THE TRANSPLANT THAT ALMOST FAILED

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Topic: Chronic Physical Illnesses and Major Depression

Abstract: Chronic physical illnesses are often complicated by psychiatric disorders. Direct effects of physical illnesses and their treatments may produce behavioral and emotional symptoms. However, primary emotional disorders must also be considered. Adam is a 9-year-old boy with chronic renal failure who is admitted to the hospital for a renal transplant. His team considers the interplay of his chronic and often life-threatening physical condition and the development of a comorbid depression.

Goal: To provide learners with an understanding of the interactions between chronic physical illness and depression in a school-age child.

Objectives: By the end of the session, learners will be able to
- Recognize the dual presentation of chronic physical illness and mood disorder.
- Understand the relationships and differences between depression due to a medical condition, a situational depression, and a primary depressive disorder.
- Understand the contribution of cognitive and emotional development to a child's ability to cope with chronic severe illness.
- Describe the appropriate management of a school age child with comorbid depression and chronic physical illness.

Themes: Children with Chronic Medical Conditions, Child Mental Health

Bright Futures Core Concepts: This case can be used to highlight communication and partnership.

Materials Provided:
- Facilitator Guide
- Three-part case narrative: Part I, Part II, Epilogue
- Handout #1: APA's DSM-IV Criteria for Mood Disorders
- Handout #2: Flow sheet of laboratory values
- Handout #3: Growth charts
- Handout #4: List of antidepressant drug interactions with the cytochrome p450 system
- References

Facilitator Preparation: Facilitator should thoroughly review this guide and the other materials provided. Facilitator can modify implementation of the case session to best fit their educational setting and learners. For a summary of recommendations on leading discussions, please see Appendix #1 in the Introduction to this manual. Participants should be familiar with how to conduct a routine medical and psychiatric interview.

THE TRANSPLANT THAT ALMOST FAILED: FACILITATORS GUIDE

Introduction

Improvements in both surgical and medical management of complex physical illness have enabled many patients to survive who in the past would have died. The effects of these illnesses and their treatments can manifest themselves in biological, psychological, social, and developmental realms. Children and their families are remarkably resilient in adapting to the challenges presented by their physical conditions. While the majority do not have identifiable emotional or behavioral difficulties, research has shown that children with chronic physical illnesses have an increased likelihood of subthreshold problems. In particular, the differential diagnosis of depressive illness can be a difficult challenge to the pediatrician requiring consultation with a child and adolescent psychiatrist.

OPEN THE DISCUSSION: INTRODUCE THE CASE TITLE AND THE SESSION GOAL. EXPLAIN THAT THIS WILL BE AN INTERACTIVE CASE DISCUSSION AND NOT A LECTURE. DISTRIBUTE PART I OF THE CASE AND ASK ONE OR MORE OF THE PARTICIPANTS TO READ IT ALOUD.

Part I: Failure and Transplantation

Adam is a 7-year-old boy who initially presented to his pediatrician with polyuria, polydipsia, pallor, and lethargy. Laboratory tests were remarkable for profound anemia, renal salt wasting, hyperkalemia, azotemia, and elevated creatinine. Renal ultrasound and abdominal CT scan revealed cysts at the cortico-medullary border of the kidneys. Renal biopsy confirmed the diagnosis of juvenile nephronophthisis, an autosomal recessive disorder accounting for 10-20% of cases of renal failure in childhood. This medullary cystic disease typically presents in the 1st or 2nd decade and progresses to end stage renal failure before the age of 20 years.

A pediatric nephrologist located at a tertiary care center 90 minutes from Adam's home takes over his care. Adam requires daily oral medication, recombinant human erythropoietin injections, dietary restriction, and regular blood tests. He is hospitalized three times during the first year of treatment for severe abdominal pain and lethargy due to metabolic acidosis. He requires peritoneal dialysis for renal insufficiency before his 8th birthday. Shortly thereafter, a gastrostomy tube is placed due to increasing difficulty maintaining nutritional status.

Adam misses many school days and does not have enough energy to play with friends. He spends most of his time at home watching television or halfheartedly trying to keep up with schoolwork. His parents are concerned that Adam seems to have little interest in anything. They believe a kidney transplant will be the answer. Adam is placed on a national waiting list for a kidney transplant. Adam is adopted; he was

found abandoned at birth and his family of origin is unknown. His parents and many other relatives undergo tissue matching, but no one is a suitable donor.

Fortunately, a suitable match is found for Adam within 6 months. His transplant operation is uncomplicated, and anti-rejection medications (cyclosporin-A and prednisone) are begun immediately. After one week on the transplant unit, Adam refuses to eat and appears glum. He is not interested in the clowns who come to visit the ward, and cannot watch even a short video without becoming distracted. He becomes agitated when his g-tube or intravenous lines are manipulated. He sometimes refuses to take oral medications, stating, "They hurt my stomach too much." When asked why he is upset, he answers, "I'm fine" or looks away. His parents are mystified, as they believed that his attitude would change once he had a new kidney.

Following the reading, ask all participants, "So what do you think about the case so far? What should we focus our discussion on today?" List agenda items on a blackboard or flipchart. Then use the questions below to guide the discussion. Remember that the key to leading a small group successfully is facilitation of the discussion rather than lecture. Draw as many participants as possible into the discussion. Allow silences while group members think about questions. Present material from the discussion guide only when needed to complement or redirect the group discussion.

GUIDING QUESTIONS FOR PART I DISCUSSION:

What are the possible causes of Adam's lack of energy and interest?
Adam's symptoms may reflect physical illness and/or psychiatric disorder. Participants may have further questions regarding his medications, laboratory values, cognitive and vegetative symptoms. Their differential diagnoses might include:

- Anemia
- Electrolyte imbalance
- Poor nutrition
- Major Depressive Disorder
- Adjustment Disorder with Depressed Mood
- Dysthymia
- Mood Disorder due to General Medical Condition
- Medication side effects
- Family dysfunction

What information would help you to better understand his difficulties?
Some participants may focus on more history, while others may focus on laboratory data. Some may believe that if laboratory abnormalities are severe enough (i.e. severe anemia) then a psychiatric disorder cannot be considered. Participants may request details about:

- Lab values
- Growth charts
- Somatic complaints
- Sleep, anhedonia, irritability, suicidality
- Anxiety
- Medication list
- Family stressors
- Family attitudes
- Family mental health history

What individual and family factors may be complicating management of Adam's renal failure?
A multidisciplinary view of Adam's presentation might include consideration of his temperament, family functioning, compliance with medication, and response to and side effects from medication. Participants may wonder about his family's fears, Adam's guilt and expectations, and the effects of his medical treatments on his physical and mental health.

What would you do next?
The discussion should allow many opinions to emerge regarding the "next step", as several areas need further exploration. Possibilities include:
- Interview child in depth
- Contact primary pediatrician and nephrologist for family insight
- Consult a psychiatrist

DISTRIBUTE PART II OF THE CASE AND HAVE PARTICIPANTS READ IT ALOUD.

Part II: Additional Background History
The medical team consults psychiatry. Prior to his initial symptoms, Adam was developing as expected. When he was 6 1/2 years old, Adam's activity level decreased, but he seemed generally happy and sociable nonetheless. Just before his 7th birthday, the first symptoms of his renal disease emerged. Within a few weeks of initial pediatric assessment, Adam underwent many tests and was hospitalized for a renal biopsy. He began to ask frequent repetitive questions about kidneys, hospitals, and the other children he saw there. He soon required medication, but hated swallowing pills and gagged often. He was reasonably cooperative with repeated blood tests, but these became more difficult and painful. Technicians often had to try three or four times before successfully obtaining a blood sample. He became progressively more fearful, and cried when going to the laboratory for phlebotomy. Erythropoietin injections presented the greatest difficulty; Adam often went days without receiving his medication.

He became more restrictive and "picky" with his food choices, but the nutritionist reassured his family that this was typical in children with renal problems. Adam missed about 30 days of school during 1st grade, but kept up academically.

Around his 8th birthday, peritoneal dialysis began, requiring catheter placement. His mother was anxious about possible infections, and often reminded Adam to "be careful!" His eating diminished, leading to gastrostomy tube placement. Adam was upset and disappointed: the dialysis was supposed to make him better but he only seemed to worsen. He felt guilty that his poor eating and trouble with medication caused him to need the gastrostomy tube, which he had not kept clean enough, leading to another hospital admission. His classmates knew about the tube, and tried not to touch him. He missed most of 2nd grade, had trouble keeping up academically, and rarely saw his peers socially.

Adam's parents hoped that they or one of their relatives would be a match for him, despite his being adopted, and they were all disappointed when that did not turn out to be the case. The failure to produce a match engendered feelings of guilt and helplessness in his mother, which she tried to mask for fear of making Adam feel even worse. Adam knows that he was adopted, but had never asked many questions about it, and his parents had avoided the topic. Over the course of his illness, Adam's mother repeatedly reminded him that it was the kidneys that were bad, and not Adam. During his interview, Adam became tearful when describing the other children on the ward, all of whom had "fat faces" and were "short." Adam said that he did not believe the transplant would help him, since the dialysis had not. He stated that the kidney was "wasted on him", and that he wishes he "never even got it."

The psychiatry team diagnoses Major Depressive Disorder, and recommends initiation of antidepressant medication. They ask the medical team about type of antidepressant that would have the least interaction with the cytochrome P450 system, and how Adam's cyclosporin levels will be affected.

GUIDING QUESTIONS FOR PART II DISCUSSION:

Do you agree with the diagnosis? Why or why not?

Distribute Handout #1 and discuss the contents:
Facilitator should read through the diagnostic criteria for Mood Disorder due to General Medical Condition and allow time for participants to review the other disorders.

- Review criteria for Major Depressive Disorder, Adjustment Disorder with Depressed Mood, Dysthymia, Mood Disorder due to General Medical

Condition Distribute Handouts #2 and 3 and discuss the contents:
The facilitator should allow participants to review the contents of the data and comment on which information might explain to Adam's energy level, appetite and mood.
- Review lab values and growth charts
- Discuss how these values might relate to his energy level, appetite, and mood

Which antidepressant medication would you choose?

Distribute Handout #4 and discuss the contents:
- Review antidepressant drug interactions with the cytochrome p450 system

What other treatments, if any, are needed?
Participants may suggest specific modes of therapy. Collaboration of providers might be emphasized if the risk of infection on return to school is considered.
- Therapy
- Support group for patient and family
- Possible treatment of parent condition
- Return to school, possibly with school intervention
- Ongoing psychoeducational sessions for family

What would you like to tell Adam's parents?
A collaborative approach to Adam's family meeting may be an efficient method to offer information, but may also overwhelm the family. His pediatricians, psychiatrists and nephrologists might meet initially to review their team meeting plan, where they should:
- Include developmentally appropriate description of his signs of depression
- Speak in a private area, first with parents alone and then with family together
- Address distinction between adjustment and depressive disorder
- Refer to his adopted status and its unclear implications
- Suggest family contact local or national organizations for kidney transplant recipients or adopted children

How can pediatrics and psychiatry best collaborate to provide continuing support for Adam and his parents?
- Make sure communication is regular
- Discuss medication changes, new symptoms, new family concerns as they arise

DISTRIBUTE THE REFERENCE PAGE AND EPILOGUE. ASK SOMEONE TO READ THE EPILOGUE ALOUD.

Epilogue

Adam started Citalopram and his mood elevated within a month. He met his outpatient therapist prior to discharge from the hospital, and saw her weekly for coping skills and insight-based therapy. His mother also sought counseling and pharmacological treatment for anxiety. With tutoring Adam brought up his academic skills and returned to school for third grade. He joined a support group for school-age adopted children as well, and with his nephrologist's approval, joined the golf team.

Refer to the learning objectives and goals, and summarize the key teaching points that were made. This will give the group a sense of accomplishment, and will reinforce the important messages. Suggest further sources of reading or other information if there are agenda items that were not covered in the discussion.

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PART I: CASE NARRATIVE

Failure and Transplantation

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Fortunately, a suitable match is found for Adam within 6 months. His transplant operation is uncomplicated, and anti-rejection medications (cyclosporin-A and prednisone) are begun immediately. After one week on the transplant unit, Adam refuses to eat and appears glum. He is not interested in the clowns who come to visit the ward, and cannot watch even a short video without becoming distracted. He becomes agitated when his g-tube or intravenous lines are manipulated. He sometimes refuses to take oral medications, stating, "They hurt my stomach too much." When asked why he is upset, he answers, "I'm fine" or looks away. His parents are mystified, as they believed that his attitude would change once he had a new kidney.

THE TRANSPLANT THAT ALMOST FAILED
PART II: CASE NARRATIVE CONTINUED

Additional Background History

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THE TRANSPLANT THAT ALMOST FAILED
PART III: CASE NARRATIVE CONCLUSION

Epilogue

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HANDOUT #1

DSM-IV Criteria for Mood Disorders
Major Depressive Disorder

1. Five (or more) of the following symptoms have been present during the same 2 week period and represent a change from previous functioning; at least one of the symptoms is either depressed mood or loss of interest or pleasure. Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.
    a. **Depressed mood** most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, can be irritable mood.
    b. **Markedly diminished interest or pleasure** in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
    c. Significant **weight loss** when not dieting or **weight gain** (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.
    d. **Insomnia or hypersomnia** nearly every day
    e. **Psychomotor agitation or retardation** nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
    f. **Fatigue or loss of energy** nearly every day
    g. Feelings of **worthlessness or excessive or inappropriate guilt** (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
    h. **Diminished ability to think or concentrate, or indecisiveness**, nearly every day (either by subjective account or as observed by others)
    i. **Recurrent thoughts of death** (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

2. The symptoms do not meet criteria for a Mixed Episode

3. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

4. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

5. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

Dysthymic Disorder

1. Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least 2 years. Note: In children and adolescents, mood can be irritable and duration must be at least 1 year.
    a. Presence, while depressed, of one (or more) of the following:
        - Poor appetite or overeating
        - Insomnia or hypersomnia
        - Low energy or fatigue
        - Low self-esteem
        - Poor concentration or difficulty making decisions
        - Feelings of hopelessness

2. During the 2-year period (1 year for children or adolescents) of the disturbance, the person has never been without the symptoms in Criteria #1 for more than 2 months at a time

3. No Major Depressive Episode has been present during the first 2 years of the disturbance (1 year for children and adolescents); i.e., the disturbance is not better accounted for by chronic Major Depressive Disorder, or Major Depressive Disorder, In Partial Remission.
    a. There may have been a previous Major Depressive Episode provided there was a full remission (no significant signs or symptoms for 2 months) before development of the Dysthymic Disorder. In addition, after the initial 2 years (1 year in children or adolescents) of Dysthymic Disorder, there may be superimposed episodes of Major Depressive Disorder, in which case both diagnoses may be given when the criteria are met for a Major Depressive Episode.

4. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode, and criteria have never been met for Cyclothymic Disorder.

5. The disturbance does not occur exclusively during the course of a chronic Psychotic Disorder, such as Schizophrenia or Delusional Disorder.

6. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

7. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:
Early Onset: if onset is before age 21 years
Late Onset: if onset is age 21 years or older
Specify (for most recent 2 years of Dysthymic Disorder): With Atypical Features

Adjustment Disorder

1. The development of emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s).

2. These symptoms or behaviors are clinically significant as evidenced by either marked distress that is in excess of what would be expected from exposure to the stressor or significant impairment in social or occupational (academic) functioning

3. The stress-related disturbance does not meet the criteria for another specific Axis I disorder and is not merely an exacerbation of a preexisting Axis I or Axis II disorder.

4. The symptoms do not represent Bereavement.

6. Once the stressor (or its consequences) has terminated, the symptoms do not persist for more than an additional 6 months.

Specify if:
Acute: if the disturbance lasts less than 6 months Chronic: if the disturbance lasts for 6 months or longer. Adjustment Disorders are coded based on the subtype, which is selected according to the predominant symptoms.

The specific stressor(s) can be specified on Axis IV.

- With Depressed Mood
- With Anxiety
- With Mixed Anxiety and Depressed Mood
- With Disturbance of Conduct
- With Mixed Disturbance of Emotions and Conduct
- Unspecified

Mood Disorder due to a the General Medical Condition

1. A prominent and persistent disturbance in mood predominates in the clinical picture and is characterized by either (or both) of the following:
    a. Depressed mood or markedly diminished interest or pleasure in all, or almost all, activities
    b. Elevated, expansive, or irritable mood

2. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct physiological consequence of a general medical condition.

3. The disturbance is not better accounted for by another mental disorder (e.g., Adjustment Disorder with Depressed Mood in response to the stress of having a general medical condition).

4. The disturbance does not occur exclusively during the course of a delirium.

5. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify type:
- With Depressive Features: if the predominant mood is depressed but the full criteria are not met for a Major Depressive Episode
- With Major Depressive-Like Episode: if the full criteria are met (except Criterion #5) for a Major Depressive Episode
- With Manic Features: if the predominant mood is elevated, euphoric, or irritable
- With Mixed Features: if the symptoms of both mania and depression are present but neither predominates

THE TRANSPLANT THAT ALMOST FAILED HANDOUT #2

Laboratory Flow sheet
Event: Presentation
Date: 1/15/99
Age: 7y-0m
Medication: None
Hgb (gm/dL): 7
HCO3-: 11
BUN (mg/dL): 90
Creatinine (mg/dL): 2.1

Event Hospitalization #1
Date: 6/15/99
Age: 7y-5m
Medication: Sodium, phosphorus and bicarbonate supplements; calcium acetate, Erythropoetin injections
Hgb (gm/dL): Same
HCO3-: 13
BUN (mg/dL): 50
Creatinine (mg/dL): 2.2

Event: Hospitalization #2
Date: 8/15/99
Age: 7y-7m
Medication: Same
Hgb (gm/dL): 9
HCO3-: 12
BUN (mg/dL): 55
Creatinine (mg/dL): 2.3

Event: Hospitalization #3
Date: 10/15/99
Age: 7y-9m
Medication: Same
Hgb (gm/dL): 10
HCO3-: 13
BUN (mg/dL): 60
Creatinine (mg/dL): 2.4

Event: Dialysis Initiation
Date: 1/15/00
Age: 8y-0m
Medication: Same
Hgb (gm/dL): 9
HCO3-: 10
BUN (mg/dL): 120
Creatinine (mg/dL): 2.9

Event: Before transplant
Date: 6/15/00
Age: 8y- 5m
Medication: Same
Hgb (gm/dL): 10
HCO3-: 17
BUN (mg/dL): 40
Creatinine (mg/dL): 1.5

Event: Transplant week #1
Date: 6/22/00
Age: Same
Medication: Prednisone, Cyclosporin-A
Hgb (gm/dL): 13
HCO3-: 23
BUN (mg/dL): 14
Creatinine (mg/dL): 0.8

Event: Transplant week #2
Date: 6/29/00
Age: Same
Medication: Same
Hgb (gm/dL): 13
HCO3-: 22
BUN (mg/dL): 13
Creatinine (mg/dL): 0.7

Event: Transplant week #4
Date: 7/14/00
Age: 8y- 6m
Medication: Citalopram
Hgb (gm/dL): 13
HCO3-: 23
BUN (mg/dL): 14
Creatinine (mg/dL): 0.7

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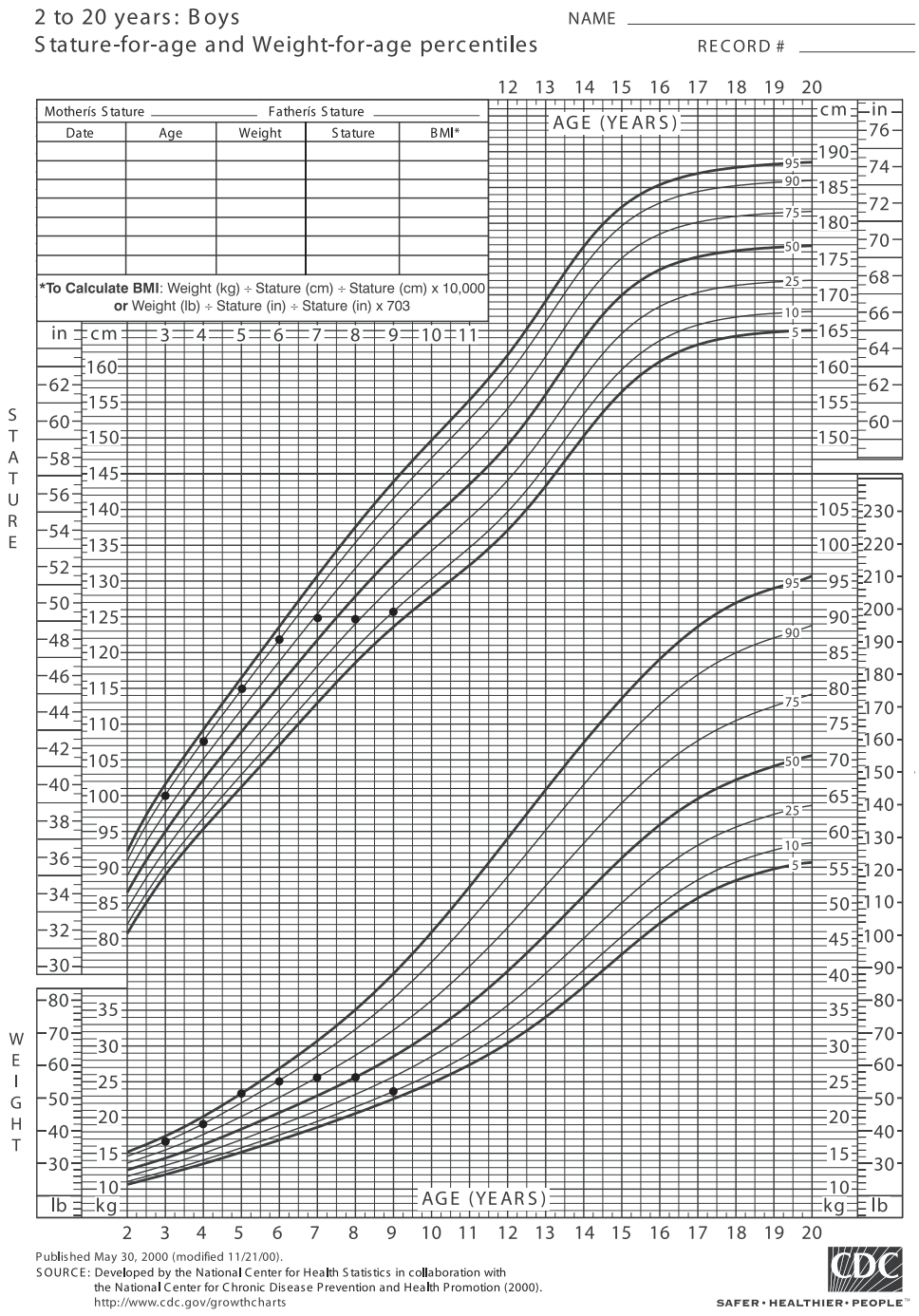
HANDOUT #3

Growth Chart



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HANDOUT #4

Antidepressant Drug Interactions With the Cytochrome p450 System
Cyclosporin is extensively metabolized by the cytochrome P-450 3A enzyme system in the liver, and to a lesser degree in the gastrointestinal tract and the kidney.

Isoenzyme: 2D6
Substrate: Tricyclics, Paroxetine, Fluoxetine, Venlafaxine, Nefazodone, Trazodone
Inhibitor: Paroxetine, Fluoxetine, Sertraline
Inducer: None
Genetics: 5-10% of whites lack enzyme

Isoenzyme: 3A 3/4
Substrate: Amytriptyline, Imipramine
Inhibitor: Fluvoxamine, Nefazodone, Fluoxetine, Sertraline
Inducer: None
Genetics: None

Isoenzyme: 1A2
Substrate: 3 tricyclics
Inhibitor: Fluvoxamine, Sertraline
Inducer: None
Genetics: None

Isoenzyme: 2C19
Substrate: 3 tricyclics
Inhibitor: Fluoxetine, Sertraline
Inducer: None
Genetics: 15-20% of Asians lack enzyme

Isoenzyme: 2E1
Substrate: None
Inhibitor: Fluvoxamine
Inducer: None
Genetics: None

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