Assessment and Treatment of Childhood Anxiety Disorders

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Disclosures for the past 12 months John T. Walkup, MD

- Lilly, Pfizer and Abbott – free medication and placebo for NIMH-funded studies. All studies completed and manuscripts are in preparation
- Royalties from Guilford and Oxford press for books and manuals related to Tourette's syndrome.

Discussion of Off Label Use of Medications

- All medication use should be considered off label unless explicitly noted otherwise

Outline

- Review of Anxiety Disorders
- Review Treatment of Anxiety Disorders
  - OCD
  - Other Anxiety Disorders
  - CAMS
- SSRI side effects

Question 1

Approximately this percentage of children with specific phobia have another anxiety disorder?

A) 10%
B) 25%
C) 50%
D) 70%
E) 90%

Question 2

- One of the following is a tool for assessment of childhood anxiety disorders:

A) SNAP-IV
B) CDRS
C) SCARED
D) WISC
E) YMRS

Question 3

Anxiety disorders in children present very commonly with:

A) Sadness of mood
B) Physical Complaints
C) Aggression
D) Hallucinations
E) Memory problems

Anxiety Disorders in Children and Adolescents

- Specific Phobia
- OCD
- Separation Anxiety Disorder
- Generalized Anxiety Disorder
- Social Phobia
- Acute Stress Disorder
- Post-traumatic stress disorder
- Panic Disorder

Specific Phobia

- Animals, insects etc.
- Environmental - thunder, water, heights
- Blood, injection or other suspected painful event
- Situational - tunnels, bridges, elevators
- 70% have another anxiety disorder

Obsessive Compulsive Disorder

- Prominent obsessions or compulsions
  - Dirt, germs, or other contamination
  - Ordering and arranging
  - Checking
  - Repetitive acts
- Impairing or time consuming

Subtypes of OCD

- Pure Obsessions
- Contamination
  - Least likely associated with other Axis I disorders
- Symmetry/Order
- Hoarding
  - Poorer treatment response.

Separation Anxiety Disorder (SAD)

- Excessive concern regarding separation from home or from attachment figures
  - Bad things happening to parent and or child
  - Cannot be alone
  - Avoidance
  - Difficulty falling asleep or sleeping with loved ones
  - Physical aches and pains
  - Accommodation by adults
- Impairment or distress.

Generalized Anxiety Disorder (GAD)

- Excessive worry and apprehensiveness
  - Restless, keyed-up or on edge.
  - Fatigued at end of school day
  - Concentration problems “choking on tests”
  - Sleep problems (falling asleep)
  - Tense and irritable
- Unable to control the worry
- Impairment or distress

Social Phobia (SoP)

- Fear of social or performance situations
  - Specific
  - Generalized

Selective Mutism

- Ability to speak
- Not speaking in social situations
- Not part of another disorder

Acute Stress Disorder

- True stressful event – life threatening
- Re-experiencing the event
- Avoidance and numbing
- Increased arousal
- Time limited

Post-traumatic Stress Disorder

- True stressful event – life threatening
- Re-experiencing the event
- Avoidance and numbing
- Increased arousal
- Risks for enduring symptoms
  - Pre-existing mental disorder
  - Proximity
  - Post-traumatic environment

Panic Disorder

- Attacks of anxiety (Physical Symptoms)
  - ⇧Heart rate, pounding heart, palpitations
  - Hyperventilation, shortness of breath
  - Choking sensation
  - Chest discomfort or pain
  - Abdominal pain
  - Some psychological symptoms
- Worry about the next one
- Avoidance behavior related to the attacks
- Agoraphobia….

Assessment Strategies

- Multidimensional Anxiety Scale for Children (MASC) – J. March
- Screen for Child Anxiety Related Emotional Disorders Scale (SCARED) – B. Birmaher
- Achenbach Child Behavior Checklist (CBCL)

What to look for

- **Physical complaints – headaches, stomach aches, dramatic presentations of pain.**
- Problems with falling asleep and middle of the night awakening, repeated visits to parents room
- Eating problems
- Avoidance of outside and interpersonal activities – school, parties, camp, sleepovers, safe strangers
- Excessive need for reassurance – new situations, bedtime, school, storms, bad things happening
- Inattention and poor performance at school
- Not necessarily pervasive – some areas of function remain

Physical Symptoms – Provoked and Spontaneous

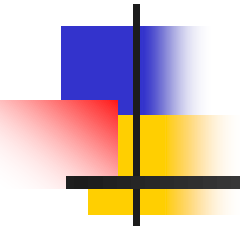
- Anxious children listen to their bodies
- Headache
- Stomachache – stomach and bowel problems
- Sick in the morning and can't fall asleep in the evening
- Frequent urge to urinate or defecate
- Shortness of breath
- Chest pain - tachycardia
- Sensitive gag reflex - fear of choking or vomiting
- Difficulty swallowing solid foods – growth inhibition?
- Dizziness, lightheaded
- Tension and tiredness – exhausted and irritable after a school day
- Derealization and depersonalization
- Avoidance to prevent above physical symptoms

What to look for

- Physical complaints – headaches, stomach aches, dramatic presentations of pain.
- **Problems with falling asleep and middle of the night awakening, repeated visits to parents room**
- **Eating problems – over and under**
- **Avoidance of outside and interpersonal activities – school, parties, camp, sleepovers, safe strangers**
- **Excessive need for reassurance –bedtime, school, storms, bad things happening**
- **Inattention and poor performance at school**
- **Explosive outbursts**
- **Not necessarily pervasive**

Epidemiology

- Very common up to 8-10% of kids
- Under diagnosed
- Under treated
- Need to look for it



The Treatment of OCD

Treatment of OCD

- Cognitive-behavioral therapy
- SRIs
  - Clomipramine
  - Fluvoxamine
  - Paroxetine
  - Sertraline
  - Fluoxetine
  - Citalopram
  - Escitalopram
- Combination treatment
- Deep brain stimulation

Serotonin Reuptake Inhibitors FDA Approvals

- Clomipramine - FDA approved to age 10 OCD
- Fluvoxamine - FDA approved to age 8 OCD
- Sertraline - FDA approved to age 6 OCD
- Paroxetine – effective for OCD and SoP
- Fluoxetine – effective for OCD; MDD to age 7
- Citalopram – No controlled trials in children
- Escitalopram – FDA approved for depression to age 12 years
- Venlafaxine – Effective for SoP and maybe childhood GAD (1 of 2 studies are positive)

Controlled Trials: Obsessive Compulsive Disorder

- Clomipramine - DeVeaugh-Geiss et al., 1992
- Fluoxetine - Riddle et al., 1992
- Sertraline - March et al., 1998
- Fluvoxamine - Riddle et al., 2001
- Fluoxetine – Geller et al., 2001
- Paroxetine - Geller et al., 2004

Sertraline In Childhood OCD

- Double-blind, placebo-controlled, 12-week, multisite trial
- N = 187; age = 6-17 years; sertraline ≤200 mg/d
- Sertraline > placebo
- Mild side effects
- Similar profile of response as clomipramine

Fluvoxamine In Childhood OCD

- Double-blind, placebo-controlled, multisite trial
- N = 120; age = 8-17 years; fluvoxamine 50-200 mg/d
- Fluvoxamine > placebo
- Mild side effects

Fluoxetine in Childhood OCD

- Geller et al., 2001
- N=103, ages 7-17 years
- 13 week double-blind placebo controlled trial
- Dose 10-60 mg/day
- Decrease CY-BOCS favored fluoxetine ($p<.026$)

Paroxetine

- Double-blind, placebo-controlled. 10 week trial
- Ages 7-17
- N=203
- Paroxetine > placebo
- Mild side effects

Geller, DA et al., 2004

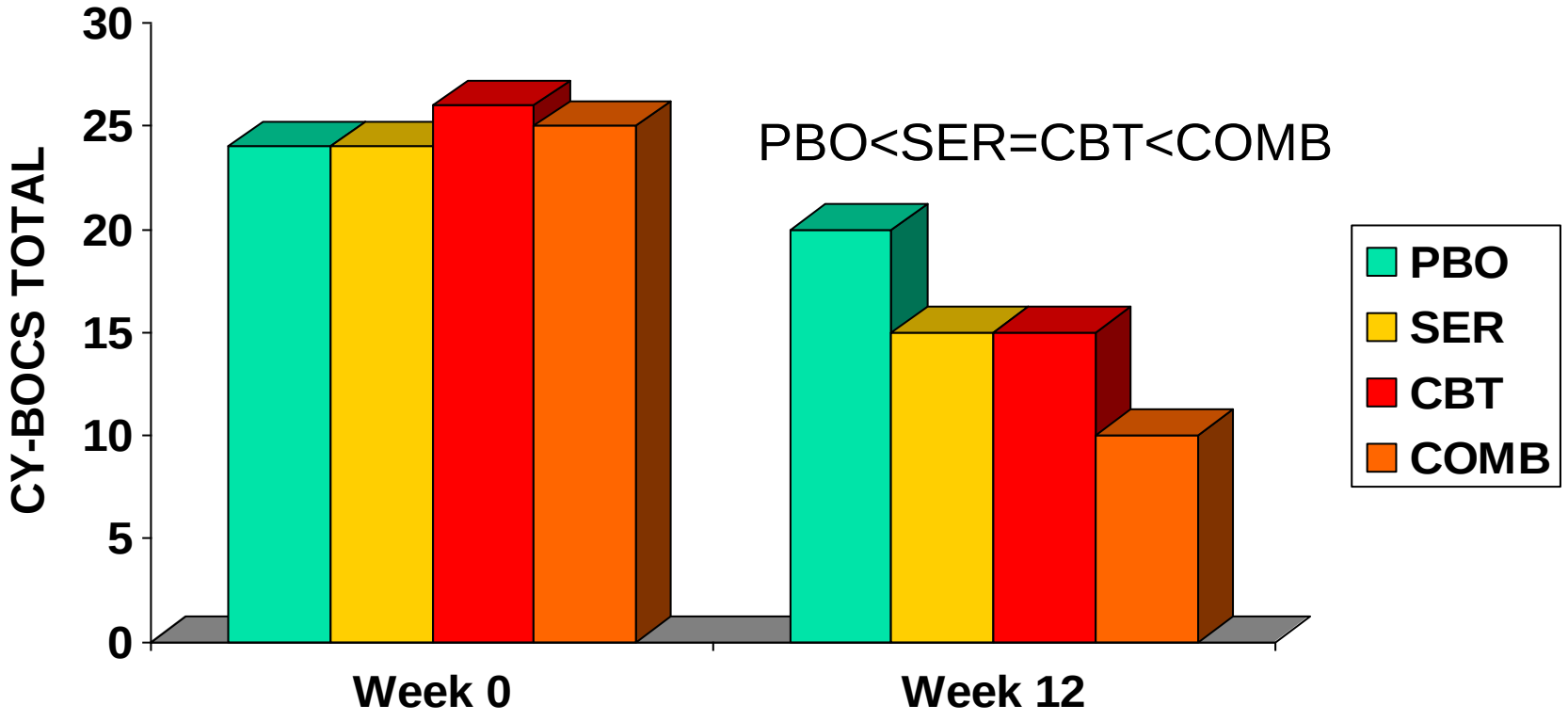
Augmentation Strategies for OCD

- Clomipramine
- Clonazepam
- Antipsychotics
- IV Clomipramine
- Buspirone
- Add second SSRI
- Lithium
- Stimulants
- Others

Pediatric OCD Treatment Study - POTS

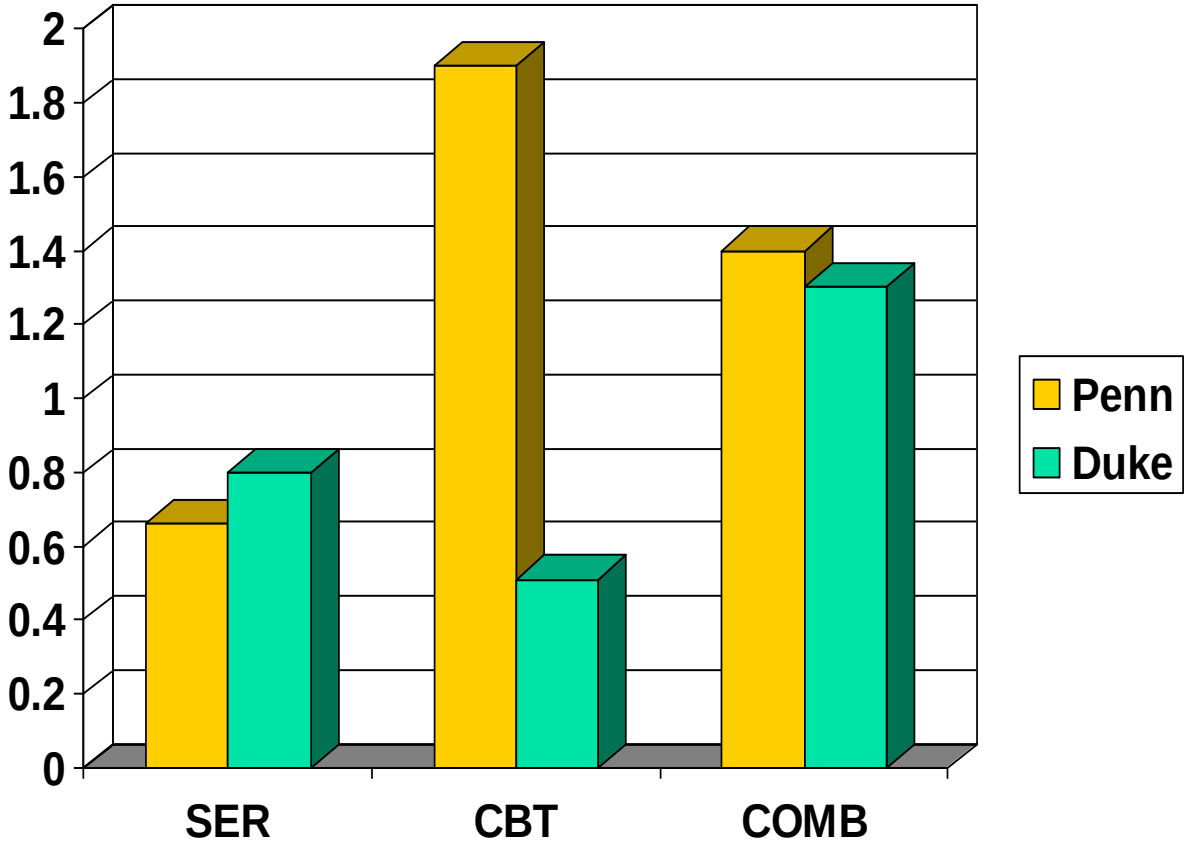
- N = 112
- Ages 7-17 years
- 3 sites, 12 weeks
- CBT, Sertraline, COMB and placebo

CY-BOCS ITT Outcomes



Pediatric OCD Study Team (2004) *JAMA*.

Site x Treatment Interaction



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Deep Brain Stimulation

- Indicated for Parkinson's, tremor and pain
- Humanitarian exemptions for dystonia and OCD
- Small number of subjects world wide for refractory depression and Tourette's syndrome

PANDAS

- **P**ediatric **A**utoimmune **N**europsychiatric **D**isorders **A**ssociated with **S**treptococcal infections
- Not a validated disorder
- Treatment outpaced our knowledge of the disorder
- Most treatments should be done as a part of a research trial
- 'Epi'-studies suggest a small group of kids may be at risk.

PANDAS

- Suspected cases
  - Throat culture
  - If positive – treat
  - Do not get spot titers
  - Probably no role in non-research settings for other immunologically-based treatments

Controlled Trials: "Separation Anxiety Disorder"

- Imipramine - Gittelman-Klein et al., 1971, 1973, 1992
- Clomipramine - Berney et al., 1981
- Alprazolam and imipramine - Bernstein et al., 1990
- Bernstein et al., 1999, 2000, 2001
- Clonazepam - Graae et al., 1994

SAD, GAD and SoP

- Pharmacotherapy
  - RUPP trial, 2001
  - Birmaher et al., 2003
- Psychotherapy
  - Kendall, 1994
  - Kendal et al., 1997
  - Many others

SAD, GAD and SoP – RUPP, 2001

- Ages 6-17 years old
- N=128
- Fluvoxamine up to 250-300 mg/day
- Randomized double-blind, placebo-controlled
- 8 weeks.
- RESULTS:
  - Fluvoxamine > placebo on CGI-I
    - 76% (48/63) > 29% (10/65)
  - Pediatric Anxiety Rating Scale
    - Fluvoxamine 18.7 to 9.0 > 50% change
    - Placebo 19.0 to 15.9 = No Change

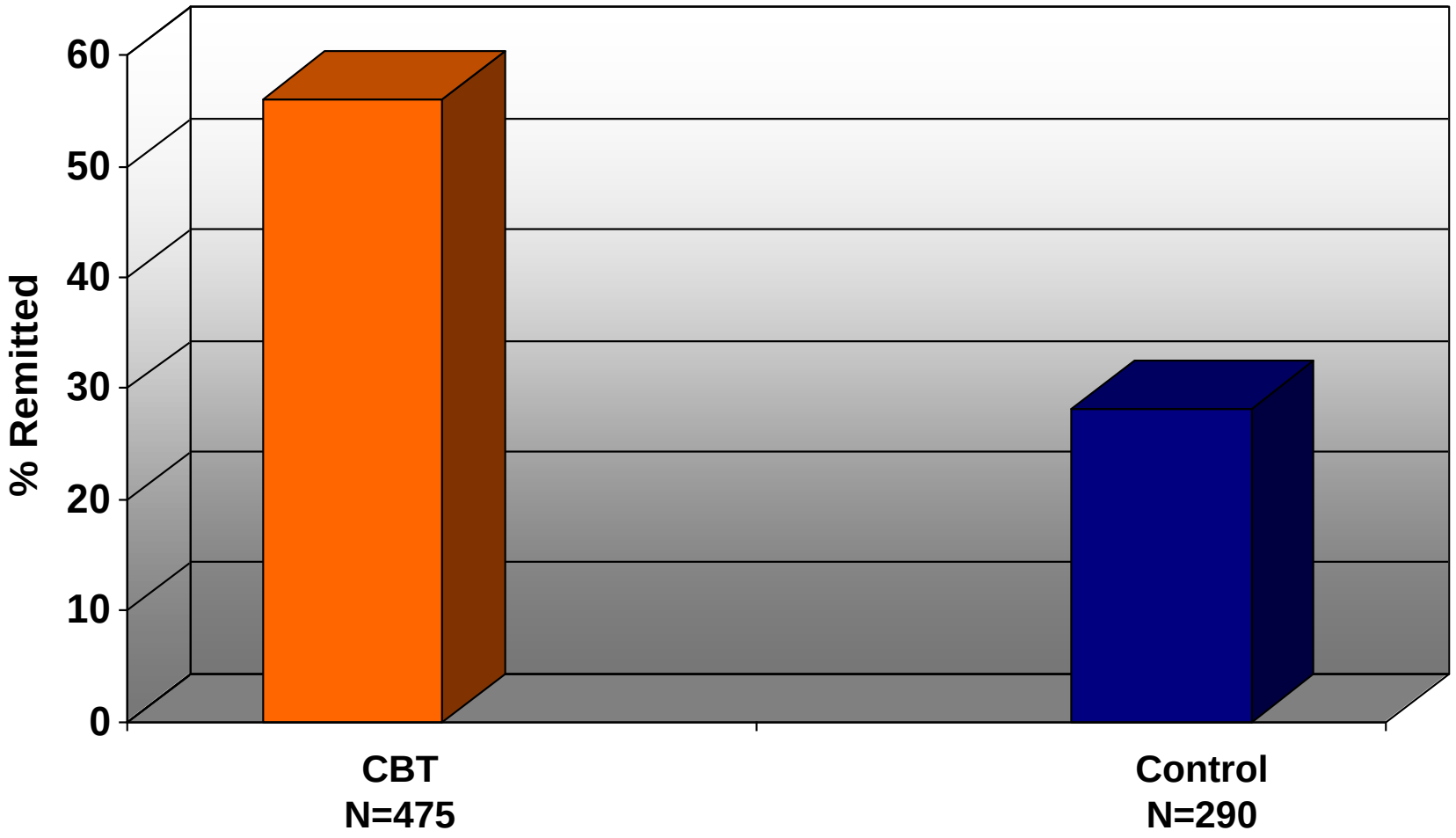
SAD, GAD and SoP

- Ages 7-17 years old
- N=74
- Fluoxetine 20 mg/day
- Randomized, double-blind, placebo controlled
- 12 weeks.
- Results
  - Fluoxetine 61% vs Placebo 35%

Birmaher et al., 2003

CBT for Child Anxiety

(ITT Outcomes)



Cochrane Report, 2006

Social Phobia

- 16-week, randomized, double-blind, placebo-controlled, flexible-dose, parallel-group,
- N= 322 children (8-11 years of age) and adolescents (12-17 years of age) with social anxiety disorder
- Medication: paroxetine 10-50 mg/d or placebo.
- RESULTS:
  - Response: 77.6% vs. 38.3%
  - CGI-I = 47.8% vs. 14.9%.

Wagner KD, et al., Arch Gen Psychiatry. 2004 Nov;61(11):1153-62.

Other Important Studies

- Sertraline in GAD - Rynn et al., 2001
- Venlafaxine in GAD, Rynn et al., 2007
- Venlafaxine in SoP, March et al., 2007
- Buspirone in GAD, unpublished

CAMS

- Aim: to compare sertraline and CBT, alone and in combination, to PBO.
- N=488 subjects with separation anxiety disorder, generalized anxiety disorder, or social phobia
- Age: 7-17 years
- Duration- 12-week trial

CAMS

- All 3 active treatments demonstrated efficacy
- 81% response to COMB, 61% CBT, 56% sertraline, 26% PBO
- COMB > CBT=Sertraline > PBO

Adverse Events

- Activation is common: 10-15% difference between groups
- Bipolar switches uncommon <1%
- Frontal lobe symptoms at higher doses
- GI issues early
- Easy bruising and bloody noses
- Some case reports about growth

Suicidality

- Risk Difference for Efficacy
  - MDD - 11.0% = NNT of 10
  - OCD - 19.8% = NNT of 5
  - Non-OCD anxiety disorders - 37.1% = NNT of 3
- Risk Difference for Suicidality 1-2%
- Overall - 0.7% = NNH 0f 143
  - But not for individual disorders
    - MDD - 0.9%; NNH ~100
    - OCD - 0.5%; NNH ~200
    - non-OCD anxiety disorders - 0.7% ; NNH ~140

Bridge et al., 2007

Summary

- Anxiety is common
- Anxiety is easy to miss
- Anxiety disorders are responsive to treatment
- Side effects with meds are minimal and can be managed with good monitoring

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Answers

1) D
2) C
3) B