Treatment of Anxiety Disorders: Psychotherapy and Pharmacological Treatment

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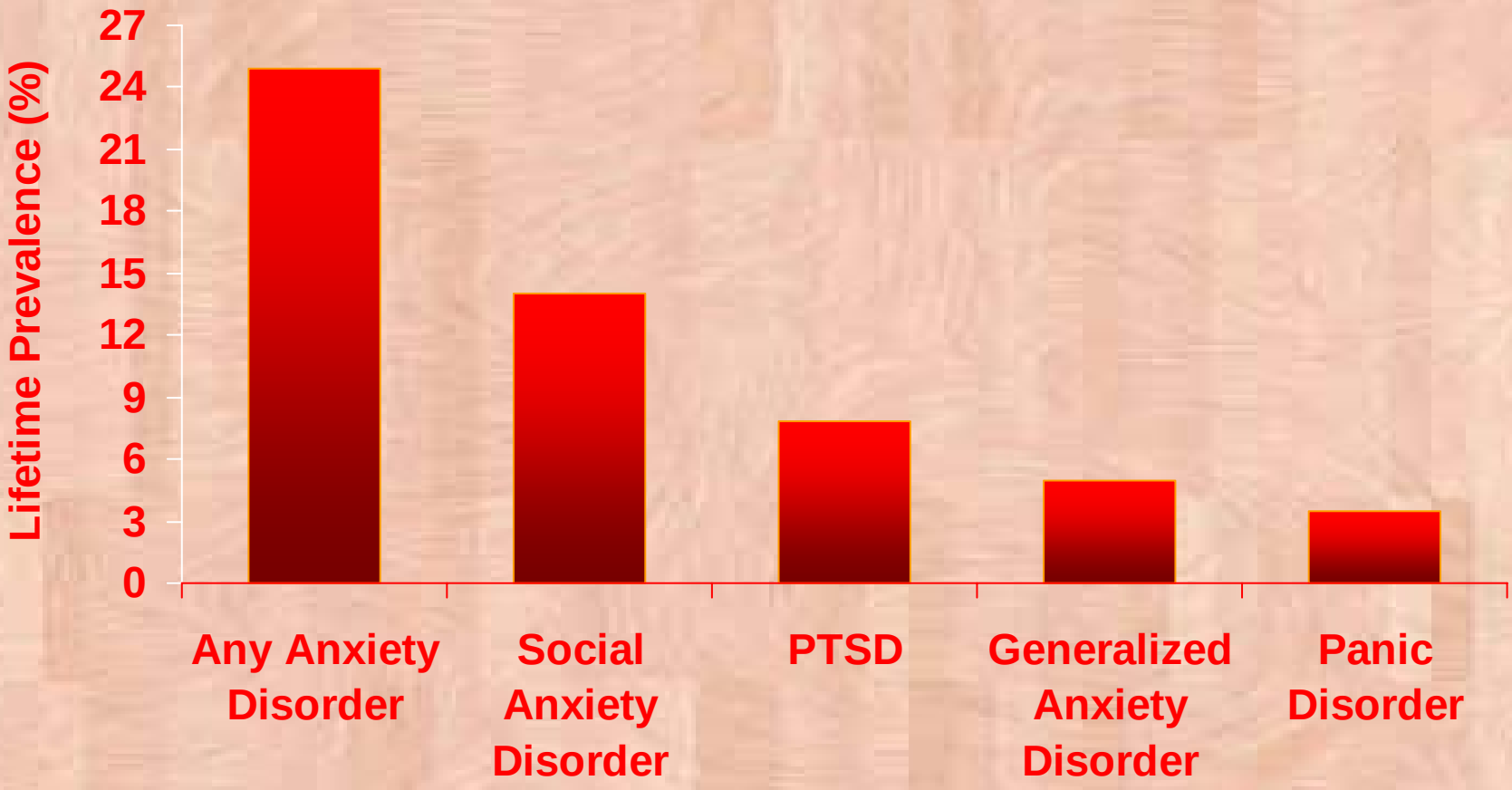
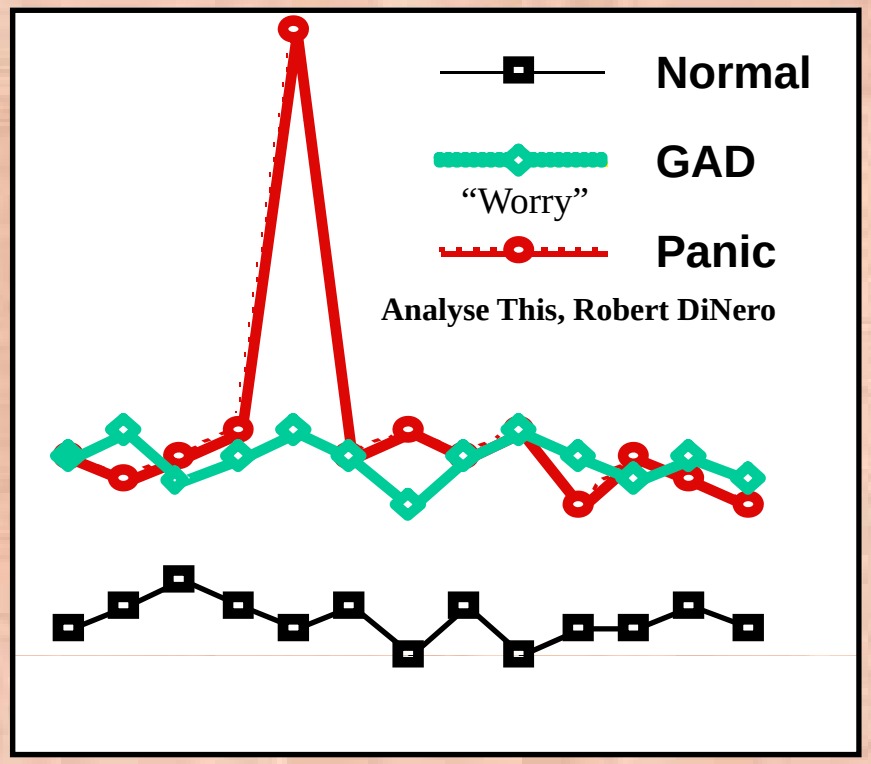
Prevalence of Anxiety Disorders



Kessler et al. *Arch Gen Psychiatry*. 1995;52:1048.
Kessler et al. *Arch Gen Psychiatry*. 1994;51:8.

Course of Illness

anxiety level



time

Phobic Disorders

- Disabling **anxiety** (at times associated with panic attacks) and **avoidance**
  - Agoraphobia (with or without panic attacks)
  - Social phobia (Social Anxiety Disorder)
  - Specific phobia

Obsessive-Compulsive Disorder (OCD)

Jack Nicholson - 'As Good As It Gets'

- Recurrent obsessions and/or compulsions:
  - Cause marked distress, are time-consuming, or interfere with functioning
  - Are recognized as excessive or unreasonable
  - Are not due to the effect of a substance or general medical condition

Posttraumatic Stress Disorder (PTSD)

E.g.: Vietnam veterans; Holocaust survivors; Rape victims

- Due to an unusual experience that would be very stressful for almost anyone Symptoms include:
  - Intrusive **recollections**; frightening **dreams**; sense of event **recurring**
  - Intensive physiological stress; **hyperarousal**
  - Persistent **avoidance** of stimuli associated with the trauma
- High **comorbidity** with other psychiatric disorders
- Increase **suicide attempt** risk
- **Female-to-male** lifetime prevalence ratio of 2:1

Sleep Disorders

- **Dyssomnias** (difficulty initiating or maintaining sleep or not feeling rested)
  - ***Primary Insomnia***
  - Primary Hypersomnia
  - Circadian Rhythm Disorder
- **Parasomnias** (abnormal event)
  - Nightmare Disorder
  - Sleep Terror Disorder
  - Sleepwalking Disorder

Education/Psychotherapy

- Education
- Behavior therapy
- Cognitive therapy
- Psychoanalysis/psychoanalitically oriented therapies
- Meditation/Relaxation/Hypnosis/Self hypnosis
- Biofeedback
- Exercise/rest

Common Misconceptions about Psychotherapy

- Substitute for pharmacological treatment
- Too time consuming (cost/benefit)
- Patients became hostile
- Requires long term training
- No community resources

Education: Objectives

- Reduce/diminish initial anxiety
- Enhance physician-patient collaboration and adherence to treatment plan
- Enhance self esteem

Behavior Therapy

- Change specific behavior (e.g. avoidance)
- Short-term approach
- Specific techniques, e.g.:
  - In vivo exposure
    - Systematic desensitization
    - Flooding

Cognitive Therapy

- **Distorted patterns of thinking**
- **Structured, specific approaches**

Psychotherapy/Counseling

- Communicate directly and honestly
- Encourage the patient to talk
- Listen actively, express empathy
- Be available

Psychotherapy/Counseling: Objectives

- Relieve symptoms
- Correct situational problems
- Restore coping/defenses
- Expand personal skills/abilities
- Prevent emotional breakdown

Meditation/Relaxation/Hypnosis

- **Patient sits quietly in a restful environment (15-20 min bid)**
- **Concentration on breathing**
- **Progressive muscle relaxation: patient alternate tensing and relaxing specific muscle groups (15-20 min bid)**
- **Hypnosis/Self hypnosis**

Biofeedback

- Use of auditory and visual signals from biological measures
- Patient learns to monitor and modulate biological responses

Exercise/Rest Prescription

- Moderate exercise enhances a sense of well-being and promotes overall fitness (but: exercise can precipitate panic attacks)
- Proper rest

Social Interventions

- **Working with the family and social system**
  - **Sharpens the diagnosis**
  - **Speeds treatment**
  - **Improves compliance**

Pharmacological Treatment of Anxiety Disorders

- When to prescribe?
- What to prescribe?
- For how long to prescribe?

When to Prescribe for an Anxiety Disorder?

- Symptom complex is severe and persistent
- Impairment of psychosocial quality of life
- To prevent the potential complications
- Potential benefit outweigh potential risks

What to prescribe?

- Benzodiazepines
- 5 HT_{1A} ligands:
  - buspiron
- Antidepressants
  - SSRI-s
    - citalopram
    - escitalopram
    - fluoxetin
    - fluvoxamine
    - paroxetin
    - sertralin
  - MAO-I (Mono Amino Oxidase Inhibitors
  - RIMA (Reversible Inhibitor of MAO-A)
    - moclobemid
  - Dual action AD-s
    - venlafaxine
    - duloxetine
  - Tri- and tetracyclic (old) agents
    - e.g. imipramin, maprotilin

Dose of medication and length of treatment is different for different anxiety disorders

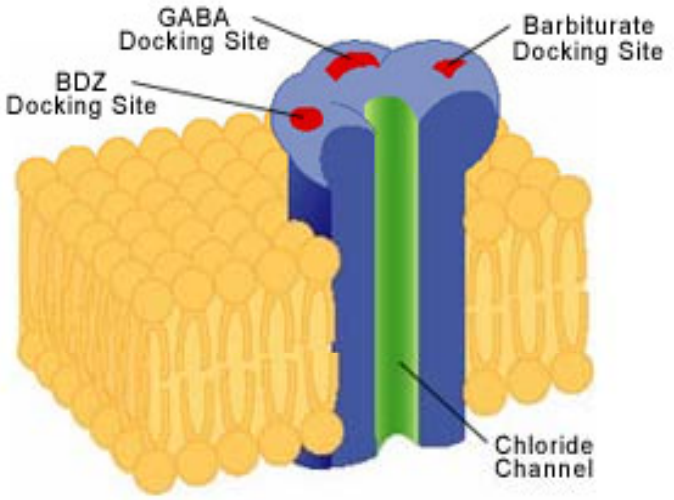
- Eg. Generalized anxiety disorder vs. Obsessive-compulsive disorder or panic disorder

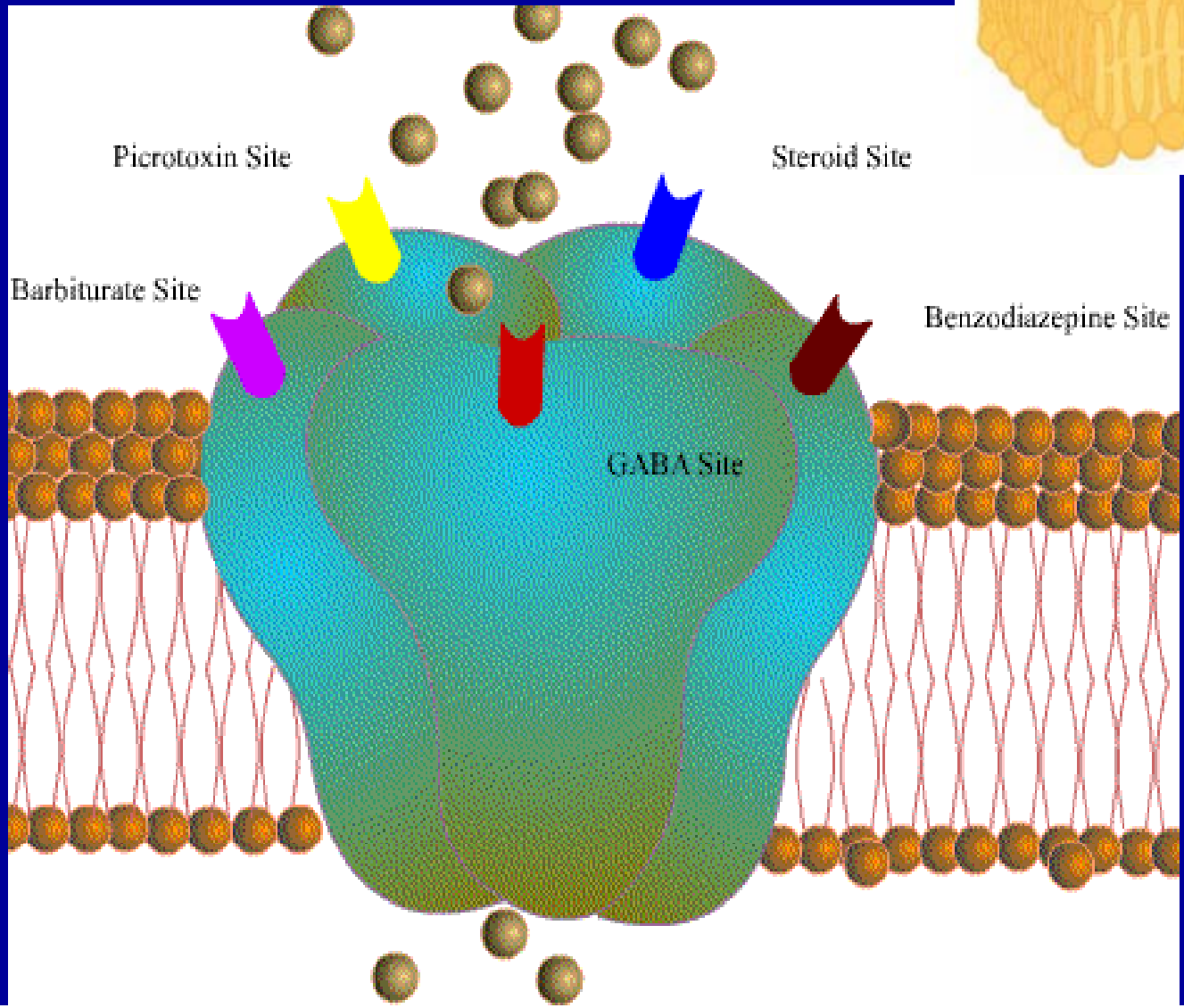
MECHANISM OF ACTION OF **BENZODIAZEPINES**

KEY CONCEPT: Benzodiazepines enhance the actions of the inhibitory neurotransmitter GABA

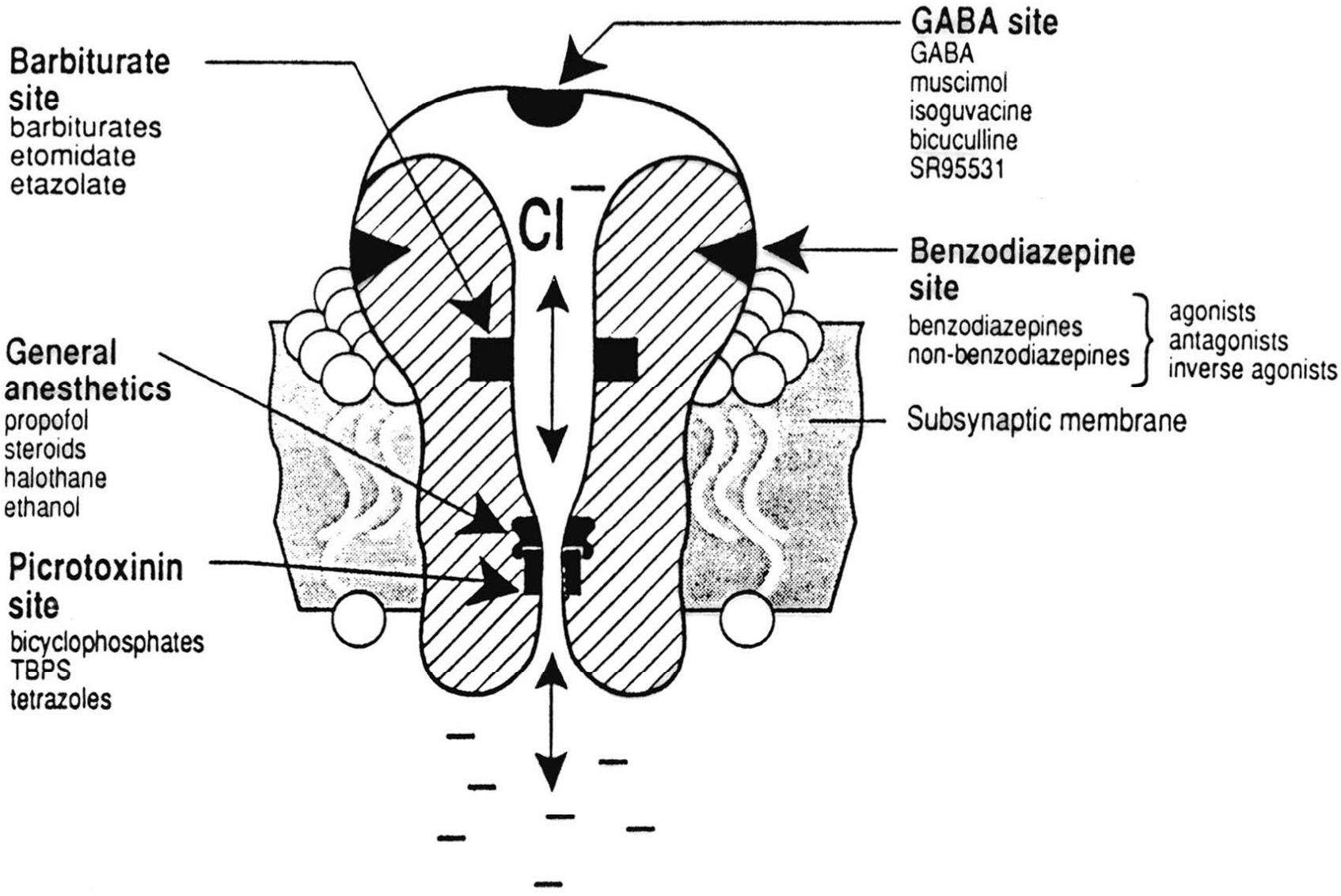
- BZD's facilitate the opening (frequency) of the Cl- ion channel in response to GABA; enhance neuronal hyperpolarization.

GABA A Receptor

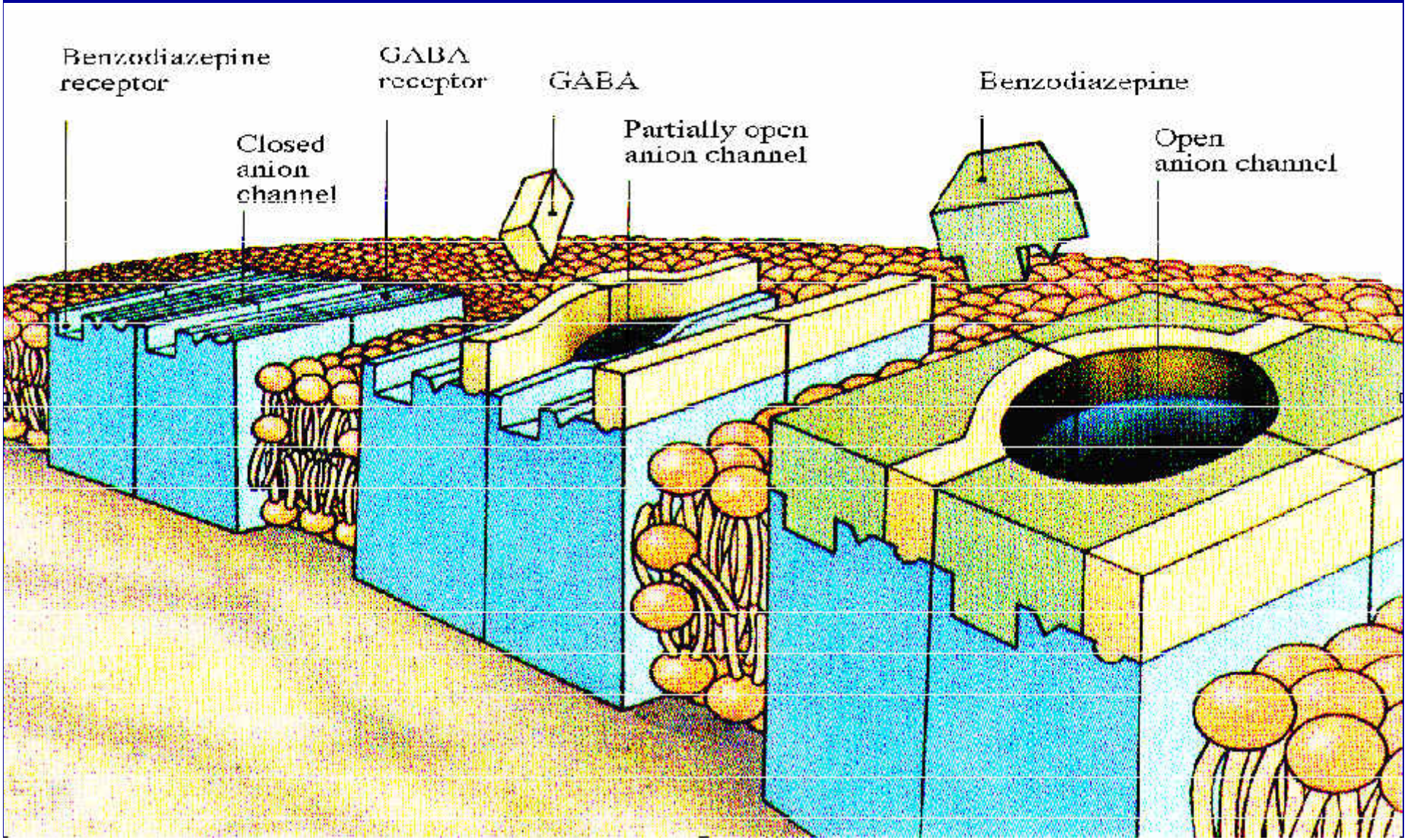




$GABA_A$ receptor



$GABA_A$-BZD Supramolecular Complex



Benzodiazepines (BZD)

- **BZD have the following (5) effects:**
  - **anxiolytic**
  - **amnestic**
  - **sedative**
  - **muscle relaxant**
  - **antiepileptic**
- **Tolerance to four effects, but clinically the tolerance is insignificant to the specific anxiolytic effect**
- **BZD bind to the BZD (omega) receptors, increase the frequency of the opening of the chloride ion channel**

BZD cont'd

- **<u>High potency</u> BZD: alprazolam, clonazepam, lorazepam (antipanic)**
- **<u>Low potency</u> BZD: e.g. diazepam, nitrazepam, temazepam**
- **Broad indication**
- **Side effects: sleepiness, dizziness, abuse potential (low as compared to barbiturates, meprobamat and alcohol)**

Abuse, Dependence, Withdrawal, and Rebound Anxiety: Benzodiazepines

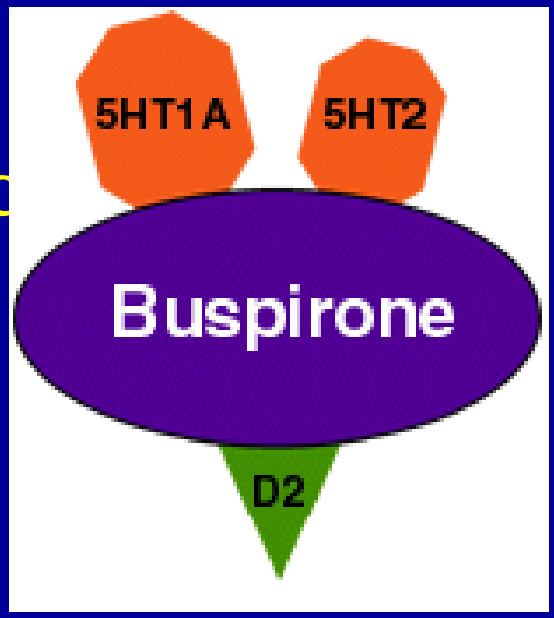
- **Abuse potential** decreased when properly prescribed and supervised.
- **Dependence** may occur at usual doses taken beyond several weeks. (REMEMBER: TOLERANCE is the main criterion!)
- **Withdrawal** may occur even when discontinuation is not abrupt (e.g., by 10-15% per week). **Symptoms** include: tachycardia, increased blood pressure, muscle cramps, anxiety, insomnia, panic attacks, impairment of memory and concentration, perceptual disturbances, derealization, hallucinations, hyperpyrexia, seizures. May continue for months.
- **Rebound anxiety**: return of target („baseline") symptoms, with increased intensity
- **Differenciate from**: **Recurrence** of symptoms (due to lack of effective treatment).

Abusers

- **Anxiolytics/sedative-hypnotic drugs are abused by two groups of people…**
  - **Individuals who overuse these drugs to reduce daily tensions and to aid in sleep**
    - These people take excessively large doses on a regular basis
  - **Street drug users**
    - Attempt to achieve a state of “relaxed euphoria” or to aid in “coming down” from a high caused by taking a stimulant

5 HT_{1A} ligands: buspiron

- **Indication: generalized anxiety disorder (only! No efficacy in panic disorder, phobia, OCD, PTSD)**
- **Late onset of action**
- **Gastrointestinal side effec**



Antidepressants

- **Different drugs used in different disorders, e.g.**
  - **OCD**
  - **Panic disorder**
  - **Phobic disorders**
  - **PTSD**

Combined Treatment - Treatment Oriented Diagnosis

PHARMACOTHEARPY

- **Diagnosis includes patient in a category.**
- **Objective of the treatment is to eliminate the causes of the syndrome (“corrects”, “restores”**

PSYCHOTHERAPY

- **Diagnosis is problem oriented.**
- **Compares recent status of the patient to the goal.**
- **Problems change over time.**
- **Objective of the treatment is to improve the health and “effectiveness” of the patient.**

Combined Treatment - Treatment Oriented Diagnosis (2)

PHARMACOTHERAPY

- **Outcome is the "product" of diagnosis and treatment (universal criteria)**

PSYCHOTHERAPY

- **Criteria for the outcome are different for each patient. The selected criteria determine the objectives and methods of treatment.**

Combination of Drugs

- **BZD + Antidepressants**
  - **late onset of action of AD**
  - **AD may worsen anxiety incl. panic in the first days/weeks of treatment**
  - **AD - warning in many countries: suicidality**
  - **BZD may alleviate the side effects of AD (GI)**
  - **BZD may be indicated as sleeping pills**

  (newer: zopiclon, zolpidem- Non BZD structures)

Drugs NOT Indicated in Anxiety Disorders

- Meprobamat
- Barbiturates
- Neuroleptics/Antipsychotics
- Antihistamins
- Antiepileptics/mood stabilizers

For How Long to Prescribe?

- As short as possible - BUT anxiety disorders may have a chronic, fluctuating course with poor outcome without treatment
- Discontinuation: Low tapering!
- Important to differentiate between:
  - Withdrawal
  - Rebound
  - Relapse