Beyond Diagnosis: Interventions for Individuals Living with Fetal Alcohol Spectrum Disorder. St. Michael's Hospital, Toronto. September, 2005.

Pharmacological therapies in FASD

There is a problem in discussing Psychotropic Medications and FASD because there is only one published prospective study on the subject, as far as I know. It relates to psychostimulants and ADHD in FASD children. All other references are retrospective and anecdotal. This is not surprising since FASD is not included in the Diagnostic and Statistical Manual of Mental Disorders and so is rarely considered by physicians who prescribe psychotropic medications.
The DSM is published by the American Psychiatric Association and has the diagnostic criteria of all the recognized mental health conditions.

The first description of the effects of drinking alcohol during pregnancy, in english, was in the Lancet in 1973, from observations made in a Seattle hospital. The publication described the characteristics of a group of infants, whose mothers were alcoholics, and they called it Fetal Alcohol Syndrome. It slowly became apparent that FAS was the tip of the ice berg and it has taken over 25yrs for the term Fetal Alcohol Spectrum Disorder to be universally accepted.

Alcohol is a teratogen that effects many parts of the developing fetus, but the part that is most affected, causing the most significant problems for the individual and society, is the neurological system. Of the neurological system, it is disruption of the central nervous system [brain] that is most disastrous.
Both gray and white matter is affected. Damage includes impaired myelin formation, glial formation, cell migration, damage to cell membranes, intracellular damage e.g. to mitochondria, altered regulation of intracellular calcium ions, interference with cell growth, division and survival and impaired production of neurotransmitters.
The latter is of special interest to the topic under discussion.

Those with FASD are often described as developmentally delayed. However. FASD is primarily a neuro-psychiatric condition, most features of which are permanent and will not be corrected by the passage of time. Using the term "developmentally delayed" has contributed to lack of awareness of the full significance of FASD.

The Seattle group followed the FAS children into adulthood.
The result was a landmark study, Understanding the Occurrence of Secondary Disabilities in Clients with Fetal Alcohol Syndrome[FAS] and Fetal Alcohol Effects[FAE], published in 1996.
The findings of this study have since been confirmed by others.

The study showed that FASD individuals had primary and secondary disabilities; primary disabilities being those inherent to the condition and secondary disabilities being those that the person is not born with and would be ameliorated or prevented through better understanding and appropriate interventions.

Mental Health Problems occurred in 95% of FASD individuals in the study. M.H.P s were considered to be a secondary disability at that time. It is now realized that they are a primary disability.
All those afflicted with FASD will have Mental Health Problems, as defined in the DSM.

The parents of FASD individuals will find accurate descriptions of their child in the DSM under various diagnoses.

It is not uncommon for FASD families to be told that there is no point in making the diagnosis because the treatment is the same for all those who are developmentally delayed.
However, it has been repeatedly shown that the earlier the diagnosis is made, with other factors, the less the FASD individual will suffer from secondary disabilities.
Nevertheless, care givers who raise FASD children are prone to blame themselves when their child grows up and displays serious behavioral problems.
It is important to understand that the measure should always be “how would the child have developed without the care and love it did receive?”
The point is that a severely damaged child who experiences abuse before adoption may have serious behavioral problems in spite of a subsequent ideal family life.

There are however other vital reasons why the FASD diagnosis should be made as early as possible.
The diagnosis of FASD clarifies and aids the use of psychotropic medications.

The medications used to alleviate the suffering of those with FASD are mostly for the relief of Mental Health Problems - attention, psychotic / personality and mood disorders.
These Psychotropic Medications appear to relieve mental health symptoms by correcting the abnormal levels of neurotransmitters [chemical imbalance] that result from the effect of alcohol on the brain of the developing fetus.

Psychotropic Medications

The first thing to note when talking about psychotropic medications is the impact of alcohol and drug abuse on mental health diagnoses.
Alcohol and street drug abuse may cause mental health symptoms, leading to diagnoses.
When the alcohol and street drugs are stopped the symptoms may disappear. Under these conditions the mental health diagnoses should be conditional.
Unfortunately, it is not unusual for me to see an adult with multiple mental health diagnosis from a time when he abused alcohol or drugs. He still carries the labels although he does not have the symptoms. The FASD individual is especially prone to this situation - at least 50% will have drug or alcohol problems.
Priority should be given to getting the person off the alcohol or drugs. Fortunately those with FASD often do not crave in the way that others do thus making the process easier.
Co-morbidity, that is multiple psychiatric diagnoses, is the FASD norm. The number and severity of the psychiatric conditions tends to increase with age.
Some of the common diagnoses are-
ADHD, dysthymia, recurrent major depression, generalized anxiety, panic attacks, obsessive/compulsive disorders, bipolar, personality disorders and the psychoses.

They are complex and difficult to treat, as is often indicated by the multiple medications they are on, the number of professionals they have seen, the clinics they have attended and number of hospital admissions they have had.
With a mixture of mood conditions, determination of the dominant mood should be attempted. This may help in deciding which medication to use.

There are a number of problems encountered in prescribing to those afflicted with FASD.
For various reasons e.g. memory disabilities, attention disorders or alcohol abuse, they are likely to take medication erratically. Censure or irritation on the part of the physician is counter productive, Inclusion of a spouse or parent in the process is often the answer.
When medications are discontinued they should be stopped gradually
Ideally, only one physician should prescribe the patient's psychotropic medications on a regular basis.

Attention Disorders

To understand the medications for attention disorders we first have to define the term 'attention disorder'

The DSM defines it as six or more of -

a] often fails to give close attention to details or makes careless mistakes in schoolwork. or other activities.

b] often has difficulty sustaining attention in tasks or play activities.

c] often does not seem to listen when spoken to directly.

d] often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace [not due to oppositional behavior or failure to understand instructions]

e] often has difficulty organizing tasks and activities.

f] often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort [such as schoolwork or homework]

g] often loses things necessary for tasks or activities[e.g. school assignments, pencils, or tools]

h] is often easily distracted by extraneous stimuli.

i] is often forgetful in daily activities.

Most people see the ADD person as easily distractible as defined in the above criteria.
However, being easily distracted is not the only kind of attention problem that can fit these criteria. It is important to understand this if we are to prescribe medications for attention disorders.

In 1892 William James published " The Stream of Consciousness". "Consciousness is always interested more in one part of its object than in another and welcomes and rejects, or chooses all the while it thinks".

In 2001 Coles and others published work that distinguished between the attention disorders of the ADHD child and FASD child.

Peter Hepper, of Belfast, Northern Ireland has shown that alcohol consumed during pregnancy interferes with the development of the startle reflect in the fetus. At five months they show fast or over habituation. That is, the infant is not acknowledging sensory information to the degree that it should. This may be translated in the adult as perseveration. That is the inability to accept / acknowledge significant information and modify the thought of the moment.

We now see that attention abnormalities can be described as -
- easily distracted- slow or under habituation
-perseveration or fast-over habituation.
To the undiscriminating observer they may look the same.

If we include perseveration as an attention disorder, and it does fit the DSM criteria, then it is apparent why the diagnosis of FASD is important in treating attention disorders.
To the observer, who does not distinguish between them, they may well appear to be the same thing.

Some of those afflicted with FASD may have both types of attention disorder. The majority of my FASD patients are adults. They all have attention problems, although they may have learned to mask or circumvent them.
Drinking alcohol during pregnancy causes over habituation/perseveration. Are there other causes of over habituation/perseveration disorder of attention? Yes, but alcohol is by far the major cause.
Does maternal drinking contribute to under habituation/easily distracted [adhd] disorder of attention? Possibly it does, it certainly needs to be investigated and clarified.

Psycho stimulants are the drug of choice for the [ADD]- under habituation patient.
What little information there is on the subject indicates that Dexedrine is more effective than Ritalin for the FASD child, if they respond positively at all.
The psycho stimulants do not help the person who has perseveration - over habituation attention problems alone. In fact they can aggravate the problem; creating mood instability and aggravating concentration and focussing problems. However, if the person displays both types then psycho-stimulants may give some relief. Certainly, the results can be dramatic on occasions.

Of all the medications I have prescribed over the years, psycho stimulants have the worse reputation and meet the most resistance from the public. Perhaps this is because many adverse reactions have occurred in the past as a result of prescribing psycho stimulants to FASD patients who had never been diagnosed other than ADHD.

FASD is not only a neuro-psychiatric condition. Other birth defects occur in FASD, in particular heart abnormalities that may be aggravated by psycho stimulants.
If psycho stimulants are being considered for the FASD patient an E.C.G should be done and the possibility of adverse affects explained. Those

who exercise or play sports should be cautioned that the medications when combined with exercise may cause symptoms. The symptoms are usually those associated with increased autonomic nervous system activity.

Psycho stimulants- C.N.S. stimulants. They can create a dramatic improvement in disorders of attention, but on many occasions have no effect. or aggravate the symptoms. In these cases increased restlessness, anger, panic and even psychosis can result. This is because the over habituation / perseveration disorder of attention is aggravated by psycho stimulants, unlike the under habituation / easily distracted [adhd] disorder of attention, that is relieved by them.
Again this may explain the significant resistance to Ritalin etc. The negative opinion of the drug coming from FASD families who have had bad experiences with psycho stimulants.
However, there are some FASD individuals who do respond positively to the psycho stimulants. They exhibit perseveration or distractibility according to the situation - if the moment is of interest they will perseverate. If it is not, they will be easily distracted.
The heightened sensitivity of the FASD individual may be compounded by the use of psychostimulants. This may a factor in rage attacks.
The neurotoxic effects of amphetamine may be enhanced if the child has had prenatal exposure to methamphetamine, as well as alcohol.

Psycho stimulants- cause mono amine neurotransmitters
[e.g. norepinephrine, dopamine and sertotonin] to be released from their storage vesicles.

Adderall [mixture of dextroamphetamine and amphetamine] -
associated with deaths of twelve children five of whom had heart defects. Could these children have been FASD and therefore possibly at risk if given psycho stimulants?

Dexedrine [dextroamphetamine] -
Studies suggest it is the most efficacious of the psycho stimulants for those FASD individuals who respond to the psycho stimulants.

Ritalin [methylphenidate]

Concerta [methylphenidate]
Has a slow delivery mechanism with more even effect. The mechanism and therefore the delivery of the drug, is interfered with if the capsule is damaged.

Norepinephrine reuptake inhibitors [NRI's]- antagonists of the pre synaptic norepinephrine transporter.

Strattera [Atomoxetine] - short acting.

Norepinephrine-dopamine reuptake inhibitors [NDRI s]
Wellbutrin [bupropion] - risk of seizures with high doses. Single dose should be no more than 150mg in immediate release form or 200mg in the SR form. The total daily dose should not be more than 450 mg. per day. Especially contraindicated in the FASD patient with over habituation/perseveration disorder of attention and who has a greater risk of seizures- a reason for identifying the FASD individual.

Psychotic Disorders -delusions / hallucinations- without insight.

The FASD individual may be psychotic. Because of the nature of psychoses they are usually treated by psychiatrists, often in clinic or hospital setting.
When there are delusional tendencies, especially when associated with inappropriate reactions e.g. anger, then an atypical anti-psychotic, seroquel, resperidone or zyprexa is indicated.
They have far less side effects than the older generation of anti-psychotics and are much safer to use.
These second generation often help calm racing thoughts and impulsivness, especially when associated with angry outbursts. The medications seem to give them time to think more clearly in the moment. It is important to explain that the term “anti-psychotic” does not mean that all who use these medications are psychotic.

Personality Disorders -DSM criteria

A - An enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual’s culture. This pattern is manifested in two of the following areas-

1] cognition [i.e. ways of perceiving and interpreting self, other people and events]
2] affectivity [i.e. the range, intensity, lability and appropriateness of emotional response]
3] interpersonal functioning
4] impulse control

B - The enduring pattern is inflexible and pervasive across a broad range of personal and social situations.

C - The enduring pattern leads to clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D - The pattern is stable and of long duration and its onset can be traced at least to adolescence or early adulthood.

E - The enduring pattern is not better accounted for as a manifestation of consequence of another mental disorder.

F - The enduring pattern is not due to the direct physiological effects of a substance [e.g. a drug of abuse, a medication] or a general medical e.g. head trauma]

Many FASD individuals and those who know them, will be familiar with these criteria.

Medications have not been found to affect the personality disorder patterns. However, psychotropic medications are often used to relieve the co-morbid psychiatric symptoms that invariably exist.

The Personality Disorder patient is most likely to make false accusations against people they are involved with.
Compare this to the confabulations of those afflicted with FASD.

Anti- psychotics.
The term is unfortunate since the many patients who need them are not psychotic. It is important to explain to the majority of FASD patients that they are not psychotic.
In fact psychosis is a contraindication to sharing the diagnosis of FASD with the patient. The psychotic patient is likely to incorporate the information into his/her gross distortions of reality with a deterioration in their condition, in my experience.
The second generation [atypical] anti psychotics are the drugs of choice. They have far less side effects and require less monitoring than the older generation drugs. This is especially important for the FASD person with memory defects etc. Once more showing the importance of identifying those psychiatric patients who are FASD.

Atypical anti psychotics - all interact with a variety of receptors.
Risperdal [Risperidone] Zyprexa [Olanzapine] and Seroquel [Quetiapine] are commonly used in Canada.
When combined with other psychotrophic medications they have a mood stabilizing effect,often with improved cognition, that seems to enhance other treatments. Thus they may be helpful for depression and bipolar conditions when used with the other appropriate medications. They should be considered when paranoid tendencies are detected. or where agitation and anger are an issue.

They should only be used in children as a last resort for serious behavioral problems.
The anti psychotics may take four to six weeks to be fully effective. It is important to remind the FASD patient of this as they may stop the drugs if they do not feel an immediate response.

Anxiety, Panic Attacks and Depression.
The SSRI s, SNRIs, are safer, and easier to monitor than the older antidepressants and are the drugs of choice for the FASD patient. However, Paxil [Paroxetine] should be used with greater caution. It is most likely to interact with other drugs. e.g. the older antidepressants, such as the Tricyclics. The NDRI, Welbutrin [Bupropion] is contraindicated because of the risk of seizures.

Again, the FASD patient needs to be cautioned that medications may take up to six weeks before having a noticeable effect.
Increased agitation and suicidal thoughts have been reported in the first few weeks and perhaps are more likely depending on the degree of agitation initially. Anger and agitation are not uncommon with depression. Anger is less likely with anxiety, but agitation can certainly occur.
The recent concern over suicides in depressed children on SSRI s raises the question whether they were FASD, a diagnosis not normally considered. Those afflicted with FASD are at increased risk for suicide.

Benzodiazepines-
bind to GABAa receptors [as do barbiturates and alcohol]. This is associated with risk of dependency and addiction and Benzodiazepines should therefore be used with caution, if at all, for the FASD patient; another reason for identifying those afflicted with the condition.

Anticonvulsants-
Used as adjunctive therapy where there is agitation.

Epival [Valproic Acid] increases levels of GABA- gamma-amminobutyric acid, the main inhibitory neurotransmitter.
It can enhance other medications when agitation is a factor.
For this reason it is effective in the bipolar patient.
The disadvantage, especially for the FASD patient, is that drug levels, liver function tests and platelet counts should done regularly. Polycystic disease of the ovaries has been associated with Epival use.
Most importantly it is teratogenic and for this reason is contraindicated for most FASD females. Again, another reason for diagnosing FASD before treating psychiatric symptoms.

Carbamazepine - similar issues.

Lamictal [Lamotrigine]- has less side effects but is said to be less effective. not recommended under 16yrs.

Neurontin [Gabapentin] less side effects - does not require monitoring.

Bipolar-

Lithium has traditionally been the drug of choice for the bipolar patient. However, blood levels have to be monitored since it has significant side effects and a low therapeutic index.
Lithium is associated with renal side effects and the those with FASD often have renal dysfunction. FASD children are particularly vulnerable to the CNS side effects of Lithium.
For all these reasons greater care is required in prescribing Lithium and consideration should be given to using one of the anti-convulants.
Again, another reason for identifying the FASD patient.

We are a long way from having all the answers. However, the sooner FASD and its significance is universally recognized, the sooner we will find the answers.

FASD is a neuropsychiatric condition.
All FASD individuals will have more than one psychiatric [DSM] diagnosis.
Knowledge of FASD is necessary, even vital in some instances, when prescribing psychotropic medications.

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per·sev·er·a·tion (pər-sĕv'ə-rā'shən)

n.

1. *Psychology*
   - **a.** Uncontrollable repetition of a particular response, such as a word, phrase, or gesture, despite the absence or cessation of a stimulus, usually caused by brain injury or other organic disorder.
   - **b.** The tendency to continue or repeat an act or activity after the cessation of the original stimulus.
2. The act or an instance of persevering; perseverance.

Thesaurus

Legend: Synonyms | Related Words | Antonyms

Noun 1. perseveration - the tendency for a memory or idea to persist or recur without any apparent stimulus for it

- inclination, tendency, disposition - an attitude of mind especially one that favors one alternative over others; "he had an inclination to give up too easily"; "a tendency to be too strict"

2. perseveration - the act of persisting or persevering; continuing or repeating behavior; "his perseveration continued to the point where it was no longer appropriate"

- perseverance, persistence
- continuance, continuation - the act of continuing an activity without interruption