Drug-drug interactions in psychopharmacology
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Drug interactions are ubiquitous
• Only rarely an absolute contraindication
• Only one of many factors involved in prescribing decisions
• More critical examples include: lithium, nortriptyline, monoamine oxidase inhibitors, pimozide, carbamazepine, ketoconazole

Other relevant factors
• Age
• Gender
• Hepatic or renal disease
• Smoking
• Alcohol use
• Diet and nutritional status
• Compliance
• Genetic polymorphisms

Examples of particular relevance
• Unexplained mental status changes
• Clinical deterioration
• Refractoriness to standard treatment
• Extreme or erratic drug plasma levels
• Issues with drug absorption, serum protein binding, altered elimination

Useful drug interactions
• Naloxone (Narcan) for opiate overdose
• Flumazenil (Romazicon) for benzodiazepine overdose
• Bethanechol (Urecholine) for anticholinergic side effects (urinary retention)
• Anticholinergics for antipsychotic induced extrapyramidal symptoms

Categories of drug interactions
• Idiosyncratic – rare, unpredictable, unexpected from pharmacokinetic and pharmacodynamic properties
• Pharmacodynamic
• Pharmacokinetic
Pharmacodynamic

- Known direct effects at biologically active receptor sites that do not involve an alteration in drug plasma levels
- May be additive, synergistic, or antagonistic

Pharmacodynamic examples

- CNS depression from alcohol, benzodiazepines and/or barbiturates
- Cardiac conduction delays from quinine-like effects i.e. low potency antipsychotics and tricyclic antidepressants
- Anticholinergic toxicity from drugs sharing antimuscarinic properties

Pharmacodynamic examples

- Hypotension with alpha-1-adrenergic blockade
  - Antidepressants – trazodone, imipramine
  - Low potency and atypical antipsychotics – clozapine, olanzapine
  - Interference with dopamine agonist or precursor for Parkinson's disease or hyperprolactinemia by an antipsychotic

Pharmacokinetic interactions

- Involve a change in the plasma level and/or tissue distribution of drugs, rather than their pharmacological activity.
- Mediated by effects on
  - Absorption
  - Distribution
  - Metabolism
  - Excretion

Children compared with adults

- Greater hepatic capacity
- More glomerular filtration
- Less fatty tissue
- Therefore more rapid elimination of stimulants, antipsychotics, TCAs, lithium
- Shorter half-life of meds in children
- Higher mg/kg dosing is usually required

Absorption issues

- Accelerated gastric emptying
  - Metaclopramide (Reglan)
- Diminished gastrointestinal motility
  - TCA's, morphine, cannabis
- Binding to other drugs
  - Cholestyramine (Questran), charcoal, kaolin-pectin, non-absorbable fats
Absorption issues

• Altered gastric pH
  – Aluminum hydroxide, magnesium hydroxide, sodium bicarbonate, potentially altering the non-polar, un-ionized fraction of drug available for absorption
• inhibition of gastric or intestinal enzymes resulting in elevated concentration of substrate
  – Monoamine oxidase – tyramine

Distribution issues

• Regional blood flow
• Lipophilicity
• Amount of drug bound to tissue and plasma proteins
• Adipose to lean body mass ratio

Competition for protein-binding sites

• Most psychotropic drugs are highly protein-bound at 80% to 90% to albumin, alpha-1-acid glycoproteins, or lipoproteins
• Effects usually have no practical significance because of offset by rapid redistribution to sites of metabolism

Minimal protein binding

• Lithium
• Gabapentin
• Topiramate
• Oxcarbazine
• venlafaxine

Effects on transport to tissue

• Amino acids competing with l-dopa for protein carrier across blood-brain barrier

Interference with metabolism

• Phase I
  – Oxidation, reduction, hydrolysis
• Phase II
  – Glucuronidation and acetylation resulting in highly polar, water-soluble metabolites suitable for renal excretion
Exceptions

- Benzodiazepines (lorazepam, oxazepam, temazepam, and clonazepam undergo only Phase II
- Lithium, gabapentin, and amantadine are excreted by the kidneys without hepatic biotransformation

Metabolic enzymes

- Cytochrome P450 isoenzymes
  - Inducing agents produce gradual decline of substrate level
  - Inhibitors produce abrupt elevations over hours to days of blood levels and levels fall rapidly upon discontinuation
- Flavin-containing monoxygenases (FMOs), N-acetyltransferase, glucuronyltransferases, methyltransferases, and sulfotransferases

Renal excretion

- Lithium interactions
- Emergency management
  - Enhanced excretion of weak bases such as PCP and amphetamines by acidification of urine with ammonium chloride
  - Enhanced excretion of weak acids such as tricyclic antidepressants and barbiturates with acetazolamide

Cytochrome P450 isoenzymes

- Over 30
- Located in the endoplasmic reticulum of hepatocytes and GI tract and brain
  - 1A2
  - 2C
  - 2D6
  - 2A3/4

2D6 polymorphisms

- 2D6
  - 7-10% Caucasians are poor metabolizers
  - 1-3% A-A or Asian
  - Have higher baseline concentrations of substrate, lower concentration of metabolites, and little effect from inhibitors or inducers

1A2 substrates

- Acetaminophen, aminophylline, caffeine, clozapine, haloperidol, olanzapine, phenacetin, procainogens, ropinirole, tertiary tricyclic antidepressants, theophylline
1A2
- Inhibitors
  - Fluoroquinolones (Cipro), fluvoxamine, grapefruit juice
- Inducers
  - Cigarette smoking, omeprazole (Prilosec), charbroiled meats

2C
- Substrates
  - Barbiturates, diazepam, NSAIDS, propranolol, tertiary TCA’s, THC, tolbutamide, warfarin
- Inhibitors
  - Fluoxetine, fluvoxamine, ketoconazole, omeprazole, oxcarbazepine, sertraline
- Inducers
  - rifampin

2D6 Substrates
- Amoxetine (Strattera), beta-blockers (lipophilic), codeine, donepezil (Aricept), dextromethorphan, encainide, flecainide, haloperidol, hydroxycodone, phenothiazines, risperidone, aripiprazole, SSRIs, TCAs, tramadol (Ultram)

2D6 Inhibitors
- Antimalarials, bupropion, duloxetine, fluoxetine, methadone, moclobemide, paroxetine, phenothiazines, protease inhibitors (ritonavir), quinidine, sertraline, TCAs, yohimbine
- Inducers ?

3A3/4 Substrates
- Alprazolam, amiodarone, aripiprazole, buspirone, calcium channel blockers, carbamazepine, clozapine, cyclosporine, diazepam, disopyramide, estradiol, lidocaine, lovastatin, loratadine, methadone, midazolam, quetiapine, sildenafil, simvastatin, tertiary TCAs, triazolam, warfarin, zaleplon (Sonata), ziprasodone, zolpidem (Ambien)

3A3/4
- Inhibitors
  - Ketoconazole, verapamil, cimetidine, fluvoxamine, grapefruit juice, erythromycin, nefazodone
- Inducers
  - Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, St. John’s wort
PSYCHOTROPIC SIDE EFFECTS

Developmental Considerations

• Developmental Issues
• Medications
• Contraindications
• Interactions
• Side effects
• Important notes

• Increased renal clearance
• Hormonal changes during puberty
• Increased hepatic metabolism

Stimulants:

• ADHD in children and adolescents
• ADHD in adults (Adderall)
• Narcolepsy

Others off label…

Contraindications:

• Hypersensitivity
• Cardiac abnormalities
• Active psychosis
• MAOI treatment
• Glaucoma

Side Effects

• Irritability, dysphoria, GI disturbance, insomnia, increased heart rate, decreased appetite, ?tics
• Sudden death risk (Adderall)-Risks when personal or family history of cardiac problems esp long QTc.

• Concerns re: clonidine and methylphenidate? …
Atomoxetine

- Rebound
- Headache
- Irritability
- Tics

- Indicated kids 6 years and over for ADHD
- Contraindication: Narrow Angle Glaucoma
- Somnolence, fatigue, decreased appetite, weight loss
- Warnings: hepatic injury and suicidality

Tricyclic antidepressants

- Indications: ADHD, OCD, Enuresis
- Contraindication: MAOI
- Relative: Pregnancy, cardiac problems, thyroid conditions

- Sudden cardiac death in children with desipramine- 7 cases. (Ref; Varley, CK(2001) Pediatric Drugs 3(8) 613. Several of the children had family history of cardiac problems

TCAs and Cardiac Monitoring

- Baseline EKG and blood pressure, pulse and repeat with increased dose and every three months.

Alpha Adrenergic Agents – Clonidine and Guanfacine

- ADHD, Tourettes, tics (all off label)
- Contraindication: cardiac problems, renal or liver disease
- Side effects: Sedation, hypotension, dizziness, abdominal pain
### Mood stabilizers

- Lithium
- Valproate
- Carbamazepine
- Lamotrigine
- Gabapentin
- Topiramate

### Lithium

- **Indication:** Acute mania and prophylaxis over 12 yrs
- **Side effects:** weight gain, psoriasis, enuresis, polyuria, polydipsia, hypothyroidism.
- **Narrow therapeutic window.**
- **Ebstein’s abnormality in pregnancy**
- **Toxicity symptoms...coarse tremor**

### Lithium

- **Increased** lithium level  
  - Thiazide diuretics, ACE inhibitors, NSAIDS (except sulindac, aspirin), metronidazole, spectinomycin, tetracycline
- **Decreased** lithium level  
  - Aminophylline, theophylline, acetazolamide, sodium bicarbonate, sodium chloride, osmotic diuretics (mannitol, urea)
- **Increased antithyroid effect**
- **Check calcium (PTH)**
- **Neurotoxicity** (rare)  
  - Antipsychotics, calcium channel blockers, carbamazepine, methyldopa
- **Prolonged neuromuscular blockade**  
  - Succinylcholine, pancuronium
- **Serotonin syndrome** (rare)  
  - SSRIs, serotonergic TCAs, tramadol, venlafaxine

### Valproate

- **Indications in adults:** migraines, partial seizures, mania or mixed episodes
- **Side Effects:** nausea, sedation, inc. appetite, hair loss, black box warnings for hepatotoxicity and pancreatitis
- **Polycystic ovary disease**

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**Informed consent re: medication interactions, ex. No NSAIDs, careful hydration, inform of new medications.**
Valproate

- Increased valproate levels
  - Aspirin (increased unbound levels), cimetidine, erythromycin, ibuprofen, phenothiazines
- Decreased valproate levels
  - Carbamazepine, phenobarbital, phenytoin, rifampin

Valproate

- Inhibited metabolism of co-administered agents
  - Lorazepam, oxazepam, tempazepam, diazepam, LAMOTRIGINE, carbamazepine, phenobarbital, tolbutamide, warfarin, AZT

Carbamazepine

- No indication in children, in adults indicated for acute manic and mixed episodes
- Cytochrome P450 interactions and autoinduction
- Hyponatremia
- Black box agranulocytosis

Carbamazepine

- Increased carbamazepine levels
  - Valproate (active CBZ-E metabolite), P450 3A4 inhibitors, antifungals, macrolide antibiotics, calcium channel blockers, fluvoxamine, grapefruit juice, isoniazid, nefazodone, protease inhibitors
- Decreased carbamazepine levels
  - Carbamazepine (autoinduction), phenobarbital, phenytoin, primidone
- Induced metabolism of co-administered agents
  - Anticonvulsants (phenytoin, lamotrigine, valproate), antidepressants, antipsychotics, benzodiazepines, cyclosporine, glucocorticoids, methadone, oral contraceptives, warfarin

Carbamazepine

- Carbamazepine– autoinduction after several weeks
  - Hyponatremia
Effects of P450 inhibition

- Antihistamines (astemizole, loratidine) 3A4
- Antipsychotics
  - 1A2 clozapine, olanzapine, haloperidol
  - 2D6 risperidone, phenothiazines
  - 3A4 quetiapine
- Benzodiazepines
  - 2C diazepam
  - 3A4 triazolam

Effects of P450 inhibition

- Codeine
  - Metabolized by 2D6 into active (morphine) metabolite
- Secondary TCAs
  - Metabolized by 2D6
- Tertiary TCAs
  - Metabolized by 1A2, 2C, 2D6, 3A4

2D6

- Most inhibition
  - Fluoxetine, paroxetine, duloxetine
- Moderate inhibition
  - Sertraline
- Negligible inhibition
  - Citalopram, escitalopram

Serotonin syndrome

- Myoclonus
- Hyperreflexia
- Nausea
- Hyperthermia
- Autonomic instability
- Agitation
- Delirium
- Coma

Serotonin Syndrome

- Monoamine oxidase inhibitors
  - Remember Demerol
- Lithium
- Serotonergic agents

TCA interactions

- Increased TCA levels
  - Methylphenidate, SSRIs
- Decreased TCA levels
  - Carbamazepine, phenobarbital, phenytoin
- Prolonged cardiac conduction
  - Type I antiarrhythmics, low potency antipsychotics, CCBs
- Hypotension
  - Antihypertensives, antipsychotics, trazodone
Antipsychotic interactions

• Increased antipsychotic levels
  – Inhibitors of 1A2, 2D6, 3A4 including fluoxetine, paroxetine, fluvoxamine, nefazodone, bupropion, duloxetine, fluoroquinolones, macrolides, antifungals
• Decreased antipsychotic levels
  – Lipophilic betablockers, carbamazepine, phenobarbital, phenytoin

Antipsychotic interactions

• Decreased absorption - antacids
• Prolonged cardiac conduction
  – CCBs, TCAs, P450 inhibitors
• Hypotension – TCAs, trazodone
• Anticholinergic toxicity
• Interference with dopaminergic effects
• Additive risk of myelosuppression
  – Carbamazepine, AZT with clozapine

Antipsychotic interactions

• Pimozide (Orap) 3A4
  – Dangerous arrhythmia potential
• Clozapine, olanzapine, haloperidol 1A2
  – Inhibited by Luvox, Cipro
  – Induced by omeprazole, cigarette smoking
• Phenothiazines are both substrates and inhibitors of 2D6

Antipsychotic interactions

• Quetiapine and ziprasidone are 3A4 substrates
  – Concentration increased by erythromycin
  – Concentration decreased by carbamazepine
• Aripiprazole substrate of 3A4 and 2D6
  – Increased by fluoxetine
  – Decreased by carbamazepine

Neuroleptic Malignant Syndrome

• CPK elevation
• Neuroleptics
• Autonomic instability
• Delirium
• Febrile
• Dantrolene

Concerns with Atypical Antipsychotics

• Metabolic syndrome
• EPS
• Tardive dyskinesia
• Hyperprolactinemia
• Cardiac
Cardiac
• Monitor baseline and when raise mediation.
• Caution with QTC $\geq 450$!
  or high HR
Or elevated PR or QRS

Monitor

Anxiolytic pharmacodynamics
• Additive CNS depressant effects
  – Barbiturates
  – Antihistamines
  – TCAs
  – Antipsychotics
  – Antiepileptic drugs
  – Hypnotics – zolpidem, zaleplon, Lunesta
  – alcohol

Anxiolytic pharmacokinetics
• Antacids may delay absorption
• Phase I inducers (CBZ, PHB) may lower blood levels except lorazepam, oxazepam, and temazepam
• Valproate inhibits glucuronide conjugation increasing levels of lorazepam, oxazepam, and temazepam

Anxiolytic pharmacokinetics
• 3A3/4 inhibitors – macrolides, antifungals, nefazodone, fluvoxamine, grapefruit juice may increase levels of alprazolam, triazolam and midazolam
• 2C inhibitors – omeprazole, ketoconazole, fluoxetine, fluvoxamine, sertraline, may increase levels of diazepam

St. John’s wort induces 3A4
• Cyclosporine
• Antiretrovirals
• Anticoagulants
• Theophylline
• Digoxin
• Oral contraceptives

Methylphenidate
• Inhibits metabolism of
  – SSRIs
  – TCAs
  – anticonvulsants
Modafinil (Provigil)
• Induces 3A4
• May lower level and effectiveness of oral contraceptives

Atomoxetine (Strattera)
• Substrate of 2D6
• Metabolism is inhibited by fluoxetine, paroxetine, bupropion

Cholinesterase inhibitors
• Rivastigmine (Exelon) has no P450 aspect

• Galantamine (Rasadyne) and donepezil (Aricept) are substrates for 2D6 and 3A4 but do not induce or inhibit P450

Codeine
• Substrate of 2D6 which converts it into its active form (morphine). Diminished analgesic effect if co-administered with 2D6 inhibitor

Disulfiram (Antabuse)
• Inhibits any array of enzymes interfering with the metabolism of a variety of drugs

SSRIs
• Indications:
  – MDD: Fluoxetine
  – OCD: Clomipramine, Fluoxetine, Flv, sertraline
  – SIDE EFFECTS: include GI, headache, and behavioral activation
  – Suicidality black box warning: extended til mid 20’s re: increased risk of suicidality 4X vs. 2X in placebo in pooled data
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ADJUSTMENT DISORDERS
Shauna P. Reinblatt, MD

Adjustment Disorder def.

- An adjustment disorder is a psychological response to an identifiable stressor or stressors that results in the development of clinically significant emotional or behavioral symptoms.
- The symptoms must develop within 3 months after the onset of the stressor(s).
- Clinical significance of the reaction is determined by either marked distress in excess of what would be expected given the nature of the stressor or by significant impairment in social, occupational, or academic functioning.
- A normal or expectable reaction to a stressor can qualify as an adjustment disorder if the reaction is sufficiently severe to cause significant impairment.

The stressor may be single or multiple, recurrent or continuous, minor or severe, common or unique – in short, the stressor need only be a psychosocial event that precedes the symptoms and that the patient and/or therapist views as stressful and responsible for the symptoms.

The maladaptive reaction must be severe enough to impair school (or work) performance, hinder social activities or interpersonal relationships, and/or be in "excess of a normal and expectable reaction to the stressor(s)."

Adjustment disorder = age independent, defined primarily by its symptom picture rather than by age

The DSM-IV also recognizes that the patient’s vulnerability is as important to symptom production as is the exact stressor

The disturbance must be something other than “one instance of a pattern of overreaction to stress” or an exacerbation of another mental illness.

Classification

Adjustment disorder is a specific diagnosis, not a nebulous category.

The current DSM-IV diagnosis is a refinement of a number of similar diagnoses developed over the years and called reactive, transient, situational, and adjustment disorders.

The Group for the Advancement of Psychiatry Committee on Child Psychiatry (GAP) in 1966 used reactive disorder to describe a generally (but not exclusively) transient disorder caused by an emotionally traumatic event that reflected a conscious conflict between the child and his or her environment. The DSM-II (1968) described a set of “transient situational disturbances”.

Classification

DSM-III (1980) renamed this category adjustment disorder and required that specific objective criteria be met to make the diagnosis. The DSM-III also defined 8 subtypes based upon symptom patterns, excluded very minor symptom pictures as well as psychotic reactions (reclassified as brief psychotic reactions), and removed the developmental stage (age) requirement. With minor variations, this is the classification in place today in DSM-IV.
Caveats

- One of the most telling problems lies not with the severity of the stressor but with its chronicity.
- If a stressor is continuously present or frequently recurrent, does the disturbance become something other than an adjustment disorder after 6 months?
- Those patients with chronic symptoms due to ongoing stress who also do not meet criteria for another diagnosis fit poorly within this nosology.
- In addition, sometimes it is exceptionally difficult in the clinical situation to differentiate between a parent-child problem or uncomplicated bereavement and an adjustment disorder. -- the severity of both stressors and symptoms is continuous rather than discrete.

DSM-IV diagnostic criteria for adjustment disorders

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. Symptoms are clinically significant as evidenced by the following:
   - Marked distress that is in excess of what would be expected from exposure to the stressor
   - 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.
5. Once the stressor (or its consequences) has terminated, the symptoms do not persist for more than an additional 6 months

Types

- Acute: if the disturbance last fewer than 6 months
- Chronic: if the disturbance lasts for 6 months or longer

With depressed mood -

- Differential diagnosis includes major depression, dysthymia, bipolar disorder (depressed), uncomplicated bereavement, mood disorder 2e GMC.
- Considered by some to be the most common subtype among adults,
- also common among children

- This diagnosis requires a predominance of symptoms of depressed mood, tearfulness, and feelings of hopelessness.
- The differential diagnosis is broad in that it includes not only key mood disorders but also uncomplicated bereavement, which can be viewed as a variant of adjustment disorder – serious depressive symptoms in response to the loss of a loved one that, however, are an expected reaction to such a severe stress.
• Axis II disorders of the borderline and histrionic types, particularly in adolescents, are likely to present with depressive symptoms and develop in an individual from a turbulent environment.

With anxiety-

• differential diagnosis=
  – generalized anxiety disorder,
  – panic disorder,
  – post traumatic stress disorder
  – anxiety disorder 2e GMC

With disturbance of conduct

• Differential diagnosis includes conduct disorder, oppositional-defiant disorder; child or adolescent antisocial behavior (V-code).

With mixed anxiety and depressed mood - differential diagnosis includes mood and anxiety disorders.

• differential diagnosis=

With disturbance of conduct

• Differential diagnosis includes conduct disorder, oppositional-defiant disorder; child or adolescent antisocial behavior (V-code).

• This subtype requires the violation of the rights of others (eg. vandalism and fighting), and conduct-disordered behavior such as truancy, reckless driving, and defaulting on legal responsibilities.

• It is particularly common in adolescents but can also occur in children. The primary differential, of course, is with conduct disorder and oppositional defiant disorder but needs also to include the lesser degree of misbehavior found in the V Code category of childhood or adolescent antisocial behavior. Limited evidence suggests a poor prognosis in children who react to stress with this behavior pattern.

• With mixed disturbance of emotions and conduct

• Differential diagnosis includes disruptive behavioral disorders. The most likely differential is with the combination of a conduct disorder and a full emotional disorder of some type.

• Includes emotional and conduct manifestations. It is presumably uncommon in adults but will find occasional use with children and adolescents. The most common pattern seems to be disordered behavior with a depressed mood, although other combinations are possible. Few data are available about this condition.

• Unspecified - "wastebasket." This may include such things as massive denial of illness, markedly regressed behavior, or a preoccupation with fantasies

Prevalence

• Between 2% and 8% in community samples of children and adolescents and the elderly.

• It has been diagnosed in up to 12% of general hospital inpatients who are referred for a mental health consultation, in 10%-30% of those in mental health outpatient settings, and in as many as 50% in special populations that have experienced a specific stressor (eg, following cardiac surgery).

• Individuals from disadvantaged life circumstances experience a high rate of stressors and may be at increased risk for the disorder. (DSM-IV-TR, pg 681) The New York Longitudinal Study of Temperament notes that adjustment disorder was the primary diagnosis in 40 of the 45 children in their study who developed a mental illness prior to 13 years of age. The majority of cases occurred in the 3-5 age group, and mild cases predominated. Although the number of afflicted children was small, the findings are particularly significant since their sample flowed from a healthy population that during the course of the study developed illness, rather than from a self-selected population of psychiatric patients. Thus their figure compares the relative frequency of children in the general population who develop an adjustment disorder to those who develop other mental illness.

Schwartz_Reinblatt_Adjustment Disorders 3
Etiology

- Vulnerability of the child is the most important factor in the development of an adjustment disorder.
- Type of stressor

Course

- By definition, the disorder begins within 3 months of onset of a stressor and lasts no longer than 6 months after the stressor has ceased.
- If the stressor is an acute event, the disturbance is usually immediate and the duration relatively brief.
- If the stressor persists, the disorder may also persist. The persistence of adjustment disorder or progression to other, more severe mental disorders (e.g., major depressive disorder) may be more likely in children and adolescents than in adults. This increased risk may be attributable to the presence of co-morbid conditions (e.g., attention-deficit/hyperactivity disorder) or to the possibility that the adjustment disorder actually represented a subclinical prodrome manifestation of the more severe mental disorder.

Three DSM-IV Disorders in Response to Stressors

- Adjustment disorder
  - Described as the development of clinically significant, emotional or behavioral symptoms in response to an identifiable psychosocial stressor, (personal misfortune) within three months of the onset of the stress.
  - The stressor may be of any degree of intensity and the degree of dysfunction does not appear to be related directly to what the stressor is.
  - Chronic stressors which may lead to chronic adjustment disorders include medical conditions that are ongoing and chronically disabling or a stressor of enduring consequences, such as financial or emotional difficulties resulting from their parent’s divorce.

Differential

- Adjustment disorder with depressed mood
  - 1. The differential diagnosis is between major depression, dysthymia or bipolar disorder, depressed phase, or uncomplicated bereavement.
    - Vegetative signs are not as prominent in children and adolescents, specifically motor retardation or weight loss or change.
    - Guilt is more typical in depressive disorders than in adjustment reaction.
Bereavement

• Viewed by some as a variant of adjustment disorder, although the diagnosis of adjustment disorder is not to be made in this circumstance. Bereavement is generally diagnosed when the reaction is an expectable response to the death of a loved one. The diagnosis of adjustment disorder, on the other hand, may be made when the reaction is in excess of, or more prolonged than, that normally expected. • Serious depressive symptoms as an expected reaction to loss do not qualify for adjustment disorder.

Bipolar disorder

• There is often a familial loading [might also be present in major depression]. • The children tend not to be normal between cycles. • Pre-pubertal children may have school phobia and evidence of impaired concentration • Adolescents appear irritable, aggressive, have increased activity, loud speech, and suicidality; Unreasonable or unpredictable explosive behavior In children, the loss of self-esteem and the presence of guilt is probably the most helpful distinctions.

Other adjustment disorder characteristics

1. In making the differential, assess whether symptoms reflect a consistent pattern of behavior over time, the quality of the family relationships, and the presence of a precipitating condition.
2. The differential diagnosis of adjustment disorders also includes certain personality disorders, specifically borderline and hysterical personality.
3. Look for specific ego deficits such as poor reality testing, and inadequate development of age-appropriate defense mechanisms. [These should be chronic and without the evidence of a specific stressor.]

Pharmacotherapy

• Drugs may be useful in treating the specific symptoms; brief periods. All drug categories are applicable but particularly the antianxiety and antidepressant medications. Antipsychotic medications may be useful for severe anxiety and decompensation, and psychostimulant medication may work for withdrawn or inhibited states or children with comorbid ADHD.

Miscellaneous Information Re: Adjustment Disorders

• Children tend to develop guilt for a personal illness. This is most likely in children who have had no previous experience with a serious illness or with younger children who are likely to assume that the illness is a punishment. Providing a child with explanations for the cause of an illness lessens the chance of this occurring.
• The birth of a child with congenital defects presents the family with a crisis similar to a premature birth. Conflicts may develop around the appearance of the baby and related social stigma.
• Families experiencing early death of an infant would benefit from interventions such as support groups, visual and physical contact with the infant, ongoing psychosocial follow-ups, and routine autopsy.
• Adolescents experience a greater amount of anxiety compared to younger children related to medical procedures and chemotherapy. A lack of protest regarding a procedure is not always synonymous with the lack of distress. In children, the thing that helps most in coping with pain experience is the presence of a parent.

• Hospitalizations occurring from the 12th to 48th month age are associated with later difficulty in adaptive functioning.

• Factors associated with increased risk for psychological morbidity in children following the death of a sibling include (a) loss that occurred when a child was under 5 years of age or during early adolescence; (b) unanticipated death or deaths from suicide or homicide; and (c) lack of adequate family or community support.

• Increased risk of morbidity also include the loss of a mother for girls fewer than 11 years of age and loss of a father for adolescent boys.

• Even though some cases remit without intervention, adjustment disorder is not a minor condition requiring no treatment. It is painful for the patient and the patient’s family, likely to worsen if the illness and its underlying causes are not addressed, and often responsive to vigorous and appropriate treatment.

• Treatment begins with a thorough evaluation, including a search for physical causes for any physical symptoms present. Because adjustment disorder can mimic so many different psychiatric disorders, such other conditions must be sought in the hope of finding a specific treatment for the child’s difficulties.

• The next step is to remove the stressor, if possible.

• The core of treatment typically centers around both working with the child individually to address his or her concerns and working with the family about many of the same issues. The conceptual approach and techniques used, of course, depend in part on the age of the child and the therapist’s assessment.

• Treatment generally should be brief and focused, with an emphasis on the child’s adjustments to the difficulties he or she has experienced. The stressor must not be ignored, particularly if chronic; rather, the child should be allowed (or encouraged) to express fear, dismay, resentment, and anger.

• Avoid, except temporarily and for very well-determined reasons, fostering regression or the hope of a magical recovery. A supportive, problem-solving approach often works well and individual therapy becomes indispensable when the family is destructive or has few resources upon which to draw.

• Because the family is bound up in so many of the stressors faced by these children, family therapy is an equally essential mode of intervention. The family should be involved in any efforts at behavioral management and environmental manipulation, if they can participate constructively.

• Limited research in this area; treatment relies on clinical judgment.
Individual Psychotherapy in Children and Adolescents

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Psychotherapy
- Individual
- Group
- Family

Goals of Psychotherapy
- Reduction in Psychiatric symptoms
- Treatment of underlying cause of symptoms

Focus of Treatment
- Cognitive functions: Thought disorders
- Affective functions: Emotional /Mood problems
- Behavior functions: Compulsions

Psychodynamic psychotherapy
- Unconscious conflict
- Unbalanced id/ ego/superego
- Defense mechanisms
- Transference/ countertransference

Play therapy
- Drawings
- Toys
- Psychodynamic, short term
Psychic Determinism

- Individuals are unaware of unconscious factors that determine their emotions, moods and behavior
- We are all unconsciously controlled

Psychoanalytic treatment

- Role of unconscious factors affecting current relationships and behavior
- Helps the individual to deal better with the realities of adult life

Transference
- Patient unconsciously reenacts the past significant relationship

Interpretation of Transference

- Feelings, Emotions, Thoughts are encouraged in Therapy
- Transference: Unconscious
- Interpretation makes it conscious for the patient and leads to recovery

Countertransference

- Psychiatrist develops Counter transference
- Patient reminds the psychiatrist about someone from his past
- Countertransference is monitored internally by the psychiatrist
- Awareness of Countertransference prevents Psychiatrist’s anti-therapeutic behavior/response

Resistance

- Patient’s attempt to oppose gaining insight and change
- Represents a compromise between forces of recovery and pathology
- Late for appointment
- Silent in Sessions
- Non compliance

Methodology: Psychoanalysis

- Typically, the patient comes four or five times a week
- Lies on a couch
- Not suitable for children and Adolescents
- Fantasies, dreams, and fears reveal clinical data
Window to Unconscious

- Uncomfortable Unconscious material or drives come out in indirect way:
  - Slip of tongue
  - Fantasies
  - Dreams.

“Defenses”:

- Opposing forces prevent expression of “Wishes”
  - Denial
  - Projection

Tripartite Structural Model of Freud

- Id
  - Unconscious
  - Discharges tension
  - Aggressive drive
  - Libidinal or sexual drive

- Ego
  - Unconscious + Conscious
  - Unconscious contains Defenses
  - Conscious integrates information, executes action and makes decision

- Superego
  - Policeman of psyche
  - Moral Conscience: internalization of parental or societal values
  - Ego ideal: role model
Ego Psychology

- Id has sexual and aggressive drives which want expression, but ego and superego opposes their expression
- Conflict produces anxiety
- Anxiety produces a defense
- Defenses lead to formation of psychiatric symptoms

Defenses

- Part of Ego
- Defenses protect ego from sexual and aggressive drives from id.

Defense: Repression

- Freud
- Expels unacceptable drives, wishes or fantasies from conscious awareness
- It produces distress “Conflict model”
- Explains Neurotic symptoms i.e. anxiety, depression and Hysterical Neurosis (Loss of strength in one arm)

Defense: Displacement

- Feelings, emotions are redirected to another target
- Angry at boss hits a dog on the street

Object Relations Theory

- Previous relationships leave mental representations of self and others
- Drives emerge in context of a relationship
- Infant-mother relationship
- Interpersonal relationships are internalized as self-object representations of relationships

Rapprochement

- Between 16 to 24 months of age
- Realizes more separateness from the mother
- Increased sense of vulnerability to separations from mother
- Checks back frequently with the mother