeting criteria for Panic Disorder **PLUS** Restriction of travel or needing a companion to leave home or endures agoraphobic situations despite intense anxiety.
- The patient considered avoiding work, which she identified as a trigger, but did not avoid going to work.
- No indication of limited travel or inability to leave her house without a companion

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**Desired Outcome:**

**What is the desired therapeutic outcome for this patient?**

- The goal is to regain control of reactions to stress and stimuli and reduce the feeling of helplessness.
- Demonstrate the ability to decrease the behaviors associated with panic and manage the panic state.
- Identify life stressors associated with panic attacks and develop a plan for managing response.
- Supportive care through Single drug therapy with cognitive-behavior therapy.
- Education related to management of symptoms, medication risk and benefits and behavior modification that provide the patient with the ability to be in control.
- Goal attainment will be measured by the client's demonstration of problem solving, decision making and structuring her environment to meet her needs and decrease anxiety.

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**Therapeutic Alternatives:**

What non-pharmacologic therapies are available for the treatment of panic disorders?

Cognitive Behavioral Therapy (CBT)

- Keeping a diary of repetitive thinking events
- Self-observation to reduce unrealistic ideas
- Restructure thoughts
- Systemic desensitization
- Exposure and response
- Breathing retraining

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### Specific CBT Therapies

#### Individual Therapy

- Teach relaxation techniques to eliminate physical tensions that precede panic attacks.
- Explore underlying conflicts and stressors.

#### Group Therapy

- Teach strategies for handling stressful life events.
- Provide safe environment to try out new behaviors and thinking about panic attacks.
- Use group for support and reassurance.
- Teach to identify when anxiety is escalating and what steps to take to interrupt the process.

#### Family Care

- Teach family about panic disorder and how to work with the client.
- Develop effective communication techniques to decrease conflicts.
- Promote honest, open expression and discussion of feelings.
- Discuss impact of clients illness on family.

### Therapeutic Alternatives:

Can or should these forms (CBT) of treatment be combined with medications?

Treatment generally includes Cognitive Behavioral Therapy and a combinations of medications for decreasing the anxiety and controlling the panic attacks.

### Therapeutic Alternatives:

What pharmacotherapeutic options are available for this patient?

#### Antidepressants:

##### Tricyclic antidepressants (TCAs)

Imipramine (Tofranil), Janamin

##### Serotonin-reuptake inhibitors (SSRIs)

Fluvoxamine (Prozac)

Sertraline (Zoloft)

Venlafaxine (Effexor)

Nefazodone (Serzone)

##### Benzodiazepines

Alprazolam (Xanax)

Clonazepam (Klonopin)

##### MAOI

Phenelzine (Nardil)

Tranylcipromine (Pamate)

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**Optimal Plan:**

Design a reasonable treatment regimen for this patient, and include the expected time to onset of beneficial effects.

**Nonpharmacological management of anxiety**

Brief Psychotherapy and education -Office counseling or referral for psychotherapy

- Education
  - Nature of panic disorder
  - Reduction of caffeine/stimulants
  - Realistic interpretation of frightening body
  - Set expectation of control of panic attacks
- Teach Behavioral Control Techniques
  - Stress Management
  - Relaxation Exercises
  - Controlled Breathing
  - Imagery and Distraction
  - Exercise
- Graded exposure to panic attacks

**Optimal Treatment Plan**

- Pharmacotherapy
  - BZ-
    - has immediate effect on anxiety (15-30 minutes)
    - Plan to use for only 2 weeks then taper off
  - Alprazolam(Xanax) .5 mg TID (Dose .5-2 mg TID/QID)
  - Antidepressant -
    - may take up to 4 weeks to reach therapeutic levels.
    - negative side effects of sedation are noticed first
  - TCA -
  - Imipramine(Tofranil ) 150 mg QD(Dose 150-300 mg)

**Optimal Therapy: Behavioral Therapy and Pharmacotherapy**

- Behavioral therapy is short-term
- Drugs are long term, panic disorder is a chronic condition
- Combined therapy - drugs & CBT - \$600/month

Drugs \$32 - \$450/month depending on use of brand names or generic, local pharmacy or ordering over internet

- Cognitive Behavioral Therapy \$300-\$350/month with maximum Medicare reimbursement of \$1000/90 days

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**Assessment Parameters:**

How should this patient be monitored for improvement and to detect adverse effects?

- Monitor for drug levels
- Monitor for liver and kidney function due to risk of toxicity with TCA, MAOI, BZ
- Monitor for symptom control
- Weekly visits that include patient counseling until symptoms are under control
- Monthly visit to monitor drug levels until therapeutic
- Every 3 month visits for at least one year due to high recurrence of attacks after treatment ( 80% recurrence within 9 months)
- If patient responds to TCA or SSRI, continue treatment for 6-12 months, then taper drugs over 1-2 months.
- If relapse, reinstitute previously effective treatment for 6-12 months
- If non-responsive to TCA or SSRI, consider MAOI as a last resort

**Patient Counseling:**

Describe how you would counsel this patient about taking her treatment regimen. Include a discussion about the possibility of becoming "dependent" on this medication.

- Cognitive-behavior therapy is intended to teach the patient to identify triggers and how to physically control the symptoms related to anxiety.
- Panic Disorder is a disease, she is not "crazy" and it may be chronic. The disease responds well to medication and therapy.
- Practice of exercises devised for her in CBT will increase her success at control of panic.
- The physical symptoms she feels are related to her chronic disease, she will not die from these symptoms- medical causes have been ruled out, she can control her response.

**TCA Monitoring & Patient Education**

- Monitoring
  - Liver/Renal function
  - ECG
  - Leukocyte & differential count
- Patient Education
  - may cause drowsiness, dizziness, blurred vision
  - Avoid ETOH and other CNS depressants
  - Abrupt discontinuation may cause nausea, headache, malaise
  - Avoid prolonged exposure to sunlight
  - Lombardi, 1999

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**Patient Counseling :**  
Drug Information  
Imipramine - Tofranil

- **Adverse Effects**
  - Anticholinergic - dry mouth, urinary retention, decreased gi motility, tachycardia, memory impairment
  - Orthostatic hypotension
  - Sexual dysfunction
  - Weight gain
  - Sedation
- Historically drug of choice to treat nonpsychotic, nonbipolar disease.
- Takes 7-21 days to reach therapeutic levels

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**Patient Counseling: Alprazolam (Xanax)**

- Caution when driving, operating machinery, performing tasks required mental alertness
- Avoid concurrent use of alcohol and other CNS depressants
- Do not stop taking drug suddenly -Needs to be tapered over weeks to month after as little as 3 weeks use

**Adverse Effects**

- Drowsiness/dizziness/ataxia
- Disorientation/Hangover
- Agitation/Excitement
- Anterograde amnesia
- Respiratory dysfunction
- Dependence/abuse/withdrawal

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**BZ Monitoring & Patient Education: Alprazolam (Xanax)**

- Contraindication - hypersensitivity, narrow-angle glaucoma, psychosis
- Intermediate acting - metabolized in liver and eliminated via urine
- Category D in Pregnancy- use only to control seizures; associated with risk of cleft lip or palate, microcephaly and retardation and pyloric stenosis

- Drug interactions **Increases CNS depression - can be deadly with CNS depressants (alcohol, barbiturates, opioids)**
  - Increases digoxin and ketoconazole
  - Many Drugs increase BZD effect: B-blockers, cimetidine, contraceptives, antibiotics,
  - Drugs that decrease BZD- anticonvulsants, ranitidine, rifampin, theophylline

- Lombardi, 1999

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**Follow-up Case Question:**

If the patient had been diagnosed with panic disorder with agoraphobia, how might her initial therapy differ from the case of panic disorder without agoraphobia?

- Cognitive behavioral therapy would have been encouraged to practice entering and staying in their feared situation. The goal would be to teach the patient to systematically expose themselves to feared situations and bodily sensation.
  - Teach the patient to become aware of irrational thoughts that accompany panic and anxiety.
  - Teach techniques to combat and correct the thoughts.
  - Relaxation training.
  - Agoraphobia involves trips to feared places outside the therapist office.
- Pharmacotherapy would have still been used to block and control the panic attacks.

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**Comparative Efficacy of Imipramine (TCA) vs. Phenelzine (MAOI)**

- Mavissakalian (1999) previous imipramine and phenelzine good results for 6-12 months of maintenance; no difference in relapse rates with that of placebo.
- Cassem, et al(1997) TCA (imipramine) has well established efficacy but has delayed onset and adverse effects especially worsening of symptoms with first dose. MAOI (phenelzine) is potentially the most comprehensive because they block panic attacks, relieve depression and offer a confidence-enhancing effect that helps the patient recover from vigilance and phobic avoidance. MAOI less side effects early in treatment than TCA and SSRI but become more problematic with long term treatment.

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**Comparative Efficacy of Imipramine (TCA) vs. Phenelzine (MAOI)**

- Vallone (1997) describes the TCA and MAOI as similar in action but TCA are preferred due to the long-term adverse effects of MAOI and the dietary restriction.
- Lombardi (1999) indicated that antidepressant were drug of choice if anxiety and depression occurred together. MAOI interact with many other drugs and food and may cause a hypertensive crisis.
- APA Clinical Guidelines (1998) Trial and error continues in treatment of panic disorder acute and long term. Best studies are those with a placebo arm - not many available.
- SSRI are pharmacologic treatment of choice; not for greater efficacy than TCA or MAOI but for least adverse affects according to all the studies.

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### Relative Cost of Pharmacologic Treatment

- Alprazolam (Xanax) 6 mg/day  
Cost of 30 day supply
- CVS Pharmacy
  - Xanax \$ 270.99
  - Generic \$ 82.99
- Internet Price ( PlanetRX.com)
  - Xanax \$ 199.27
  - Generic \$ 15.39
- Imipramine (Tofranil) 150 mg/day  
Cost of 30 day supply
- CVS Pharmacy
  - Tofranil \$176.99
  - Generic \$62.99
- Internet Price ( PlanetRX.com)
  - Tofranil \$ 88.71
  - Generic \$ 17.54

### Cost of Behavioral Therapy Sessions

- Medicare Reimbursement for Behavior Management & Rage Therapy
  - based on 90 days of treatment with weekly sessions of 48-58 minutes.
  - Reimbursed at \$75.00 - 85.00 per session
  - Max. \$1000.00 reimbursement/90 day period
  - Can repeat treatment for new episodes
  - Max. reimbursement- 270 days of tx. per year
- Medicaid does not pay for Behavior Management & Rage Therapy in Michigan. Individual cases may appeal the general ruling.
- Blue Cross/Blue Shield
  - HMO - pays 50% of the physician fees
  - Standard - pay based on individual coverage contract

### Comparison Monopharmacotherapy vs. Weekly Behavioral Therapy Session

- Pharmacotherapy Alone:
  - Monthly cost CVS \$ 447.98 to Internet \$287.00
  - Xanax \$199.27 for 4 week supply
  - Tofranil \$88.71 for 4 week supply
- Behavioral Therapy Along:
  - \$300 - \$340 for 4 weeks
  - \$75-85/session
  - One session per week for four weeks

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## The Cost of Panic Disorder

Combination Therapy:  
Xanax and Tofranil plus  
Cognitive Behavioral Therapy

\$587 - \$780/month



### Clinical Pearl:

Optimal therapy often includes non-pharmacologic treatment such as behavioral therapy, in addition to pharmacotherapy. treatment regimens should be considered for a long-term basis.

## Patient Education Resources

- **Internet - Caregiver Info & Support:**  
[www.webofcare.com/Lycos\\_WebMD](http://www.webofcare.com/Lycos_WebMD) - [www.webmd](http://www.webmd)
- **Support Groups**
  - National Alliance for A.I.M. (Agonophobia in Motion), 1729 Crooks Road, Royal Oak, Michigan
- **Books**
  - Beckfield D.F. (1994). Master your Panic...and Take Back Your Life. San Luis Obispo, CA: Impact Publishers.
  - Handly, R., & Neff, P. (1985) Anxiety and Panic Attacks. New York: Fawcett-Crest.
- **National Institute of Mental Health Panic Information Line: (800)64-PANIC**
  - Panic Disorder (NIH-93-3508) available in Spanish -SP-92-1869)
  - Understanding Panic Disorder - NIH-93-3509
  - Getting Treatment for Panic Disorder: Information for Patients, Families, and Friends - NIH-94-3642

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