

Anxiety Disorders: An Overview

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Objectives

1. List anxiety disorders commonly encountered in a primary care environment.
2. Cite the diagnostic criteria for several anxiety disorders and differentiate each from similar presenting clinical situations.
3. Demonstrate the ability to use screening tools appropriately for anxiety disorders.
4. Be aware of psychological treatments of anxiety disorders
5. Cite the current FDA approved and evidence-based guidelines for psychopharmacological treatments for anxiety disorders.

Case 1

A 24-year-old female comes to your office for evaluation. She complains of an 8-month history of insomnia, difficulty concentrating, fatigue, irritability, and is constantly stressed out. She has trouble falling asleep, awakens after 2 or 3 hours, and has difficulty returning to sleep, worrying about all the things she needs to get done.

The patient is concerned that her impaired concentration is interfering with her work as a receptionist and is threatening a long-term relationship with her boyfriend. She has occasional episodes of nausea, crampy abdominal pain, but her appetite is unchanged and her weight has been stable.

On physical examination, her BP is 122/72 mm of Hg; pulse rate is 96/min and regular. Her thyroid gland is within normal limits and nontender.

The remainder of physical examination including cardio-respiratory examinations is WNL. Results of routine laboratory studies are normal.

Generalized Anxiety Disorder

Diagnostic Criteria

- A. Pervasive, excessive worry, at least 6 months across many life domains.
- B. Uncontrollable worry.
- C. Concomitant symptoms, at least three (one for children), some present for prior 6 months:
 - Note: only one item is required in children.
 - 1. Edginess
 - 2. Easy fatigue
 - 3. Impaired concentration
 - 4. Irritability
 - 5. Muscle tension
 - 6. Trouble with sleep
- D. Above symptoms significantly impair social and occupational functioning.
- E. The above-mentioned symptoms are not attributed to drug abuse, medications, or medical condition.
- F. Other mental disorders do not explain these symptoms.

(Am Psychiatric Association, 2013)

Generalized Anxiety Disorder

Differential Diagnosis

1. Anxiety Disorder due to another medical condition
2. Substance/medication-induced anxiety disorder
3. Social anxiety disorder
4. Posttraumatic stress disorder and adjustment disorders
5. Depressive, bipolar, and psychotic disorders

Case 2

Jane, a 27-year-old woman, is married with two children. Shortly after the birth of her second child, with no apparent precipitant, she experienced her heart “racing,” was short of breath, lightheaded, unsteady, and was afraid of going crazy. She experienced another attack a few weeks later with a desire to flee. She described it as “out of the blue.” She also felt that she could die and began to think about the world ending. She began to avoid situations where she thought she could not escape, and her life became more limited. The fear of having another attack with similar feelings contributed to her avoidance of any situation where she might be out of control and has limited her socializing with friends.

Panic Disorder

Diagnostic Criteria

- A. Frequent panic attacks that occur “out of the blue,” characterized by brief but intense fear peaking within minutes, accompanied by four of the following symptoms:
1. Cardiac: chest pain or discomfort, increased heart rate, palpitations/pounding heart.
 2. Abdominal: abdominal discomfort, nausea, increased sympathetic activity—trembling, sweatiness, and breathlessness.
 3. Neurological: dizziness, feeling unsteady and lightheaded.
 4. Alterations in perception—derealization and alterations in sensation.
 5. Fear of out of control or dying.
- B. For 1 month following the attack, one or both of the following may occur:
1. Continual worry about another attack.
 2. Patient alters behavior in a maladaptive way.
- C. Attack is not secondary to a medical or substance abuse problem.
- D. There is no other DSM V disorder that explains these symptoms.

(Am Psychiatric Association, 2013)

Panic Disorder

Differential Diagnosis

1. Other specified anxiety disorder or unspecified anxiety disorder
2. Anxiety disorder due to another medical condition
3. Substance/medication-induced anxiety disorder
4. Other mental disorders with panic attacks as an associated feature

Case 3

John is a 22-year-old man, complaining of difficulty in his social relationships and loneliness. He said that he has always been shy, not wanting to be the center of attention. He spends most of his time alone, having few friends. John states that he would like to have a partner but feels that a woman would not find him interesting and would think he's ignorant. He therefore avoids social situations where others may judge him. At work, when he has to make a presentation, his anxiety becomes overwhelming and increases as the time gets closer.

Social Anxiety Disorder (Social Phobia)

Diagnostic Criteria

- A. Anxiety as a response to situations where a person feels judged.
- B. A person feels his behavior will be judged poorly by others.
- C. Anxiety and social situations.
- D. Avoidance or fear of social situations, where the fear is out of proportion to the actual threat
- E. Symptoms last for more than 6 months.
- F. The anxiety experienced in social situations causes difficulties in other areas of functionality.
- G. Substance use is not the cause of anxiety.
- H. The DSM V mental disorder does not explain the symptoms better.
- I. The patient's fear, anxiety, or avoidance is out of proportion when another medical condition is present.

(Am Psychiatric Association, 2013)

Social Anxiety Disorder (Social Phobia)

Differential Diagnosis

1. Normative shyness
2. Agoraphobia
3. Panic disorder
4. Generalized anxiety disorder
5. Separation anxiety disorder
6. Specific phobia

Case 4

A 32-year-old woman is evaluated for a 3-month history of increased sweating, heart racing, increased appetite, and 8 lb. weight loss over 6 months. The patient also reports a 3-month history of amenorrhea, before which time she felt completely healthy. She also reports increased worry, restlessness, and lack of proper sleep for the past 6 months.

Medical history is otherwise unremarkable and she takes no medications.

Physical examination shows a thin, restless woman with smooth, fine moist skin and fine hair. BP is 132/86 mm of Hg, pulse rate is 112/min, RR 16/min and BMI 18.5. Mild lid lag is noted, but no proptosis, diplopia, or conjunctival injection are noted.

Examination of the neck reveals a smooth enlarged non-tender thyroid gland. There is a mild, fine tremor of the outstretched hands. Reflexes are brisk.

Cardiac examination reveals a regular tachycardia without any murmurs. Her lungs are clear to auscultation.

Group 4 (Contd)

Lab Studies:

CBC with Differential : WNL

Urine B HCG : < 5

Urine Toxicology Screen: Negative

TSH: 0.008 (0.270-4.200 uIU/ml)

Free T4 : 6.54 (4.5-11.7 MCG/DL)

T3 Uptake 49.7 (28.0-41.0 %)

Free Thyroxine Index 10.7 (1.6-3.7)

EKG: Sinus Tachycardia

Anxiety Disorder Due to Another Medical Condition

Diagnostic Criteria

- A. Panic attacks or anxiety as a predominant feature.
- B. Another medical condition clearly explains anxiety.
- C. Another mental disorder is ruled out.
- D. The disturbance is also present without delirium.
- E. The above symptoms significantly impair social and occupational functioning.

Following aspects should also be considered:

1. The onset, exacerbation, or remission of the medical condition strongly correlates with anxiety symptoms.
2. Known association of a medical disorder with anxiety, eg, hyperthyroidism.
3. All other DSM V anxiety disorders are ruled out.

(Am Psychiatric Association, 2013)

Anxiety Disorder Due to Another Medical Condition

Differential Diagnosis

1. Delirium
2. Mixed presentation of symptoms
3. Substance/medication-induced anxiety disorder
4. Anxiety disorder
5. Illness anxiety disorder
6. Other specified or unspecified anxiety disorder

GAD-2 and GAD-7 Scales

Screening Anxiety

GAD-2 and GAD-7 Scales:

Over the past 2 weeks, how often have you been bothered by the following problems?

(0=Not at all; 1=Several days, 2=more than one half of the days, 3=Nearly everyday)

1. Feeling nervous, anxious, or on the edge
 2. Being unable to stop or control worrying
 3. Worrying too much about different things
 4. Having trouble relaxing
 5. Being so restless that it is hard to sit still
 6. Becoming easily annoyed or irritable
 7. Feeling afraid, as if something awful might happen
- **A Positive GAD-2 (Items 1 and 2) result is a score of at least 3 points**
 - **A positive GAD-7 result is a score of at least 8 points**
 - ◆ **These are screening tools only and NOT Diagnostic tools; confirmatory interview is necessary to diagnose the condition**

(Spitzer et al., 2006)

Psychological Treatment

- Cognitive Behavioral Therapy
 - Cognitive Restructuring
 - Exposure
 - Breathing/relaxation/mindfulness skills

Cognitive Restructuring

- Thoughts/beliefs with anxiety disorders = fear based, worst case scenario
- Change to have thoughts/beliefs based on data & likelihood of events occurring
- Change thoughts -> change emotion

Exposure

- Most potent component of treatment
- Set up practice of facing fear – extinction learning
- More you face fear, more you overcome fear
- Phobias
- Interoceptive exposure
- Social anxiety exposure
- GAD exposure
- Issue of Benzodiazepines

Breathing/relaxation/mindfulness

- Diaphragmatic breathing
- Box breathing
- Progressive muscle relaxation
- Guided visualization
- Thought river
- Thought/emotion labeling

Medical Management (* FDA Approved)

1 st Line Medications	2 nd Line Medications	Norepi-Serotonin Modulator	Others	CAM
SSRI	TCA s	Mirtazapine	Buspirone *	Kava Kava
Sertraline *	Amitriptyline		Pregabalin	Valerian root
Citalopram	Nortriptyline		Hydroxyzine	Passion Flower
Escitalopram *	Imipramine			Acupuncture
Fluoxetine *	Desipramine			Aroma Therapy
Paroxetine *	Benzodiazepines			Meditation
Fluvoxamine *	Alprazolam *			Exercise
SNRI	Diazepam			
Venlafaxine *	Clonazepam *			
Duloxetine	Lorazepam			
	Clorazepate			

Medications: Not FDA Approved

Medications under CAM category are NOT FDA approved and therefore due precautions should be discussed while suggesting their use.

FDA Approved Medications: Anxiety Disorders

Medication	GAD	Panic Disorder	Social Phobia
Sertraline	50-200 mg/day	50-200 mg/day	50-200 mg/day
Escitalopram	10-20 mg/day	10 mg/day	10 mg/day
Fluoxetine	20-80 mg/day	10-60 mg/day	10-80 mg/day
Paroxetine	20-50 mg/day	10-60 mg/day	20-60 mg/day
Fluvoxamine	100-300 mg/day	150 mg/day	100-300 mg/day
Venlafaxine	75-225 mg/day	75-225 mg/day	75 mg/day
Alprazolam	1-4 mg/day	0.5 to 1.5 mg/day	0.5-1.5 mg/day or prn
Clonazepam	0.5-4 mg/day	0.5-1.5 mg/day	0.25-1.5 mg/day or prn
Bupirone	20-30 mg/day	20-30 mg/day	20-30 mg/day
Propranolol	-----	-----	10-40 mg/day

Medications and Potential Adverse Effects

SSRI

GI side effects (nausea, diarrhea, heart burn); Sexual Dysfunction(decreased libido, delayed orgasm); headache; wt gain; insomnia; somnolence; serotonin syndrome

SNRI

Hypertension; Sweating; nausea; constipation; dizziness; sexual dysfunction; weight gain; serotonin syndrome

TCAS

Dry mouth; constipation; blurry vision; orthostatic hypotension; weight gain; somnolence; headache; sweating; sexual dysfunction; urinary retention

BENZODIAZEPINES

Respiratory depression; Sedation; Fatigue; ataxia; slurred speech; memory impairment; weakness;
Risk of dependence or abuse

**NOREPI-
SEROTONIN
MODULATOR
(MIRTAZEPINE)**

Somnolence; increased appetite; weight gain; dry mouth;
Agranulocytosis

Efficacy & Tolerability Comparison

- A systematic review & network meta-analysis comparing randomized trials of adults with GAD in outpatient settings
- Primary outcomes were efficacy (mean difference [MD] in change in Hamilton Anxiety Scale Score) and acceptability (study discontinuations for any cause)
- Summarized mean treatment differences and odds ratios using network meta-analyses with random effects
- Analysis included 89 trials, 25441 patients randomly assigned to 22 different active drugs or placebo

Findings: Duloxetine, pregabalin, venlafaxine and escitalopram were more efficacious than placebo with good acceptability

Slee, A., Nazareth, I., Bondaronek, P., Liu, Y., Cheng, Z., & Freemantle, N. (2019). Pharmacological treatments for generalised anxiety disorder: A systematic review and network meta-analysis. *The Lancet*, 393(10173), 768-777. doi:10.1016/s0140-6736(18)31793-8

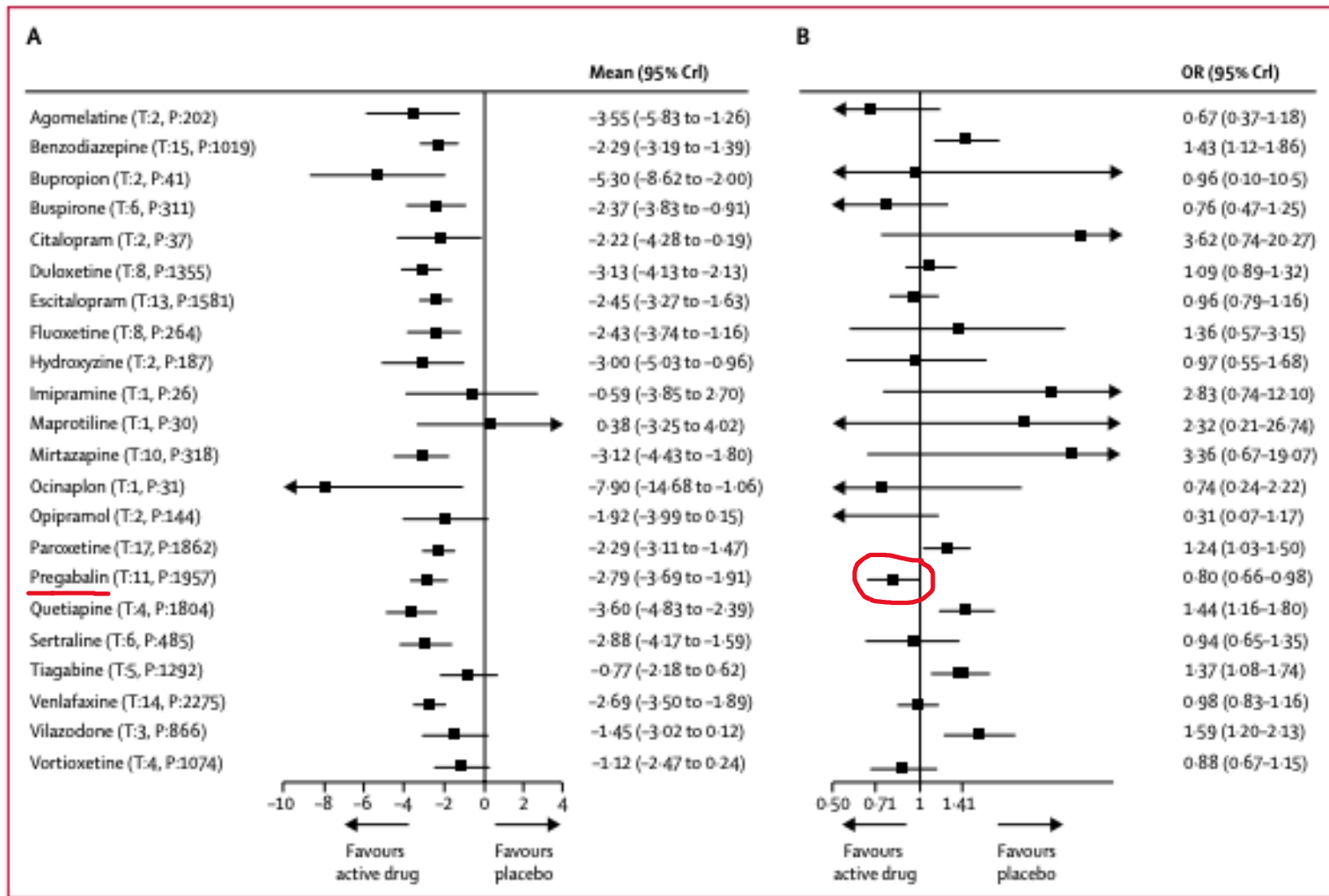
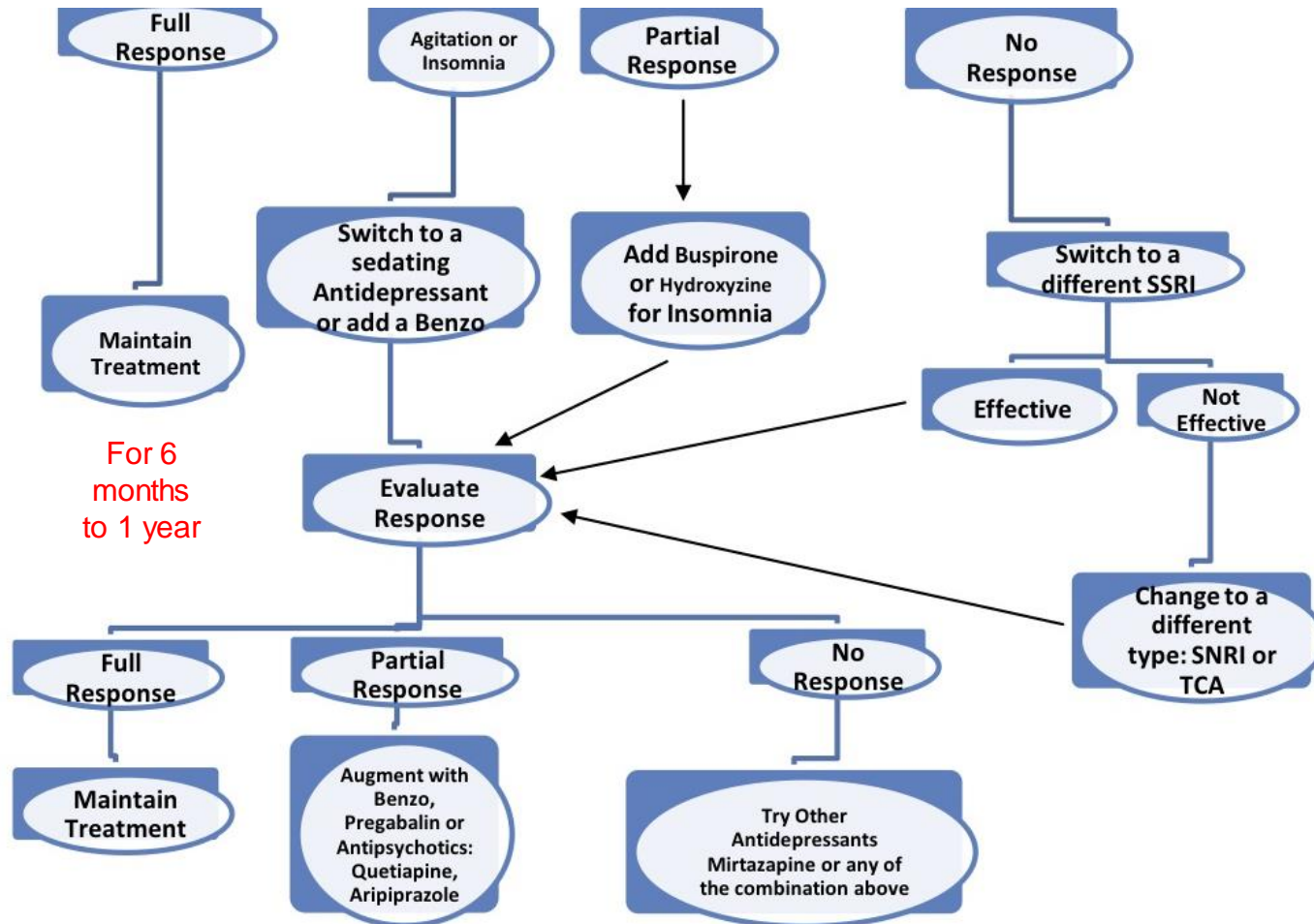


Figure 3: Forest plot of network meta-analysis of all trials for efficacy and acceptability

Efficacy (A) measured as mean difference in change in HAM-A from baseline, and acceptability (B) measured as odds ratio for patients not completing study. Drugs compared with placebo, which was the reference compound. CrI=credible interval. T=number of trials. P=total number of patients. OR=odds ratio.

Management of GAD: Algorithm



Summary and Recommendations: Generalized Anxiety Disorder

- SSRIs and SNRIs are considered first-line treatments for generalized anxiety disorder, with starting dose typically half that used in depression (SOR: A)
- TCAs are effective in treatment of GAD (SOR: A), but their side effect profile and potential lethality have relegated them to second- or third-line agents
- Benzodiazepines offer the advantage of rapid effect and proven efficacy (SOR: A) but carry risk of abuse and dependence.
- Other agents for treatment of GAD include Hydroxyzine (SOR: A), buspirone (SOR:B), and pregabalin (SOR:B)
- Psychotherapy is an important and effective treatment strategy for anxiety disorders. Psychotherapy combined with pharmacotherapy yield superior results to either treatment alone (SOR: A)
- Maintenance treatment of GAD reduces the likelihood of relapse (SOR: B)

(Rothberg, 2011)

Summary and Recommendations: Panic Disorder

- SSRIs, SNRIs, and benzodiazepines have all been found to be effective in the treatment of panic disorder (SOR: A)
- First-line agents for panic disorder are SSRIS and SNRIs, with starting doses typically half that for depression (SOR: A)
- Benzodiazepines can be used as first-line agents when no comorbid issues are present, including issues of substance abuse and dependence (SOR: A)
- Maintenance of treatment of panic disorder has been shown to reduce the likelihood of relapse (SOR: B)

(Rothberg, 2011)

Quiz # 1

A 36-year-old woman comes to your office for evaluation of episodic chest pain associated with dyspnea, tachycardia, diaphoresis that occurs a couple of times each week. The symptoms develop suddenly, and are so severe that she feels that she is going to die, and improve significantly within 20-30 minutes. She denies any precipitating factor and does not know if anything makes the symptoms better or worse.

The patient has been evaluated in the past for EKGs, stress test, echocardiography and 24-hour holter monitor, and upper endoscopy. The patient does not take any medications. Physical examination is within normal limits.

Which of the following is the most effective treatment for this patient?

- A. Cognitive-behavioral therapy
- B. Cognitive-behavioral therapy with Citalopram
- C. Buspirone
- D. Venlafaxine
- E. Citalopram

Quiz # 2

According to DSM V, which of the following symptoms is generally not characteristic of GAD?

- A. Easily fatigued
- B. Impairment in social, occupational, or other important areas of functioning.
- C. Excessive sleep
- D. Irritability
- E. Muscle tension

Quiz # 3

A 26-year-old single woman presents to the emergency department relating that over the past four nights she has been awakened by discrete episodes of a palpitating heart, choking sensations, sweating, trembling. She is worried that another episode may occur at any time.

Which of the following is the most likely diagnosis?

- A. Specific phobia
- B. Panic attack
- C. Generalized anxiety disorder
- D. Hyperthyroidism
- E. Substance-induced anxiety disorder

Quiz # 4

Which of the following pharmacologic agents is not recommended in the treatment of Generalized Anxiety Disorder?

- A. Paroxetine
- B. Venlafaxine
- C. Clozapine
- D. Buspirone
- E. Benzodiazepines

Quiz # 5

An 18-year-old woman is evaluated because of perceived halitosis that she first became aware of at age 12 years, when a friend told her that she had bad breath. The patient subsequently became very self-conscious about her breath. She covers her mouth when talking to anyone, brushes her teeth repeatedly, and constantly chews gums and mints. Because of her concern about her breath she has never had a boyfriend. Medical history is unremarkable. She does not snore, have difficulty breathing, smoke, or drink alcohol. She gets regular dental check ups.

Evaluation of the nose, mouth, and posterior pharynx is normal. There is no noticeable odor when the patient breaths out through the mouth or nose at a distance of 5 to 10 cms from the examiner. Scrapings from the back of the tongue do not have an odor.

Which of the following is the most likely diagnosis?

- A. Gastro esophageal reflux disease
- B. Nasal polyps
- C. Obstructive sleep apnea
- D. Halitophobia
- E. Periodontal disease