Psychiatric Intervention In Chronic Disease Management
Depression & Anxiety

• Depression and Generalized Anxiety Disorder are frequently overlap

• Mixed anxiety and depression disorder (MAD) has been recognized in ICD-10 as a diagnostic group including those anxious and depressed patients which do not fit sufficient criteria for any major axis I disorders

Anxiety Disorders Can Impact Everyday Life

- For many patients, anxiety disorders are a significant cause of disability

A review of current research findings on generalized anxiety disorder and its associated burden, cost, and resulting disability. Significant impairment in work productivity defined as ≥10% reduction. Significant social impairment defined as "marked impairment" based on clinician ratings.

- 88% of the per capita cost of employees with anxiety disorders is due to lost productivity while at work and 12% is due to the cost of missed work

Importance of Proper Diagnosis of Anxiety Disorders

- About 1 in 5 to 1 in 12 patients presenting to primary care will have symptoms of an anxiety disorder.

- Anxiety disorders are often misdiagnosed because the patient presents with somatic complaints:
  - 87% of patients with generalized anxiety disorder show primary symptoms that are not considered “anxiety”.

- In patients with depression, a coexisting anxiety disorder is often missed and therefore not treated.

- The goal of treatment is for the patient to recover the ability to interact normally with his/her environment.

### Association of Mental Disorders with Chronic Physical Conditions

<table>
<thead>
<tr>
<th>Type of physical condition</th>
<th>Non-comorbid depressive disorder</th>
<th>Non-comorbid anxiety disorder</th>
<th>Comorbid depression-anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>1.1 (0.9, 1.2)</td>
<td>1.2 (1.1, 1.4)</td>
<td>1.2 (1.0, 1.4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.3 (1.1, 1.6)</td>
<td>1.3 (1.1, 1.5)</td>
<td>1.4 (1.1, 1.8)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.7 (1.4, 2.0)</td>
<td>1.6 (1.4, 1.8)</td>
<td>1.6 (1.4, 1.9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.5 (1.4, 1.8)</td>
<td>1.7 (1.5, 1.9)</td>
<td>1.8 (1.5, 2.1)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>1.6 (1.4, 1.8)</td>
<td>1.7 (1.5, 1.9)</td>
<td>2.5 (2.2, 2.9)</td>
</tr>
<tr>
<td>Ulcer</td>
<td>1.8 (1.6, 2.2)</td>
<td>1.9 (1.7, 2.3)</td>
<td>2.7 (2.3, 3.2)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>2.0 (1.7, 2.3)</td>
<td>1.9 (1.6, 2.3)</td>
<td>2.8 (2.3, 3.4)</td>
</tr>
<tr>
<td>Back/neck problems</td>
<td>2.2 (1.9, 2.4)</td>
<td>2.0 (1.8, 2.3)</td>
<td>2.9 (2.5, 3.3)</td>
</tr>
<tr>
<td>Chronic headache</td>
<td>2.5 (2.2, 2.8)</td>
<td>2.3 (2.1, 2.5)</td>
<td>4.0 (3.5, 4.7)</td>
</tr>
<tr>
<td>Multiple pains</td>
<td>2.5 (2.2, 2.9)</td>
<td>2.3 (2.1, 2.6)</td>
<td>4.5 (4.0, 5.1)</td>
</tr>
</tbody>
</table>

1. Both anxiety and depressive disorders are independently associated with chronic physical conditions.

2. Having both depression and anxiety further increases the risk of a number of physical conditions co-occurring.

* p<0.05

The Association of Depression & Anxiety with Medical Symptom Burden in Patients with Chronic Medical Illness

Examine the association of comorbid depression or anxiety with medical symptom burden in patients with arthritis, DM, heart disease and pulmonary disease.

Bidirectional effects depression/anxiety vs severity of medical illness

- Higher numbers of medical symptoms when controlling for severity of disease
- Increased medical complications
- Heightened awareness of physical symptoms
- Provoke or worsen episodes of anxiety and/or depression
- Higher medical costs
- Repeated medication changes and polypharmacy

W. Katon et al. / General Hospital Psychiatry 29 (2007) 147–155
Risk Factors

• Family history of anxiety (or other mental disorder)
• Personal history of anxiety in childhood or adolescence, including marked shyness
• Stressful life event and (or) traumatic event, including abuse
• Being female
• Comorbid psychiatric disorder (particularly depression)
When does anxiety become a disorder?

- Greater intensity and (or) duration than usually expected
- Leads to impairment or disability in occupational, social, or interpersonal functioning
- Daily activities are disrupted by the avoidance of certain situations or objects in an attempt to diminish the anxiety
- Includes clinically significant, unexplained physical symptoms and (or) obsessions, compulsions, and intrusive recollections or memories of trauma
Implication of Comorbidity

- Epidemiologic surveys have shown that comorbidity has a negative impact on:
  - Elevated rates of suicide
  - Greater severity of primary disorder
  - Greater impairment in social and occupational functioning
  - Poor response to treatment
  - Unexplained somatic symptoms
  - High use of nonpsychiatric medical care
  - Long-lasting symptoms
  - At risk for more severe psychiatric disorders

Anxiety disorders included panic disorder, agoraphobia without panic disorder, social phobia, simple phobia, and GAD.


Comorbidity
Majority with AD develop lifetime MDD; >50% with MDD develop lifetime AD

Major Depression
17% lifetime prevalence

Anxiety Disorders*
25% lifetime prevalence

*Anxiety disorders included panic disorder, agoraphobia without panic disorder, social phobia, simple phobia, and GAD.
Comorbidities Between Depression and Anxiety

Major Depression

- PTSD: 50%
- Panic Disorders: 30–60%
- SAD: 70%
- GAD: 62.4%
- OCD: 19–90%

Symptoms of Anxiety and Depression is Overlapping

Social Anxiety Disorder
- Fear/avoidance of social situations
- Blushing
- Trembling/shaking
- Stuttering

Generalized Anxiety Disorder
- Palpitations
- Sweating
- Worry
- Anxiety
- Muscle tension
- Dry mouth

Depressive Disorder
- Low self-esteem
- Anhedonia
- Depressed mood
- Suicidal ideation
- Worthlessness
- Appetite disturbance

Difficulties concentrating
GI complaints
Interpersonal sensitivity
Agitation
Irritability
Sleep disturbance
Fatigue
Pain
Worry
Anxiety
Muscle tension
Dry mouth

Psychopathology: Nature and Nurture

Genetic factors

Vulnerability and resistance genes

Vulnerability/Phenotypic plasticity

Developmental trajectory

Enriched environment

Social support

Psychiatric intervention

Psycho-immune disease

Trauma

HPA axis dysfunction

Anxiety Symptoms

Depression

90% Patients with Anxiety Disorders Co-morbid with Depression Symptoms or MDD

Anxiety Disorders
- Worry
- Muscle Tension
- Palpitations
- Sweating
- Dry Mouth
- Nausea

MDD
- Depressed Mood
- Anhedonia
- Appetite Disturbance
- Worthlessness
- Suicidal Ideation

Sleep Disturbance
- Psychomotor Agitation
- Concentration Difficulty
- Irritability
- Fatigue

90%

Depression and Anxiety Comorbidity: 4 Common Clinical Presentations

A. Anxiety Disorder With Depressive Symptoms

- Social phobia
- Panic disorder
- Generalized anxiety disorder
- Posttraumatic stress disorder
- Obsessive-compulsive disorder

B. Major Depressive Disorder With Anxiety Symptoms

- Major Depression
- Anxiety

C. Coexisting Anxiety Disorder and Major Depressive Disorder

- Social phobia
- Panic disorder
- Generalized anxiety disorder
- Posttraumatic stress disorder
- Obsessive-compulsive disorder

D. Anxiety Symptoms and Depressive Symptoms (subsyndromic)

- Depressive Symptoms
- Anxiety Symptoms

*Note: Obsessive-compulsive disorder and Posttraumatic stress disorder are no longer included as anxiety disorder in DSM-V
How Depression and Anxiety May Be Mismanaged
Treating the Symptoms, Not the Syndrome

- 66% patients with somatic complaints remain undiagnosed for anxiety and depression and it lead them to visit their doctors >6 times/year

- Multiple agents used to treat symptoms, not syndrome, unnecessary consultations and hospitalizations

- Overuse of anxiolytics/hypnotics/ analgesics/ narcotics

Consequences of Depression/Anxiety Co-morbidity

- More severe/chronic anxiety
- Greater social impairment
- Higher rates of alcohol/drug abuse
- Increased risk of suicide
- Poorer response to acute & long-term treatment

Lydiard RB, Brawman-Mintzer O (1998), J Clin Psychiatry 59(suppl 18):10-17
Anxiety, Depression and Stress: Brain and Body Affected
Somatic Presentation of Anxiety Disorders

1,000 Patients at 4 Primary Care Clinics

Prevalence of Anxiety Disorders in those with symptoms (%)

- Chest Pain: 33%
- Fatigue: 26%
- Headache: 28%
- Insomnia: 35%
- Abdominal pain: 31%

Kronke K et al. (1994), Arch Fam Med 3(9): 774-779; Weisberg R et al. (2004). Presented at the 24th Annual Meeting of Anxiety Disorders Association of America, Miami; March 11-14
Somatic Presentation of Anxiety Disorders (Cont.)

Primary Care Anxiety Project

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restlessness</td>
<td>91</td>
</tr>
<tr>
<td>Irritability</td>
<td>83</td>
</tr>
<tr>
<td>Difficulty Concentrating</td>
<td>82</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>81</td>
</tr>
<tr>
<td>Muscle Tension</td>
<td>74</td>
</tr>
<tr>
<td>Easily Fatigued</td>
<td>71</td>
</tr>
</tbody>
</table>

Kronke K et al. (1994), Arch Fam Med 3(9): 774-779; Weisberg R et al. (2004). Presented at the 24th Annual Meeting of Anxiety Disorders Association of America, Miami; March 11-14
Symptoms

• Anxiety symptoms are common in patients with Major Depression Disorder:
  – Worry (72%)
  – Psychic Anxiety (62%)
  – Somatic Anxiety (42%)
  – Panic Attacks (29%)

Aina & Susman, JAOA 2006;106(suppl 2)(5):S9-S14
Suicide Risk in Patient with Depression and Anxiety Co-morbidity

- 70% suicides revolves around depression illness
- Anxiety disorder pose a significant risk of suicide
- Risk of suicide is increase in patient with comorbidityity
  - Panic disorder risk of suicide 7%
  - Comorbid panic disorder with depression 23.6%
  - MDD risk of suicide 7.9%
  - MDD with comorbidity risk of suicide 19.8%

Aina & Susman, JAOA 2006;106(suppl 2)(5):S9-S14
Treatment of Co morbidities Depression and Anxiety

• There are a number of general principles of treatment of depression and anxiety disorder co morbidity
• Cognitive-behavioral therapy (CBT) is one option with well-documented efficacy for both depression and anxiety disorders
• Antidepressants are now first-line treatments for anxiety disorders, with or without co morbid depression
• Antidepressants such as SSRIs (Sertraline, escitalopram/citalopram, paroxetine) and SNRIs (venlafaxine) are first-line treatment for GAD, which commonly presents co morbid with depression
• Benzodiazepines are useful for the acute treatment of anxiety symptoms

Naomi M. Simon, MD; Jerrold F. Rosenbaum, MD Psychiatry & Mental Health 8(1), 2003

Therapy

- Increase Quality of Life
- Decrease/Cease Symptoms
- Recover Function Peran dan Fungsi
- Decrease Suicidal Risk
- Decrease Relaps / Recurrence
- Decrease risk of Disability/ Mortality

Modifikasi dari:
Pharmacotherapy
Benzodiazepines

- Benzodiazepines, which include diazepam, lorazepam, and alprazolam, have been popular for the treatment of anxiety since they were introduced in the mid-1960s.
- Benzodiazepines tend to have a rapid effect and are well tolerated when used appropriately for short-term anxiolytic therapy.
- Long-term use can lead to physical dependence.

Benzodiazepines - two groups:
- Predominantly *hypnotic or sedative* - treatment of insomnia
- Predominantly *anxiolytic* - treat anxiety disorders.
Benzodiazepines

• By binding to the GABA-benzodiazepine receptor, benzodiazepines dramatically increase the actions of GABA.

• This in turn stimulates the chloride ion channel to open, allowing entry of more chloride ions, which sends an inhibitory signal to slow the firing of that neuron. Therefore, neuron firing is decreased, which is thought to be related to a calming or anxiolytic effect.
BENZODIAZEPINE

- Potential anti anxiety
- Quick onset of action
- Long term treatment
- > 4 months treatment → withdrawal (40%-80%)
- 2 - 4 weeks treatment + Antidepressant
- Withdrawal → COGNITIVE BEHAVIORAL THERAPY
- Alprazolam, Clonazepam, Lorazepam, Diazepam
Selective Serotonin Reuptake Inhibitors (SSRI)

- The SSRIs are selective in that they affect only serotonin reuptake to achieve their therapeutic effects.

- Most SSRIs are indicated for the treatment of depression, with some showing effectiveness for both depression and anxiety and in “pure” anxiety disorders.

- SSRIs achieve significant therapeutic responses in most patients, but they may not always produce remission of symptoms.

- Common side effects include nausea, headache, dizziness, nervousness, insomnia, daytime drowsiness, diarrhea, and sexual dysfunction.
Selective Serotonin Reuptake Inhibitors (SSRI)

- **Increase Serotonin**
- **Decrease Cortisol (Long term)**
- **Serotonin → Amigdala projection (Anxiety ↓↓↓)**
- **Sertraline, Fluoxetine, Paroxetine**
- **Combine with Benzodiazepine**
Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

• In normal situations, serotonin and norepinephrine are continually taken up by reuptake pumps on the presynaptic neuron. The neurotransmitter is then destroyed by monoamine oxidase or recycled into storage vesicles. This reuptake process is thought to lead to inadequate amounts of neurotransmitters in the synapse.

• SNRI are drugs that block the reuptake of these neurotransmitters into the presynaptic neurons. The net effect is an increased amount of neurotransmitters available for impulse conduction.

• The neurotransmitter availability is thought to lead to its antidepressant and anxiolytic activity.
Psychotherapy & Other Therapy

- **Cognitive Behavioral Therapy**
  
  Cognitive-behavioral therapy helps patients separate realistic thoughts from unrealistic, anxiety-provoking thoughts. Patients are also trained to use simple techniques, such as deep breathing and muscle relaxation, to calm themselves in anxious moments. Behavioral therapy helps people change specific behaviors by using techniques such as systemic desensitization (i.e., gradually exposing the patient to a feared object or situation, until the patient becomes desensitized).
Psychotherapy & Other Therapy

• **Supportive Therapy**
  Regular contact with a sympathetic clinician, repeated reassurance about the nature of anxiety, and guidance in confronting and alleviating stressful situations can lead to a significant reduction in the patient’s anxiety level

• **Relaxation**

• **Psychoeducation**
Special Considerations Concerning Pharmacotherapy in Women

- Anxiety disorders generally have been found to occur more often in women (16%) than in men (9%)
- It is important to review the special issues surrounding the use of pharmacotherapy during pregnancy and breastfeeding
- When pharmacotherapy is indicated for a pregnant or breastfeeding woman, the potential risks of medication exposure in the fetus and infant must be weighed against the risks inherent in untreated maternal illness
### Medications to avoid during pregnancy

<table>
<thead>
<tr>
<th>Phase of pregnancy</th>
<th>Medication to avoid</th>
</tr>
</thead>
</table>
| First trimester                            | • Carbamazepine  
• Divalproex  
• Lithium  
• Conventional antipsychotics  
• Paroxetine  
• Benzodiazepines can be used with caution |
| Third trimester and labour-delivery        | High dose benzodiazepines should be used with caution                                |
| All trimesters                              | MAOIs                                                                               |
Summary

• High degree of overlap among anxiety and depressive symptoms in SAD, GAD, and MDD
• These disorders frequently occur in a comorbid fashion
• Associated with considerable impairment
• Effective treatment early in the disease may improve the long-term clinical course