



Intellectual Disability



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Introduction

As many as 50% of young people with intellectual disability have autistic spectrum disorder or specific delay in social development and empathy skills (Wing & Gould, 1979). Conversely, 70% of young people with autism have a degree of intellectual disability. In a combined child psychiatry and developmental paediatric clinic for children with intellectual disability, 80% had autistic features (Dossetor, 1997). Both are problems of slowed, distorted and incomplete development. Thus autistic features are an important consideration in assessing and treating children with intellectual disability. In general no pharmacological treatments have been found to reverse these processes, despite continued reports of "miracle cures" proposed to treat the underlying disorder. The role of pharmacologic treatment is in the targeted management of specific symptoms or associated disorders. Psychiatric or emotional and behavioural disorders co-occur in about 40% in those with intellectual disability (Volkmar & Dykens, 2002). This chapter focuses on these associated disorders that cause additional impairment to daily functioning significantly impacting on their quality of life and that of their carers.

'50% of young people with intellectual disability have autistic spectrum disorder or specific delay in social development and empathy skills'

Assessment

"The hit and miss of magic bullets" describes the author's experience of prescribing for the psychiatric disorders of young people with intellectual disability. The point made then was that psychotropic medication can be essentially helpful and or be of little benefit and this is difficult to predict (Dossetor, 1997). Diagnostic validity and treatment selection is complex and requires an openness of inquiry. It is widely accepted that there is a major biological or

neuropsychiatric component to many or even most of the psychiatric problems presenting in young people with intellectual disability and autistic spectrum disorders. Einfeld and colleagues' longitudinal study of behaviour disturbance in young adults with intellectual disability found that family factors contributed to 4% of the variance of behavioural change over 4 years (Tonge, 1999). The greatest predictor of continued behaviour disturbance was previous behaviour disturbance, which in turn has an impact on family function.

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Family Factors

Although biological factors are thought to be central in causing psychiatric symptoms in intellectual disability and autism, it is essential to look at the well being of carers and other family members in an evaluation, as this is one of the predictors of breakdown of families or out of family placement.

'The presence of autism significantly affects the prognosis and treatment of those with intellectual disability, and must be specifically sought'

Psychiatric Diagnoses

It is now clear that all the main diagnostic categories experienced by those with normal intellect such as anxiety disorders, PTSD, adjustment reactions, grief, depression, bipolar disorders, attention deficit hyperactivity disorder and schizophrenia are experienced by those with intellectual disability and the autistic spectrum. The presence of autism significantly affects the prognosis and treatment of those with intellectual disability, and must be specifically sought. There are also some specific diagnoses, which may be suggested by the behavioural presentation, which may be described as the behavioural phenotype, these are discussed at the end of this chapter. The Royal College of Psychiatrists (2001) has developed DC-LD (diagnostic criteria for psychiatric disorders for use with adults with learning disabilities/mental retardation) which include learning disabled-sensitive criteria to aid diagnosis. DC-LD is a multiaxial diagnostic system:

Axis I: severity of learning disability

Axis II: causes of learning disability

Axis III is divided into 5 levels:

- A: Developmental Disorders
- B: Psychiatric Illness
- C: Personality Disorders
- D: Problem Behaviours
- E: Other Disorders

However these disorders are more easily recognised in those with mild intellectual disability. In those with severe intellectual disability this is more difficult. Eliciting and recognising

subjective mental phenomena is unreliable in those with severe intellectual disability and in children under the mental age of 7 years. This means that the child psychiatric models of diagnosis based on indirect methods of inquiry, behavioural observation and information from multiple sources and informants are an essential part of good practice to build up an accurate impression of a problem. There is also a new diagnostic category in ICD10 of "overactive disorder associated with mental retardation and stereotyped movements".

'Eliciting and recognising subjective mental phenomena is unreliable in those with severe intellectual disability and in children under the mental age of 7 years'

Clinical Rating Scales

Behavioural rating scales are also used to supplement the assessment, and ensure a wide spectrum of symptom investigation. This has led to an additional approach of categorising difficult behaviour in the intellectually disabled by a factor analysis of the symptoms.

1. **Developmental Behavior Checklist** (an equivalent to the Child Behavior Checklist (CBCL) developed for an intellectually disabled population)

Tonge (1999) using the Developmental Behavior Checklist found positive scores on the following factor-analysis-derived subscales on a clinical group:

- Anxiety (23.2%)
- Disruptive (22.7%)
- Self-absorbed (13.4%)
- Social relating (10.8%)
- Language disturbance (6.7%)
- Antisocial (3.6%)

Total with positive score on only one scale: 80.4%, on two scales 14.4% and on three scales 2.1%.

2. **The Handicaps Behaviour Skills Schedule** (HBS) (Wing, 1981)

The Handicaps Behaviour Skills Schedule is recommended as a comprehensive semi-structured interview, which enables a clinician to assess development and a wide range of symptoms while making them aware of the developmental age equivalents of different domains of development.

Sensitivity to developmental stage (as well as chronological age) is critical to using all diagnostic categories appropriately. Training and a longer interview are disadvantages of the DISCO (Diagnostic Interview for Social and Communication Disorders) the current successor of the HBS.

3. **The Social Reciprocity Scale** (SRS) (Constantino, Przybeck, Friensen & Todd, 2000).

The SRS allows scoring of autistic features or social intelligence as a range. The presence of even mild autistic features has been shown to have a strong influence on prognosis for psychiatric disorder, both with intellectual disability and without it.

Symptoms in a Developmental Context

A study of teenagers with intellectual disability (Dossetor, 1991) showed that the behavioural disturbance as measured by the HBS was a single statistical factor that correlated with developmental age not chronological age. This study demonstrated that behaviour disturbance peaks in developmental toddlerhood and starts to improve after the developmental age of 2-3 years, as is found in those with normal development. Developmental explanations help us understand the empirical dimensions from the Developmental Behavior Checklist.

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Anxiety and disruptiveness - increase with greater mobility and children’s growing awareness of other people and themselves. Behaviour starts to improve with the development of an internal imaginary world, play and interactive skills.

Self-absorption, social impairment and language disturbance - are related to the specific delay in social development or autistic type behaviours. Language disturbance requires sufficient skill to have language and yet suffer autistic type abnormalities.

Antisocial behaviour - requires enough ability to appreciate that you are harming someone else or their possessions.

Hyperactivity - The demandingness of developmental toddlerhood, say in a 15 year old with high levels of activity and little awareness of the impact on others, is a common problem. Treating hyperactivity pharmacologically in this context requires cautious expectations over the degree of effect and of side effects as opposed to toddlers of normal intellect. Chronological adolescence has an influence on increasing agitation and moodiness until hormones, frontal lobe development and lifestyle settle down in the early twenties. Accordingly assessment involves using these epidemiological approaches to deviant/difficult behaviour within a developmental context.

‘The demandingness of developmental toddlerhood, say in a 15 year old with high levels of activity and little awareness of the impact on others, is a common problem’

Symptoms, syndromes and the emergence of a new speciality

In the challenge to understand the significance of disturbed behaviour, frequently clinicians focus on target symptoms rather than symptom clusters or syndromes. In the last 20 years behavioural approaches have been the dominant approach to treating emotional and behavioural disturbance in those with intellectual disability. This is partly through a functional analysis of the behaviour causing distress and partly by approaches enabling skill enhancement in the context of impairment of communication. While this is useful as part of the approach, it is important to recognize that this does not equal a "diagnosis" of the underlying cause/s of the behaviour, and therefore does not exclude the use of other approaches.

Over the last 5-10 years there has been a re-emergence of the recognition of the need to consider a greater diversity and balance of approaches. Possible approaches include preventive, psychotherapeutic, behavioural, family oriented, dietary, or pharmacological therapies to mention a few. Perhaps the biggest pressure for this greater collaboration of approaches is the rise of parental advocacy groups, often governed and communicating through the Internet, but also working hand in hand with professionals through research and academic meetings. The deinstitutionalisation of people with intellectual disability has led to an increased awareness of the biological contribution in children and adolescents with psychiatric disorder and conversely an awareness of the importance of attachment, relationships and sociological factors in those with intellectual disability. This has led to an intellectual enrichment, with stronger roots in basic sciences, for both the psychiatry of intellectual disability and of community child psychiatry. It has also led to a new overarching convergence of child mental health under the rubric of *developmental neuropsychiatry*.

Table 1

The Integration of the Psychiatry of Intellectual Disability and Child Psychiatry

Psychiatry of Intellectual Disability

Institution based

Biased to biology and genetics
 Concerned about biological disadvantage
 Diagnosis based on syndrome recognition
 Treatment bias to psychopharmacology,
 Including segregation & passive eugenics

Child Psychiatry

Community based

Biased to sociology
 Concerned about emotional deprivation
 Diagnosis based on epidemiology
 Treatment bias to psychotherapies
 Attributing responsibility to families & communities

**The Social Acceptance of Difference with Biological Variation
 Integrating Medical Sciences with Social Psychology**



Developmental Neuropsychiatry

The integration of developmental processes in all young people:
 biological underpinnings in a context of family and community
 with expansion of aetiological and therapeutic models

Behavioural Phenotypes

Working in this little researched field of therapeutics provides the opportunities for major advances in understanding. Behavioural phenotypes - the genetic basis of certain clinical presentations of development, abilities, and behaviours is one such opportunity. Opportunities for understanding more about the genetic and molecular nature of behavioural syndromes and disturbance illustrate the importance of single case or small case series for unusual behaviours or disorders.

Textbox 1

Behavioural Phenotypes

Syndromes of specific behavioural phenotypes have done much to increase the interest and understanding of the biology of behavioural problems in those with intellectual disability.

Fragile X and trinucleotide repeats

Sometimes the causal pathway is so close as to have a "dose-related" outcome of genetic abnormality to behaviour. One example is the number of CGG nucleotide repeater sequences; more than 320 is proportional to the level of intellectual disability in Fragile X children.

Prader Willi and schizophrenia

The rarer genetic cause of Prader Willi Syndrome, of maternal uniparental disomy of chromosome 15 in adults suggests it may be the highest risk of schizophrenia in any population (Dykens, 2001).

Sphrintzen's syndrome and psychosis

Similarly Velo Cardio Facial Syndrome (Sphrintzen's Syndrome) with a deletion of 22q11 was been found in adult populations to have a prevalence of:-

- 42% major psychiatric disorder
- 30% psychosis
- 24% had schizophrenia (with stronger positive symptoms and weaker negative symptoms than is normally seen)

Syndrome specific symptoms and signs:

- Hyperphagia of Prader Willi
- "Cry of the cat" of 5p Syndrome
- Self-hugging in Smith Magenis Syndrome (Dykens, 2001).

Symptom over representation in syndromes

Some symptoms are over-represented in several conditions such as: -

- Overactivity and inattention seen in Fragile X and William Syndrome
- Self injurious behaviour in seen in different syndromes: -
 - Extreme lip and finger biting in Lesch Nyhan Syndrome. The specificity of SIB in Lesch Nyhan Syndrome raises the suspicion of abnormalities of purine or dopamine function in this pattern of SIB
 - Hand biting in Fragile X
 - Skin picking in Prader Willi Syndrome
 - Head banging, nail biting and gauging, and insertion of objects in orifices in Smith Magenis Syndrome
- Anxiety disorders seen in William syndrome present with different subtypes of anxiety disorder. The behavioural phenotype can lead to the genetic diagnosis, and not always the other way round

Mental health workers may not be skilled at recognising physical or anatomical characteristics of genetic syndromes, but they should maintain their expertise in the characteristic behavioural phenotype patterns. In our department, a clinical description of a case of Smith Magenis Syndrome led to the identification of 3 further cases, which were subsequently confirmed by genetic testing.

- Autistic spectrum disorder, intellectual disability and motor incoordination in Joubert's Syndrome where cerebellar (vermal) agenesis and the chromosome abnormality will often only be suspected on clinical grounds

‘The behavioural phenotype can lead to the genetic diagnosis, and not always the other way round’

Differential Diagnosis and the Multidisciplinary Team

A multidisciplinary team can be very helpful in diagnosing potentially treatable medical causes of psychiatric symptoms including:-

- oesophageal reflux
- constipation
- dental problems
- impediments to communication such as visual and hearing impairment
- co-occurrence of neurological problems such as epilepsy, space occupying lesions (eg Tuberous Sclerosis) and cerebral palsy

Multiple social disadvantages may also exacerbate difficulties for the child with intellectual disability.

Approaches to psychopharmacological treatment and levels of evidence

Even where aetiology is biological this does not necessarily mean the treatment should also be biological. Biological features of depression or basal nuclei changes on SPECT scans in OCD also respond to CBT; the severe intellectual disability of Phenylketonuria (due to absence of Phenylalanine dehydroxylase) is prevented by diagnosis on a screening test at birth and providing a phenylalanine free diet. A "prosthetic environment" has major effects in reducing handicap or even disability but is not a "miracle cure" and thus will seldom change the impairment.

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Table 2

Impairment, Disability and Handicap

Impairment:	Aetiological deficient mechanism; eg. absence of Phenylalanine dehydroxylase in PKU
Disability:	The consequent loss of function or ability; eg. the deficit of language, intellect or mobility for age and circumstances
Handicap:	The loss of social role due to interaction with context; eg. the inability to access community facilities from lack of wheel chair ramps, or adequate staffing/carer supervision for behaviour.

The Evidence

There is very limited evidence available on which to make most treatment decisions about children and adolescents with autism or intellectual disability. While there have been few randomised control trials (RCTs) reported in the medical literature in the last 5 years, a few important studies have been published. Most publications to date are case reports or open label studies. There have been several barriers to research and publishing in autism and intellectual disability:-

- A) The lack of financial incentive for pharmaceutical companies
- B) A professional bias against publishing
- C) The inherent complexity of the area.

One reviewer commented that there were no ethical grounds to publish a study of risperidone in an open label or non-randomised trial as there was no scientific evidence that it could be helpful in this population (Ismail I, personal communication). In contrast to this a recent publication in the New England Journal of Medicine showed that risperidone was effective in managing aggressive behaviours in autism (RUPP, 2002). Thus, relative absence of evidence must be distinguished from an evidence of absence of effectiveness.

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It may be dubious medical practice to prescribe when there is Cochrane level I evidence (meta-analysis of several high quality relevant RCTs) that indicates that a treatment doesn't work for a specific condition in a comparable population. However an evidence-based approach uses the best level of evidence available in the clinical context for that individual. This includes open label cohort studies and even expert opinion. A number of clinician's reviews indicates that clinical experience continues to be the main ethical guide in this area of practice (Einfeld, 2001; Tyrer, 1997). The relative lack of evidence makes it critical that clinicians working in this area contribute to research, as single case studies or small series may be extremely useful for other clinicians and their patients.

"Psychotropic Medications and Developmental Disabilities: The International Consensus Handbook" (Reiss & Aman, 1998) has been a valuable collection of public debate, scientific examination, and expert opinion on the use of drugs at least in adults with intellectual disability, collating the psychotropic evidence to date.

Psychotropic Medications and Intellectual Disability

The complexity of diagnosis or, more accurately, formulation of disordered behaviour in young people with intellectual disability results in psychotropic treatment trials. Medications often have to be used consecutively based on one of a number of alternative explanatory hypotheses. The choice of medication is influenced by core symptoms, acceptance of the medication, the likely size of helpful effect and the level of risk from adverse effects.

Central Nervous System Stimulants (Dopamine agonists)

Dexamphetamine and methylphenidate are helpful in ADHD or aggression but are more likely to be ineffective and have significant side effects than in a population of average IQ. Cautious dosing and expectations are recommended. Amantidine (an antiviral agent) has an interesting but limited literature in ADHD. The newer slow release stimulants of Adderall, Concerta or Ritalin LA are likely to be helpful and studies are in progress on efficacy. Comorbid autistic spectrum disorder makes the response less predictable.

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Mood stabilisers

Lithium, as used for Bipolar Disorder (also called manic depression) is the best of this group for instability of mood and aggression in those with intellectual disability, but also subject to the problems of monitoring (response to taking blood in some young people with autism is unpredictable) and side effects. Lithium citrate is a liquid preparation, a useful alternative where large tablets cannot be swallowed, so long as there is good quality supervision of dosing.

Carbamazepine, "the universal second line psychotropic drug" (Tyrer, 1997), has a long-standing track record in adults with intellectual disability for aggression and related symptoms and I find it useful in approximately 50% of those with Intellectual Disability/Autism. Gradual increase in carbamazepine to 100-200mg bd, and the use of higher doses only if some indication of benefit is shown. Higher doses can be monitored with drug levels but clinical observations remain paramount. Valproate is now gaining greater usage and as experienced is gained with lamotrigine and topiramate as mood stabilisers, they are likely to be useful in this population.

Antidepressant Medications

Tricyclic Antidepressants (Reuptake inhibitors of noradrenalin and serotonin)

The *tricyclic antidepressants* have a valuable role in ADHD related symptoms. Amitriptyline may be preferred for impulsivity-related aggression, anxiety and inattention and is often more useful than stimulants because of its longer half-life. The different spectrum of side effects may be therapeutic where sedation, reduced nocturnal frequency of urine or increased firmness of bowel action may be desirable.

Sudden death reports on desipramine, though increasingly considered over stated, makes an ECG check of the QT interval worthwhile with tricyclics.

Atamoxetine is keenly awaited with its reported success for ADHD in the general childhood population.

Clomipramine is sometimes a useful compromise as a tricyclic serotonin reuptake inhibitor.

Serotonin specific reuptake inhibitors

SSRIs may be helpful in Autistic Spectrum Disorders, which are discussed in the following chapter. McDougle and colleagues' RCT showed fluvoxamine to be effective in adults with

autism for aggression, stereotypies, anxiety, language and socialisation, enhancing their level of social and community independence (response in 8/15 vs 0/15) (McDougle et al., 1996). This confirms the benefit of the other SSRIs shown in less rigorous studies. With this level of evidence it may be acceptable to trial all with autism on an SSRI, but I find it only beneficial for targeted psychiatric symptoms and particularly for aggression or self-injurious behaviour that is driven by anxiety or stereotypic pressure. SSRIs are not generally helpful for hyperactivity-related symptoms. However, they may be used for depression or anxiety as in the general child population. In children with intellectual disability in particular SSRIs can cause dose-related agitation and activation. It is reported that benefits may accrue even after 12 weeks. Preference for which SSRI is suggested by strength of SSRI (citalopram and paroxetine may be more anxiolytic), potential drug interaction (sertraline probably has least drug interaction due to P450 system), pharmacokinetics (fluoxetine's long half-life is better for inconsistent compliance, sertraline's shorter half-life enables quicker withdrawal if there are unwanted effects), side effects (fluvoxamine is said to be more often sedating and less often insomnia inducing but this has been questioned of late), and preparation (fluoxetine syrup enables ease of administration in those who can't swallow tablets and who require very small doses, especially for initiation). Although generally safe, experience of rarer side effects such as spontaneous bruising, serotonergic syndrome or withdrawal syndrome, encourages caution.

Venlafaxine is a newer medication with noradrenalin and serotonin reuptake inhibitor characteristics. Literature in this population is lacking but its side effect profile in other populations is much safer than tricyclic antidepressants such as amitriptyline.

Reversible monoamine oxidase inhibitors

Moclobemide may be useful where side effects from other antidepressants have prevented compliance. It has a role in anxiety, social phobia, depression, ADHD (eg associated with tics), and possibly cannabis craving.

5HT/Serotonin agonists

Buspirone (used for anxiety) has a limited literature and can be helpful in anxiety, self-injurious behaviour and aggression. Fenfluramine is no longer available as it was implicated in valvular disease and pulmonary hypertension in women (using it for dieting).

Major tranquilisers or antipsychotics (Dopamine antagonists)

It is worthwhile noting that the more old fashioned term of major tranquilliser is preferable in childhood where antipsychotic action is rarely the target symptom.

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Traditional or typical antipsychotics

As in other settings, the risks of extrapyramidal adverse drug reactions (ADRs) such as acute

dystonic reactions, or the rare but serious tardive dyskinesia or neuroleptic malignant syndrome must be considered when prescribing antipsychotic medication. Although thioridazine is the best-studied traditional major tranquilliser, it has been withdrawn from distribution because of reports of effects on cardiac conduction. Along with haloperidol it was shown to be helpful for aggression, agitation, excitability, screaming, hyperactivity, self-injurious behaviour and stereotypies. High doses were shown to be no more effective than low doses for these chronic symptoms.

Other traditional major tranquilisers also have a role, if a different pattern of effects or side effects is required eg increased sedation with chlorpromazine, improved mood on flupenthixol, pimozide for resistant tics or less lactation with stelazine. Aman showed that below an IQ of 45 or a mental age of less than 4.5yrs that thioridazine is more likely to be helpful for ADHD than stimulants (29% vs 8%). However, given the concern about cardiac effects, this is no longer available. They argued that lowering general arousal levels allows attention to a wider range of stimuli in those with restricted or stereotypic patterns of interest, which may be made worse by stimulants.

Parenteral droperidol with diazepam is our preference for acute sedation, but a general anaesthetic can be preferable for staff occupational health and safety when a secure placement is needed urgently! (Midazolam is useful for short-acting sedation eg for procedures).

Atypical antipsychotics or major tranquilisers

These are probably the greatest therapeutic advance in this population in the last few years, because of their reduced rate of extrapyramidal ADRs. Risperidone has been found in multicentre RCTs in young people to be effective for irritability/aggression, hyperactivity and stereotypies (but not social withdrawal and inappropriate speech) in those with intellectual disability and in those with autism (RUPP Study, 2002). Mild or moderate increased appetite was found in 73% of children (average weight gain 2.7kg in 8 weeks); fatigue and drowsiness, although often short-term (less than 4 weeks), were common. Drooling, dizziness, dyskinesia, tremor and tachycardia were also significantly increased. Three of 49 children withdrew from the study because treatment was ineffective, versus 17 in the placebo group.

Our own retrospective cohort study supports the need for close attention to side effects (Zwi, King, Longworth, Nunn, & Dossetor, in press). Other atypical antipsychotics also have a similar role, although there is limited literature in this population.

Olanzapine is more sedating and obesity/diabetes inducing but the wafer version is useful when oral administration is compromised.

Quetiapine and ziprasidone are hoped to have less weight induction and have been shown effective in hostility in schizophrenia, improving mood. Ziprasidone was used in an open label cohort of maladaptive youth with autism, and aggression improved in 6/12 (McDougle et al, 2002), whereas in a similar study with quetiapine only 2/6 were seen to be responders with problems of tolerability and sedation (Andres et al, 1999).

Clozapine has a growing literature on its cost effectiveness for extreme behaviour

disturbance in adults with intellectual disability, often permitting release from a high security environment. Clozapine is the only specific D1 receptor antagonist we have which fits the D1 antagonist animal model for self-injurious behaviour. However clozapine is associated with agranulocytosis and is subject to strict protocols.

Beta-adrenergic blockers

Propranolol has a valued role in aggression, explosive personality and anxiety. Experience suggests that it is useful in moderating these problems rather than being seen as a specific treatment. Morning beta-adrenergic blockade in Smith Magenis Syndrome is observed to improve the inverted circadian cycle in this condition and improves the extreme nocturnal insomnia, and to a lesser extent the hyperactivity (De Leersnyder et al., 2001).

In those at risk of asthma a cardio-selective (beta 2 subtype) medication such as metoprolol is safer.

Alpha-2 Agonists

Alpha-2 agonists such as clonidine and guanfacine (which is still not available in Australia) have a role in oppositional defiant disorder, acute anxiety and tics, although sedation is often a limitation. Sedation is often used therapeutically especially with the insomnia of stimulants. The risk of tachycardia and rebound hypertension on withdrawal of these medications requires gradual tapering of doses when withdrawing and caution with anticholinergic medications. Clonidine may be helpful occasionally in cases of hyperactivity, inattention and impulsivity, and it may be the coincident underlying anxiety that distinguishes these cases (Agrawal, Sitholey, Kumar & Prasad, 2001).

Opioid Antagonists

Naltrexone is of theoretical interest, especially in self-injurious behaviour, but a further 10 years of experience has not reinforced its utility. It may still be helpful for a clinical subgroup, perhaps self-injury with social withdrawal and self-preoccupation.

Night Sedatives

Nocturnal insomnia can often be tricky to treat and yet major sleep problems have significant social costs. Sedation side effects can be useful in amitriptyline, clonidine and atypical major tranquilisers.

Trimeprazine (antihistamine) has had long clinical usage for night sedation.

Short-term benzodiazepines such as temazepam (half-life 2-4 hours) or nitrazepam (half-life 12-24 hrs) can be used to establish sleep patterns along with a behavioural program, but caution is recommended with their use because of disinhibition, and habituation.

Chloral is valuable and has a long track record of safe use despite the more recent debate about safety.

The hormone melatonin is attracting increasing plaudits although the right preparation is required and not the homeopathic version. Doses up to 3mg given as late at night as possible is closest to recreating physiological pharmacokinetics.

Antiandrogens

In teenagers sexualized aggression is often a manifestation of a lack of opportunity to develop social skills and confidence. However a trial of cyproterone or medroxyprogesterone may be indicated where the consequences of untreated sexual behaviour are unacceptable for the teenager (repeated law breaking) or where a younger sibling is at risk. Reduction of testosterone to a third of pre-treatment serum level is the guide to sufficient dosage. Advice of a paediatric endocrinologist is valuable with such a rarely used treatment.

Anticholinergics

Benztropine and others are useful for extrapyramidal/parkinsonian side effects, but may also be helpful to moderate repetitive autistic spitting (also oral atropine drops).

Combinations

Clinicians must be acutely aware of placebo effects and avoid the pressure to accumulate medications without good documentation of benefit. On the other hand, we all wish we could be "pharmacologically pure" in our treatment and monotherapy is one advocated principle of treatment. However audit and reported experience suggests that the risks of increased side effects are not gross (beware the addition of 2 drugs of similar mechanism). It is not uncommon to obtain greater benefits or fewer side effects from a combination of 2 or 3 drugs. Interactions require caution and watchfulness.

In complex psychopharmacology telephone access to the clinician is the best means of monitoring the clinical condition while making one drug change at a time. Each drug change requires a minimum of 3 weeks before drawing conclusions, subject to modifications for side effects. Einfeld (2001) provides a useful guide on how to monitor change and Burbidge, Brady and Davis (1999) provide a brief summary of the legal issues with regard to consent and guardianship, and the contact details for the relevant state and territory authorities are listed in the chapter on Psychiatric Emergencies.

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