

**Medication Management  
in FASD**

**Presenter:** Dr. David Shih, MD, FRCP  
**Date:** November 25, 2009

**Government  
of Alberta**

The FASD Learning Series is part of the Alberta government's commitment to programs and services for people affected by FASD and those who support them.

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**Learning Objectives**

- Learn the steps before using medications
- Learn the basics of medication choices for treating insomnia, aggression, Anxiety Disorders, ADHD, and Mood Disorders in FASD
- Understand what medications can do and cannot do

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**Before Using Psychiatric  
Medications**

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### ***Before Using Psychiatric Medications***



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### ***Psychological Interventions***

- Review and enhance life-style changes
- Behavioral modification
- Psychotherapy to work through emotions and past trauma (e.g. Play Therapy or Talk Therapy)
- Group therapy or family therapy
- Psychotherapy to work on attachment for younger children
- Specific treatment of certain conditions e.g. treat concurrent substance abuse (AADAC)

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### ***Social Interventions***

- Environmental modification (e.g. visual cues)
- Consider a case conference with school or other providers
- Encourage parents to talk to friends and pharmacists, to consult parent groups, and to check internet resources for information on medications

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*Psychotropic Medications*

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*Psychotropic Medications*



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*Medical check to make sure the problems are not due to a physical problem.*

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## Medical Tests

Recent medical examination

And

Basic blood tests

➤ To rule out other medical problems

- Anemia
- Hypothyroid

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## Medical Tests

Basic blood tests (continued)

➤ As baseline if anticipating the use of certain medications

- CBC
- TSH
- Prolactin
- Fasting blood sugar
- Lipid profile

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## How Psychiatric Medications Work

➤ Increase amount of neurotransmitters

- Serotonin
- Dopamine
- Noradrenaline

in the synapse

- SSRIs
- Stimulants

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### **How Psychiatric Medications Work**

- **Improve the function of Inhibition circuits in the brain**
  - Clonidine
- **Block the effects of neurotransmitters on certain brain cells**
  - Risperidone

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### **Psychiatric Medications**

- Improves the connections and regulation of existing brain cells and circuitry
- They do not teach the brain how to work better
- They do not create new circuits
  
- **Only environmental teaching and learning creates new brain circuits**

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### **Making Sure You Have the Right Diagnosis**

- **Full psychiatric history** and mental status examination
- And
- **Formulation** (biological-psychological-social understanding of the child or teen)
  - **DSM IV Multi-Axial Diagnosis**

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**Disclosure to Parents**

- Inform parents of the **level of evidence** in the use of medications
- Often medications are use in an “**off-label**” manner in treating disorders in children and teens
- Provide **medication information sheets**
- **Disclose any side-effect that may be fatal no matter how rare**

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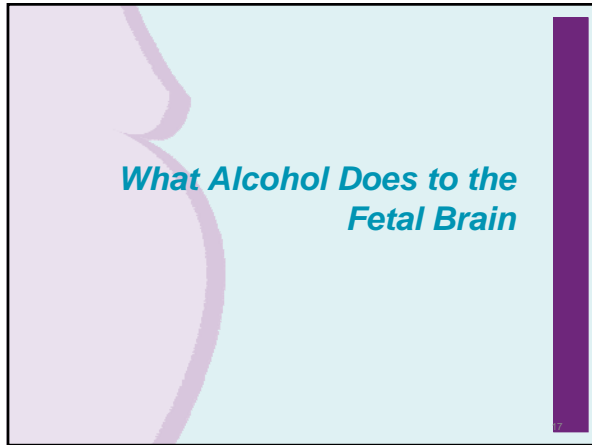
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**What Alcohol Does to the Fetal Brain**



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**What Alcohol Does to the Fetal Brain**



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### **Alcohol As Neurotoxin on the Developing Brain**

#### **Alcohol damages**

- The inside of brain cells
- The positioning of cells during brain growth
- The brain circuits
- The Serotonin and Dopamine brain circuits
- Alcohol kills brain cells

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### **Medications Used in Persons with FASD**

#### **Because of the damage to the brain cells and circuits**

- Medications may not work the way we expect
- Lower doses may help
- Higher doses may be needed
- There may be more side-effects than expected

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### **Points to Remember**

- Many organs in the body can be damaged
- Make sure the child has been fully examined by a Pediatrician
- FASD is not just a pediatric condition – it is a medical condition that impacts the individual across the lifespan

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***FASD and Accompanying Conditions***

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***FASD and Accompanying Conditions***



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***Accompanying Conditions***

- **Insomnia**
- **Aggression**
- **MOOD DISORDERS**
  - Major Depressive Disorder
  - Bipolar Disorder
- **ANXIETY DISORDERS**
  - Generalized Anxiety Disorder
  - Obsessive-Compulsive Disorder
- **Attention Deficit Hyperactivity Disorder (ADHD)**

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**Presentation Framework for Each Condition**

- What are the medication choices?
- What is the evidence for this medication?
- What are the common and serious side-effects of the medications?
- Assessing response and when to stop?

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**Levels of Evidence for Medications**

1. Randomized double blind placebo-controlled trial "RDBPC" (best evidence)
2. Open studies (where the people know what medications they are taking)
3. Case reports

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**Medications Used for Insomnia**

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### Medications Used for Insomnia



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### Sleep Hygiene

- No television/ computer/ videogames in the bedroom
- Avoid caffeine four (4) hours before bedtime
- A light snack before bedtime is alright
- Hour before bedtime should be a quiet time
- Use the bed only for sleeping
- Sleeping is better in a cool room

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### Medications That Have Been Used for Sleep Problems in Children and Teens

#### OVER the COUNTER

- Antihistamines
  - Benadryl
- Melatonin

#### PRESCRIPTION

- Chloral Hydrate
- Clonidine
- Trazadone
- Zopiclone
- Neuroleptics
  - Neuleptil
  - Risperidone
  - Seroquel

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### **Medications Used for Sleep in Children**

- There are no medications for sleep approved by Health Canada for use in children
- There are no adequate studies in children of medications for sleep

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### **Side-Effects of Medications Used for Sleep**

#### **Antihistamines**

- Anticholinergic side-effects such as constipation
- May cause paradoxical excitation
- Overdose causes hallucinations and convulsions

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### **Side-Effects of Medications Used for Sleep**

#### **Chloral hydrate**

- Discontinuation after long term use might cause withdrawal delirium and seizures

#### **Clonidine**

- Sudden stoppage can cause rebound hypertension

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### Side-Effects of Medications Used for Sleep

#### Melatonin

- Largely unknown
- Abdominal cramps with large doses
- Fatigue
- Headache
- Dizziness
- Irritability

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### Update or Unique Characteristics of Medications Used for Sleep

- It is really not ideal to use medications for sleep for children unless there is **parental exhaustion**
- **Relief for a side-effect from another medication which is required** (e.g. insomnia caused by stimulant)
- Often **unknown environmental factors or family factors** are influencing the sleep of children and we may never know what they are

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### Additional Medications for Sleep in Adults

#### Sedative antidepressants

- Trazadone
- Amitriptyline
- Mirtazapine/ Remeron

#### Anticholinergic side-effects

- Dry mouth
- Constipation
- Urination difficulty

#### Side-effects

- Can be fatal in overdose

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**Additional Medications for Sleep in Adults**

**Benzodiazepines**

- Diazepam
- Valium
- Oxazepam
- Temazepam

**Side-effects**

- Can cause habituation (need more and more)

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**Medications Used to Reduce Aggression**

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**Medications Used to Reduce Aggression**



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### Theory of What Medications Do in Treating Aggression

- The medication **reduces impulsivity**
- The medications **lengthen the fuse**, thereby giving the person more time to make a choice
- The person still makes the choice and can be aggressive
- “Chemical restraint”

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### Choices and Evidence for Medications Used to Control Aggression

#### NEUROLEPTICS

- **Risperidone**
  - Has the best evidence from many large RDBPC trials showing it reduces aggressiveness in children over placebo
- **Olanzapine (Zyprexa) and Quetiapine (Seroquel)**
  - Have no RDBPC trials for aggression
- **Chlorpromazine**
  - Oldest medication

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### Side-Effects of Neuroleptics

- **Extrapyramidal** side-effects (muscle stiffness)
- Significant **metabolic** side-effects
  - Excessive weight gain
  - Alterations in glucose metabolism
  - Increase lipids
- Long term use of Neuroleptics increase the emergence of **Tardive Dyskinesia**

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**Choices and Evidence for Medications Used to Control Aggression**

**MOOD STABILIZERS**

- **Divalproex (Epival)**
  - One RDBPC trial of explosive youth found 80% response versus 25% on placebo
- **Carbamazepine (Tegretol)**
  - Some case reports
- **Lithium**
  - Two RDBPC trials of hospitalized children with conduct disorder lithium better than placebo

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**Choices and Evidence for Medications Used to Control Aggression**

**PSYCHOSTIMULANTS**

- **Methylphenidate and Dextroamphetamine**
  - Nine studies show some decreased aggression response in children with both Attention Deficit Hyperactivity Disorder and Conduct Disorder

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**Update on Medications Used for Aggression**

- **Rapid-onset preparations of Risperidone** (Risperidal M tabs) and **Olanzapine** (Zyprexa Zydis) **used sublingually** can provide quick pharmacological control (without using injections) if the person cooperates with taking the medication
- Regular medication management visits, fasting blood work, height and weight (BMI), and case conferences are essential

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*Medications for Anxiety Disorders*

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- Purpose of Medications in Anxiety Disorders*
- Reset the “panic alarm” so that it goes off less easily
  - Turns down the volume of the anxiety signal by reducing the physiological responses
  - Reduces the intensity of the cognitive worrying

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*High anxiety is like walking down a river with the water level high, making it harder to walk forwards.*

*The medication lowers the level of water in the river, making it easier to walk forwards.*

Dr Shih's "Walking Down The River Metaphor"

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### **Choices and Evidence for Medications Used for Anxiety Disorders in Children**

#### **For Generalized Anxiety Disorder**

- Positive RDBPC trial evidence
  - Sertraline (Zoloft)
  - Fluoxetine (Prozac)
  - Fluvoxamine (Luvox)
- No evidence for Venlafaxine (Effexor)

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### **Anxiety Disorders in Children**

*Do not use Benzodiazepine for anxiety disorders in children because of habituation and risk of disinhibition.*

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### **Choices and Evidence for Medications Used in Obsessive Compulsive Disorder (OCD) in Children and Teens**

USA FDA labeling approval for

- **Sertraline** (Zoloft)
- **Fluoxetine** (Prozac)
- **Fluvoxamine** (Luvox)

In several studies

- **Cognitive Behavioural Therapy (CBT)** is as good as Medication for OCD

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### **Unique Characteristics of Medications Used for Anxiety Disorders and OCD**

- **Start lower and slower in anxiety kids to reduce adverse effects**
- **Lower doses may be helpful**
- **Need higher doses for OCD**
- **Look at functional outcomes and not just reduction of anxiety or symptoms**

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### **Medications for Attention Deficit Hyperactivity Disorder**

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**Medications for Attention Deficit Hyperactivity Disorder**



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**Two Guidelines for Using Medications in ADHD**

Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (CADDRA)

[www.caddra.ca](http://www.caddra.ca)

Texas Department of State Health Services algorithm for ADHD

[www.dshs.state.tx/mhprograms/adhdpage.shtm](http://www.dshs.state.tx/mhprograms/adhdpage.shtm)

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**Factors in Choosing a Medication for ADHD**

- Duration of action
  - 4 hours
  - 6 hours
  - 12 hours
  - 24 hours
- Types of side-effects
  - Stimulant
  - Versus non-stimulant
- Flexibility
- Tablets or Capsules or Sprinkle
- Cost

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**Approach to Medications for ADHD**

- First choice is a Stimulant medication
  - Ritalin
  - Dexedrine
- Second choice is a Non-stimulant medication
- Ritalin, Dexedrine, Strattera, and Desipramine all have very good positive RDBPC trials

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**First Choice Is a Stimulant Medication**

**METHYLPHENIDATE (RITALIN)**

- Regular fast acting tablets (4 hours)
- 6 hours **Ritalin 20 mg SR tablet**
- 12 hours **Concerta** or **Biphentin** (sprinkle)

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**First Choice Is a Stimulant Medication**

**DEXTROAMPHETAMINE (DEXEDRINE)**

- Regular fast acting tablet (4 hours)
- 6 hours **Dexedrine Spansule**
- 12 hours **Adderall XR capsule** (sprinkle)

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### Side-Effects of Psychostimulants for ADHD

- May slow growth but ultimate height is not affected
- High doses associated with compulsive behaviours in vulnerable individuals with movement disorders
- Very high doses especially Dexedrine can cause damage to CNS and Cardiovascular system such as hypertension
- **Main side-effects are insomnia, decreased appetite, and tics**

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### Discussion on CADDRA Guidelines

The **CADDRA guidelines** recommend starting first line with the new long acting preparations

- Adderrall XR
- Biphentin
- Concerta
- Strattera

My concerns are that these are expensive medications that the family may not be able to afford, and if there is a disturbing side-effect during the day, it will last for 12 hours.

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### Second Non-Stimulant Choices for ADHD

#### ATOMOXETINE (STRATTERA)

- Begins working after 10 days
- 24 hours duration/ take every day

#### BUPROPION (WELLBUTRIN)

#### DESIPRAMINE or IMIPRAMINE

#### CLONIDINE

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**Side-Effects of Non-Stimulants Used for ADHD**

Strattera's most common side-effects are

- Decreased appetite
- Vomiting
- Somnolence
- Irritability
- Two cases of liver failure reported worldwide

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**Side-Effects of Non-Stimulants Used for ADHD**

Desipramine/ Imipramine can cause

- A tachycardia
- In some cases a dangerous heart block
- Slow metabolizers can have toxic serum concentrations

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**Unique Characteristics of Medications Used for ADHD**

The effectiveness of medications used for ADHD is measured by

- Using rating scales (e.g. Conner's, SNAP)
- Or asking for feedback from the teacher

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*Medication for ADHD is like a bicycle.*

*Child says he has to push the pedals to make the bicycle move.*

*The metaphor bicycle helps the child to get the work done faster in the time allocated.*

*Therefore the improved school marks are credited to the motivation of the child and not to the medication.*

Dr Shih's "Bicycle Metaphor" for ADHD Medications

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### **Unique Characteristics of Medications Used for ADHD**

- Medications may produce **unpredictable and paradoxical effect** in preschool children
- Medications are not as effective in adults

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### **Medications for Mood Disorders**

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### Medications for Mood Disorders



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### Mood Disorders

- Major Depressive Disorder
- Dysthymia
- Bipolar Disorder



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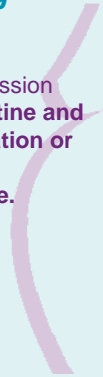
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### Research Evidence in Treating Depression

The Treatment for Adolescent with Depression Study (2006) showed **Combined Fluoxetine and CBT** appears superior to either medication or CBT alone, had a faster response, and improved functioning and quality of life.



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**Medications in Major Depression in Children and Adolescents**

**Selective Serotonin Reuptake Inhibitors (SSRI)**

- Prozac
- Zoloft
- Paxil
- Luvox
- Celexa

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**Medications in Major Depression in Children and Adolescents**

**Norepinephrine Dopamine Reuptake Inhibitor (NDRI)**

- Wellbutrin

**Selective Serotonin Norepinephrine Reuptake Inhibitor (SNRI)**

- Effexor

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**Selective Serotonin Reuptake Inhibitors (SSRI)**

- Fluoxetine (Prozac)\*\*
- Sertraline (Zoloft)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Citalopram (Celexa)
- Escitalopram (Lexapro)

\*\*Only Fluoxetine has RDBPC trial evidence in children and teens

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### **Unique Characteristics of Medications Used in Major Depression**

SSRI's inhibit the P450 liver enzyme and slow down the breakdown of many other medications  
**(watch for drug interactions)**

SSRI's or Venlafaxine (Effexor) if taken alone in **overdose has very low risk of being fatal**

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### **Unique Characteristics of Medications Used in Major Depression**

Fluoxetine (Prozac)

- **Has long half life**, which is useful if there are concerns about compliance

Bupropion (Wellbutrin)

- Has **strict dosage guidelines** because **doses above 300 mg daily can increase risk of seizures**

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### **Precautions for Using SSRIs**

- Recent concern about emergence of **suicidal ideation** with use of antidepressants especially SSRIs
- Serotonin syndrome (diarrhea)
- Withdrawal syndrome (flu-like)
- First trimester use of SSRIs and risks of birth defects

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### **SSRIs and Suicide**

- Every year, 19% of teenagers in the general population think of suicide and 9% make an actual attempt
- Antidepressant 2 - 9% had suicidal ideation, and Placebo 0 - 7%

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### **Careful Monitoring of SSRI Treatment**

- Measure the symptoms of depression using **rating scales**
- Check for suicidality
- Provide details on side-effects and expected time-lines on improvement

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### **Medication Management SSRI Treatment**

- Give small test dose of medication, and if OK, start with very low dose, and if possible see within 3-4 days of starting treatment
- Increase dose slowly every 3-4 days to therapeutic dose and wait 6-8 weeks with weekly visits or telephone check-ins

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### ***Bipolar Disorder***

- Remember the diagnosis of Bipolar Disorder in children is controversial and difficult
- Classic Bipolar Disorder is not an outcome of manic symptoms that occur in childhood
- No medications have been approved by the FDA for pediatric Bipolar Disorder
- Only Lithium was grandfathered in with approval for treating teens over age 13 years old

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### ***Medications Used in Bipolar Disorder in Children and Adolescents***

There are **no RDBPC trials done in children and teens**, and evidence is derived from adult studies

- Valproate/ Divalproex
- Carbamazepine
- Lamotrigine

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### ***Medications Used in Bipolar Disorder in Children and Adolescents***

#### **Lithium**

- Only medication approved by FDA for treating acute mania and maintenance in children

#### **Clonazepam**

- No evidence

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**Double-Blind Placebo-Controlled Trials on Medications for Bipolar Disorder**

DRUG	Age 18 and Over	<u>Age under 18</u>
Lithium	<b>Beneficial</b>	2 studies pending
Valproex	<b>Beneficial</b>	FDA study No benefit
Olanzapine	<b>Beneficial</b>	<b>Beneficial</b>
Risperidone	<b>Beneficial</b>	Data being analyzed
Quetiapine	<b>Beneficial</b>	Being studied
Topiramate	No benefit	No benefit

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**Side-Effects of Medications Used in Bipolar Disorder**

**Anti-convulsants**

- Can have serious adverse effects on the blood production system in the bone marrow
- May cause fatal conditions with reductions in white blood cells, red blood cells, and platelets

**Lithium**

- Can cause hypothyroidism and kidney changes with long term use

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**Unique Characteristics of Medications Used in Bipolar Disorder**

- Avoid using Valproate in girls and women because of risk of polycyclic ovaries
- **Response to medication is not proof of diagnosis**
- Periodic blood tests are mandatory

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**Conclusion**

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**Conclusion**



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**Practical Points About Medications**

- **Talk to your pharmacist**
- **Special packaging**
  - Stripes
  - Bubble packs
- **Safe storage**
  - Locked up
- **Compliance**
  - Supervise taking of medication
- **Compounding**
  - Tablets
  - Capsules
  - Liquids
  - Sprinkle
  - Special formulation

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**STATIC:** Alcohol damaged the hardware and wiring circuits (every person with FASD is different). Medications try to patch or boost some of the hardware.

**DYNAMIC:** Environmental stimulation, strategies and teaching are the software that programs the brain, and can change some of the circuits.

Dr Shih's "Computer Metaphor" for FASD

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**Take Home Messages**

- Medical check to make sure the problem is not due to a physical problem
- Try environmental and social changes first
- Medications may not work the way we expect in a person with FASD because of the different ways the alcohol damages the brain

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**Take Home Messages**

- Start low and go slow
- Medications patch hardware not software problems
- Medications provide a more solid biological platform for thinking and decision making

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**Thank You for Your Attention and Questions Please**



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**Reference**

- Contact Information
- Source Material

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**Contact Information**

**Dr. David Shih**  
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780-438-0011



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***For Information on Upcoming  
Sessions in the Series:  
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***Please Take the Time to Fill Out  
the On-Line Evaluation***

***Thank You!***

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