Depression in Children / Adolescents

Background

1. Definition[1]
    - Depressive symptoms that are present daily for at least 2 weeks and
        - Cause clinically significant social, occupational impairment
        - Cannot be explained by other psychiatric illness, other medical condition or use of medications, or substance abuse
2. General info
    - Episodic dz
    - Often persists into adulthood
    - Common condition
    - Often delayed diagnosis and treatment
    - Poor function in family, school and social settings
    - At risk for suicide, substance abuse

Pathophysiology

1. Pathology of disease
    - Combination of genetic and environmental factors
    - Disturbances in neurological pathways primarily involving neurotransmitters norepinephrine, serotonin & dopamine
2. Incidence / prevalence
    - Lifetime incidence
        - 10-30%
        - Median incidence 15-18 years of age
    - Estimated prevalence
        - Pre-school age 1%
        - School age 2%
        - Adolescents 5-8%
3. Risk factors[3]
    - Genetics
        - Depression in parents increases risk
    - Female sex
    - Environment
        - Marital conflict
        - Caregiver - child conflict
        - Abuse (physical, emotional, sexual)
        - Death of parent or family member
        - Peer group difficulties
        - Academic difficulties
    - Co-morbid medical illness
    - History of other psychiatric conditions
        - Substance abuse
        - Anxiety disorders
        - ADHD

        - Learning disabilities
        - Prior depressive illness
4. Morbidity/ mortality[4]
    - 3rd leading cause of death in adolescents
        - Completed suicide rate age 15-19 = 8.2/100,000
        - Completed suicide rate age 10-14 = 1.3/100,000
        - 25 suicide attempts for every one completed suicide
    - Males have higher rate of death from attempts than females
    - High school students
        - 6.9% at least one attempted suicide in last 12 months
        - 14.5% seriously considered suicide in last 12 months
    - If untreated, may have poor long term outcomes
        - School failure
        - Adverse consequences of risk-taking behavior
        - Increased substance abuse risk

Diagnosis

1. History
    - Same diagnostic criteria as for adults with a few variations due to ability of children to describe inner emotions (often require multiple sources for information)
    - DSM-IV criteria[1,3]
        - Depressed mood or anhedonia present for 2 weeks and causing clinically significant impairment
            - Depressed (or irritable) mood
                - In children and adolescents this may be vague physical symptoms, poor eye contact, acting out or hostile/angry interactions
            - Loss of interest or pleasure in activities
                - May present as social withdrawal
        - In addition to depressed/irritable mood or loss of pleasure, at least 4 symptoms present for at least 2 weeks
            - Sleep disturbance
                - Insomnia or hypersomnia
            - Weight change or altered appetite
                - Failure to meet expected weight gain during childhood or failure to thrive
            - Decreased concentration
                - Poor school performance
            - Suicidal ideation
                - May be non-verbal clues such as giving away possessions or illustrations
                - Preoccupation with music, literature, movies with morbid themes
                - Feelings of hopelessness / helplessness

- Psychomotor agitation or retardation
    - Uncharacteristic hyperactive mood / behaviors may be noted
- Fatigue
    - Frequent school absences for fatigue or withdrawal of school activities
- Feelings of worthlessness or guilt
    - Self-deprecation ("I'm stupid")
- Not explained by other psychiatric disorder
    - 40-70% of depressed adolescents have comorbid psychiatric conditions
- Not caused by effects of medical illness, medications or other illicit drugs
- Not caused by bereavement

- Depression can be characterized as
    - With psychosis
        - Primarily auditory hallucinations in children, but must be differentiated from true psychotic disorder such as schizophrenia
        - Psychotic symptoms are associated with increased risk of suicide
    - Without psychotic symptoms

2. Physical exam
    - Thorough exam to rule out medical cause
3. Diagnostic testing
    - Laboratory evaluation if warranted by physical exam
        - CBC
        - TSH
        - Basic metabolic panel
        - Liver function tests
        - EEG
    - Diagnostic imaging
        - Not indicated
    - Depression scales[5]
        - Primarily used in research settings and useful for screening
            - Dx depends on detailed clinical interview
        - Generally have sensitivity and specificity ranging from 70% to 100%
        - Examples
            - Beck Depression Inventory (BDI), BDI-PC (BDI for Primary Care)
            - Children's Depression Inventory (CDI)
            - Center for Epidemiologic Study Depression Scale (CES-D), CES-D-C (CES-D for children).
            - Patient Health Questionnaire (PHQ-9)

Differential Diagnosis

1. Organic medical problems:
    - Iron-deficiency anemia

- Hypothyroidism
- Diabetes mellitus
- Medications
  - Beta-blockers
  - Sedatives
  - Corticosteroids
  - Anti-seizure medications
  - Analgesics
  - Isotretinoin (Accutane)
  - Acyclovir
- Nutritional deficiency
  - Folate
  - B-12
  - Niacin
  - Vit C
  - Iron
- Chronic infection
  - Mononucleosis
  - HIV
- Chronic systemic dz
  - Lupus
  - Addison's dz
  - Cushing's dz
  - Wilson's dz

2. Other psychiatric disorder
   - Bipolar disorder
   - ADHD
   - Adjustment disorder
   - Anxiety / panic disorder
   - Schizophrenia
3. Bereavement
4. Substance -induced mood disorder
   - Or withdrawal from substances
5. Chronic learning deficiency
6. Epilepsy
7. Brain tumor

Therapeutics

1. Acute treatment
   - Suicidal ideation
     - Identify if present, hospitalize and refer to mental health professional
   - Safety plan
     - Requires discussion with patient and family how to anticipate increased suicidal urges

        - Use of "safe" words to communicate about suicidal ideation to responsible adult if urges become overwhelming
        - Steps to take to help alleviate these urges
2. Further management (24 hrs)
    - Suicidal ideation:
        - Safety plan in place, have a practitioner available 24 hrs a day to address any concerns for safety /suicidality
3. Long-term care
    - Guidelines for Adolescent Depression in Primary Care II (GLAD-PC II)[6]
        - Mild depressive illness
            - Receive 6-8 weeks of active support and regular monitoring of symptoms
            - Education for patient and family
        - Moderate/severe depressive illness
            - Receive psychotherapy (CBT or IPT) either as primary treatment or in conjunction with antidepressants
            - Initiation of antidepressant therapy
            - Consider consultation of mental health specialist
            - Education of patient and family
                - Improvement in parental depression associated with improvements in child's psychopathology
    - Psychotherapy[7]
        - In adolescents, most effective when combined with pharmacotherapy
            - NNT 4 when CBT combined with fluoxetine at 12 weeks
            - Typical response rate to psychotherapy or pharmacotherapy alone is 60% (35-40% remission)
        - Cognitive behavioral therapy (CBT)
            - Most studied form of psychotherapy for depression
            - Helps patients recognize and counteract distorted patterns of thinking that relate to depression
            - Indicated for moderate depression in adolescents
            - Insufficient evidence to recommend CBT monotherapy for severe depression in adolescents
    - Interpersonal therapy (IPT)
        - Addresses depression in terms of dysfunctional relationships and teaches patient awareness and skills to change these patterns
    - Pharmacotherapy[7]
        - SSRI therapy is only appropriate in the context of ongoing education, clinical monitoring and safety plan provisions
        - SSRIs appear to be the safest for Tx of depression in adolescents
        - Fluoxetine only SSRI with FDA approval for Tx of depression in patients 8-18 yo
            - Initial dose 5-10 mg/d
            - May increase q7days to target dose 10-20 mg/d
            - Do not exceed 20 mg/d
            - NNT 7 at 12 weeks when compared to CBT alone

- Other SSRIs not approved by FDA for children or adolescents, but may weigh benefits / risk and side effect profiles
    - Generally lower doses than in adults
- Requires close follow-up during initiation phase for side effects
    - Should have weekly follow up in person for 1 month, then biweekly, then monthly when stable dosage and symptoms
    - GI side effects common and tend to dissipate
    - Activation is also common, should raise concern for suicidal ideation
        - 4% risk od suicidality with SSRI treatment
        - 2% risk of suicidality in placebo
        - No suicides occurred during studies however
    - Watch for induced mania / hypomania
    - Warn patients against abrupt discontinuation
        - Discontinue SSRI with taper over course of several weeks
    - Continuation of antidepressant therapy for 6 months after remission may reduce relapse rates
        - Patients with recurrent depression and those who had difficulty achieving remission should receive continuation therapy for at least 12 months
        - Medication switch plus addition of CBT may improve remission rates for adolescent nonresponders to first-line SSRI
        - Compared to medication change alone
        - If response is still inadequate, should refer to pediatric behavioral specialist
- TCAs
    - Generally not indicated due to unclear efficacy and side effect profile
- Black box warning (2004)
    - FDA mandated warning on all antidepressants: increased suicidality , small, but real increase shown in meta analysis

Follow-Up

1. Return to office
    - Weekly during 1st month, then every other week x2 months (FDA recommendation)
    - Need to have 24 hour contact availability for emergency
    - Return to office more urgently if suicidal ideation, manic symptoms, or serious adverse events
        - 1-800-273-TALK National Suicide Prevention Hotline
2. Refer to specialist
    - Consider for all cases of pediatric depression
    - Access may be a barrier: need for PCP ability to diagnose and treat

- Indications for referral
  - History of suicidality
  - Co-existing anxiety disorder
  - Co-existing substance abuse disorder
  - Psychosis
  - History of mania / family history of bipolar disorder
  - Non-response to initial treatment trial

3. Admit to hospital
   - Any current / active suicidal ideation

Prognosis

1. Untreated major depressive episode can last 7-9 months
2. Recurrence
   - 40% within 2 years
   - 70% within 5 years
3. Common sequelae
   - Impaired social functioning
   - Poor academic performance
   - Increased risk for drug, alcohol, and nicotine use if left untreated
   - Increased risk for eating disorders
   - Increased risk for somatization disorders
4. Poorer prognosis
   - Multiple major depressive episodes
   - Comorbid anxiety
   - Comorbid substance use disorder
   - Male sex

Prevention

1. Community based identification and treatment for at-risk children may be effective
2. Screening
   - Insufficient evidence for or against routine screening of children & adolescents
   - Affirmative answer to either of two questions effective for general screening
     - "Over the past 2 weeks have you ever felt down, depressed or hopeless?"
     - "Have you felt little interest or pleasure in doing things?"
   - Affirmative answer to either question should lead to further screening with depression scales (BDI, etc) or detailed clinical interview

Patient Education

1. AAFP- Depression in Children and Teens
   - http://www.aafp.org/afp/20020915/1048ph.html
2. Family Doctor.org
   - http://familydoctor.org/online/famdocen/home/children/parents/special/common/641.html

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8. USPSTF. Screening: Major Depressive Disorder in Children and Adolescents. March 2009. http://www.ahrq.gov/clinic/uspstf/uspschdepr.htm

Evidence-Based Inquiry

1. Which drugs are safest for moderate to severe depression in adolescents?
2. Should we use SSRIs to treat adolescents with depression?
3. Which drugs are most effective for moderate to severe depression in adolescents?

PURLs

1. Treat depressed teens with medication and psychotherapy

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