Learning Objectives

• Describe changes to categories and criteria for eating disorders in DSM-5

• Implement evidence-based treatment in the management of patients with eating disorders
Pretest Question 1

Which of the following is the most prevalent eating disorder?

1. Anorexia nervosa
2. Binge eating disorder
3. Bulimia nervosa
Pretest Question 2

Which of the following is the only medication that has FDA approval for the treatment of bulimia nervosa?

1. Citalopram
2. Fluoxetine
3. Lisdexamfetamine
4. Sertraline
Eating Disorders

- Complex systemic diseases
- Comorbid with many psychiatric and somatic disorders
- Tendency for chronicity
- Significant medical and psychiatric consequences
- High socioeconomic impact
Eating Disorders: Lifetime Prevalence

Prevalence (%)

- Anorexia nervosa
- Bulimia nervosa
- Binge eating disorder

Why Are Diagnostic Criteria Important?

They define

• What is normal and what is not
• What requires treatment
• Who pays for treatment
• Who may be eligible for disability benefits
• Who can be awarded damages in case of litigation
Changes From DSM-IV-TR to DSM-5

• Chapter called "Feeding and Eating Disorders"

• Major change: official recognition of binge eating disorder

• "Feeding disorder of infancy and early childhood" renamed "avoidant/restrictive food disorder"
Goal of Revisions

Currently 60% of Dx in some centers

Eating disorder NOS

Anorexia nervosa

Bulimia nervosa

Binge eating disorder

DSM-IV-TR to DSM-5

• Criteria for anorexia nervosa broadened

• Reduced the frequency of diagnostic criteria for bulimia nervosa
DSM-5 Diagnostic Categories

• Anorexia nervosa (AN)
• Bulimia nervosa (BN)
• Binge eating disorder (BED)
• Avoidant/restrictive food intake disorder
• Other specified feeding or eating disorders
Anorexia Nervosa

• Characterized by self-induced starvation and excessive weight loss

• Third most common illness in adolescents
Anorexia Nervosa

- Restriction of energy intake relative to requirements
- Intense fear of gaining weight or becoming overweight, even though underweight
- Disturbance in how one's body weight or shape is experienced
Anorexia Nervosa

- Core diagnostic criteria unchanged
- Exception: requirement for amenorrhea eliminated
- Criterion A wording for low body weight changed
- Criterion B expanded to include persistent behavior that interferes with weight gain
Anorexia Nervosa

• Removed: "refusal to maintain body weight at or above a minimally normal weight for age and height"

• Misperception: people with AN choose to keep their weight in a certain range
Anorexia Nervosa

• Remains: "intense fear of gaining weight or becoming fat"

• Added: "persistent behaviors that prevent weight gain, even though at a significantly low weight"
Anorexia Nervosa

- Division of anorexia into 2 subtypes, restricting and binge eating/purging, remains
- Distinction between anorexia nervosa and bulimia nervosa
Bulimia Nervosa

• Reduction in minimum required average frequency of both binge eating and inappropriate compensatory behavior → from twice to once weekly

• Scheme distinguishing purging and non-purging types eliminated
Former EDNOS

- "Other specified feeding or eating disorders"
- Purging disorder
- Night eating syndrome
Addition of Binge Eating Disorder

• Has been around for decades
• Formally recognized in 1994
• Part of eating disorder NOS in DSM-IV-TR
• Often underdiagnosed and undertreated
• Impact on quality of life
• Lifetime prevalence is 1.9–3%
• More prevalent than AN or BN
• Fewer than 40% of affected individuals receive treatment
• If untreated, poses significant public health challenge
BED

- Recurrent binge eating episodes
- Occur during discrete periods of time
- Consumption of more food than is typical for most people
- Associated with feelings of impaired control over eating
• Episodes must occur at least once a week for a minimum of 3 months

• Feeling of loss of control during eating episodes
• Diagnostic crossover between BED, BN, and AN occurs in a small percentage of individuals

• Distinguishing characteristic of patients with BED: lack of recurrent inappropriate compensatory behavior
Comorbidities Associated With BED

• Hypertension, diabetes mellitus type 2, dyslipidemia

• Disturbed sleep

• Obesity

• Obesity NOT a defining characteristic of patients with BED
BED and Psychiatric Comorbidities

Risk Factors Associated With BED

- Strong genetic component
- Childhood obesity
- Parent with a mood disorder or substance use disorder
- Exposure to traumatic life events or life stressors
Obesity

Not included in DSM-5 as a mental disorder
Neurotransmitters and Food Intake

• Dopamine (DA), serotonin (5HT), and noradrenaline in hypothalamic and striatal regions regulate food intake
  – Affect hunger and satiety
  – Mediate reward and motivation of feeding
Dysregulation of Brain Reward Systems

- Alterations in dopamine, acetylcholine (ACh), and opioid systems in reward-related areas observed in patients with eating disorders
Neurotransmitters and AN

• Reduced dopaminergic, serotonergic, and noradrenergic neurotransmission in hypothalamic and striatal regions

• Changes in dopamine D2 receptors and 5HT2C/2A receptors; compensatory changes
AN and Animal Models

- Restricted access to food enhances the reinforcing effects of DA when animal eats.

- Alterations in mesolimbic DA and 5HT occur as a result of restricted eating.
Neurotransmitters and BN and BED

- Monoaminergic neurotransmission is downregulated in hypothalamic and striatal regions
- Overactive alpha-2 adrenoreceptors may contribute to an attenuated response to food
- More support for the treatment of BN and BED with monoaminergic drugs
Animal Models for BE

- Bingeing on palatable foods releases DA
- Purging attenuates the release of ACh that might signal satiety
Neurobiology of Binge Eating

• Alterations within endogenous opioid system

• Disparities in dopamine receptor and dopamine receptor transportation gene expression

• Alterations within dopaminergic reward pathway
Treatment of Eating Disorders

• Multidimensional
• Psychotherapy
• Nutritional rehabilitation
• Medication treatment
AN Treatment

- Effect of all antidepressants has generally been disappointing

- Meta-analysis of 8 studies of antipsychotics for the treatment of anorexia nervosa failed to demonstrate efficacy for body weight and related outcomes in females

Role of Oxytocin in AN

• Animal data suggest that oxytocin is a satiety hormone

• Higher oxytocin levels were associated with the severity of disordered eating psychopathology in AN

• Treatment implications?
BN Treatment

Reduce the frequency of bingeing and purging in both depressed and non-depressed persons with bulimia

Fluoxetine in the Treatment of BN

- One and only treatment for any eating disorder authorized by regulatory authorities
- 8-week, double-blind trial comparing 20 and 60 mg/day with placebo in 387 women
- Fluoxetine 60 mg/day superior to placebo
- Insomnia, nausea, asthenia, and tremor more common with fluoxetine

Arch Gen Psychiatry 49(2):139-47.
BN Treatment Topiramate

- Multiple behavioral dimensions improved
- Binge and purge behavior reduced
- Improvement in self-esteem, eating attitude, anxiety, and self-image
- Side effects limit usefulness
Topiramate

- First double-blind study: 2003
- 64 patients: 31 topiramate, 33 placebo
- Dose
- Primary efficacy measure: Eating Disorder Inventory (EDI)
- Significantly greater improvement in topiramate group

GOAL

• Reduce binge eating behavior

• Reduce risk of medical and psychiatric comorbidities
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<th>Treatment</th>
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<th>Reduced associated pathology</th>
<th>Weight loss</th>
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<td>Bariatric surgery</td>
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Topiramate

- First study: McElroy et al. 1983
- Wide spectrum of actions
- Antipicking eating and antipurging actions
- Promotes weight loss
**BED Treatment**

**Topiramate**

- 16 weeks, multicenter, randomized controlled trial with 407 patients

- Marked reduction in the frequency of binge eating episodes with significant weight loss

- Final average dose: 300 mg/day

BED Treatment

Zonisamide

• Significantly greater reduction in binge eating episode frequency, body weight, and scores on several rating scales

• Efficacious but not well tolerated

• Mean daily dose: 436 mg

Atomoxetine

• Significantly greater reduction in binge eating episode frequency, body weight, and scores on rating scales than placebo

• Efficacious and fairly well tolerated

• Mean daily dose: 106 mg

BED Treatment

Sibutramine

• Serotonin and norepinephrine reuptake inhibitor
• 12-week study: reduces the frequency of binge eating, promotes and maintains weight loss
• Dose: 10 mg/day
• Withdrawn from market due to safety issues

Psychostimulants

• Methylphenidate produced greater decrease in appetite in 1 case-controlled study (Davis et al. 2007)

• Lisdexamfetamine dimesylate (LDX): significantly greater reduction in binge eating days per week (McElroy at al. 2012)
BED Treatment

- LDX: phase 2, multi-center, randomized, double-blind, placebo-controlled study
- 11-week
- Forced titration
- LDX 30-, 50-, and 70-mg/day groups and placebo
- LDX 50- and 70-mg groups statistically superior to placebo on primary endpoint

Memantine

- Open-label trial
- Significantly reduced frequency of binge eating days and episodes

Eating Disorders and Peptide Hormones: New Treatment Targets

- Ghrelin agonists
- Neuropeptide Y1 and -5 antagonists
- Orexin receptor antagonists
- CRF receptor 2 antagonists
- Histamine 3 antagonists
Summary

• Biggest news: addition of binge eating disorder as independent category in DSM-5

• At the moment, there are no effective treatments that address all the clinical features of eating disorders

• Lack of dose standardization in RCT
ONLY FLUOXETINE is approved by regulatory authorities for the treatment of BN
Summary

• Significant progress made in recent decades
• More extensive RCT needed
• Focus on potential new targets