SCHIZOPHRENIA IN CHILDHOOD

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CHAPTER ONE

CLASSIFICATION

1.1. Introduction:

The diagnosis of Schizophrenia in children has historically been the source of much psychiatric controversy, especially with regard to classification, treatment and prognosis. This was further complicated by the broad category for the diagnosis of psychotic disorders in childhood in the Diagnostic and Statistical Manual of Mental Disorders (DSM II).This included Schizophrenia in childhood, autism, and other psychotic conditions. The work of Kolvin (1971a-f) and Rutter (1972), have been instrumental in separating autism and Schizophrenia into distinct categories.

This review is not aimed at being an exhaustive coverage of all the literature on Schizophrenia in childhood, but is focused on classification, phenomenology, epidemiology, differential diagnosis, etiology, course, cross-cultural factors, and treatment. The adult literature has been referred to, when there is no appropriate reference in the literature on children with Schizophrenia, in certain focused areas. Specific research questions will be discussed in depth in the appropriate sections. These are:

1) Is Schizophrenia with childhood onset a discretely homogenous entity or is the condition on a continuum with adult Schizophrenia?
2) Are the current classification systems diagnostically valid in children with Schizophrenia?

3) Do phenomenological descriptions of the condition assist the clinician diagnostically, given the financial constraints limiting the extent of special investigations, in the South African context?
4) The evidence concerning the etiology of Schizophrenia in childhood will be critically evaluated.
5) Do current treatment models have any relevance to clinical practice in South Africa, especially with regard to the need for cost-effective solutions?
6) Two cases obtained from the in-patient Unit of the Red Cross Hospital's Child and Family Unit will also be examined, in the light of the literature.

As much of the literature prior to DSM III generally did not clearly differentiate between childhood Schizophrenia, autism and other heterogeneous conditions (Rutter, 1972), they have not been included, except for seminal papers. In addition the age groups in the papers do not always mention the pubertal status of the children, thus for the purpose of the review, primarily studies focusing on samples with onset prior to 13 years are included. These have lately been characterized in the literature as 'VEOS'[1] (Very Early Onset Schizophrenia).

In one of the few longitudinal studies of children with Schizophrenia, Werry, McClellan and Chard (1991), reported that more than half the sample (55%) which had been diagnosed as schizophrenic at first presentation, was found to have Bipolar Disorder at follow-up. It is possible that the papers reviewed may also reflect this once longitudinal follow-up has been completed. The results of longitudinal studies are awaited.

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[1] * EOS = Early Onset Schizophrenia (13 to 17 years approximately). (Werry et al, 1991).

1.2. Historical Background to Classification:

Asarnow and Asarnow (1994) have succinctly summarized the historical overview of childhood-onset Schizophrenia and this is briefly presented. Kraeplin observed that dementia praecox could begin during childhood and estimated that at least 3.5 percent of his cases had onset before age 10 with another 2.7 percent of cases developing between ages 10 and 15. Similarly, Bleuler estimated that between 0.5 and 1 percent of schizophrenic cases had onset before age 10, with 4 percent of schizophrenic psychoses beginning before age 15 (Cited in Asarnow and Asarnow, 1994).

With the emergence of child psychiatry as a medical sub-specialty in the 1930's early child psychiatrists saw children with a range of conditions, from profound mental retardation, developmental problems, to autism and childhood onset-Schizophrenia. For the next 40 years, which included the publication of the DSM II, childhood-onset Schizophrenia had been: "used as a generic term to include an astonishingly heterogeneous mixture of disorders with little in common other than their severity, chronicity, and occurrence in childhood. To add to the difficulty, the term has been employed in widely divergent ways by different psychiatrists." (Rutter, 1972)

Rutter's (1972) seminal review 'Childhood Schizophrenia Reconsidered' clearly argued that infantile autism was a distinct category separate from childhood Schizophrenia. Kolvin (1971a) (using clearly defined diagnostic criteria), demonstrated that not only were infantile psychoses of early onset different from later onset psychoses, but also the later onset group presented with the clinical symptoms of Schizophrenia (formal thought disorder, delusions and hallucinations), similar to adults (Talay-Ongan, 1998).

The publication of the Diagnostic and Statistic Manual of Mental Disorders (DSM)- DSM III and III-R reflected this changed thinking, and Schizophrenia in children was diagnosed using the same criteria as in adults. The current situation in DSM-IV and International Classification of Diseases (ICD 10), continue to reflect that Schizophrenia in childhood can be diagnosed by using the same criteria as in adults. These criteria are specified on the following page.

1.3. Classification Systems:

The two major classification systems which will be considered are the American Psychiatric Association's Diagnostic and Statistical Manual, version four (DSM-IV), and the World Health Organization's International Classification of Mental and Behavioural Disorders, version ten (ICD-10).

1.3.1. Diagnostic Criteria for Schizophrenia- DSM-IV:

A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1- month period (or less if successfully treated):

(1) delusions

(2) hallucinations

(3) disorganized speech (e.g., frequent derailment or incoherence)

(4) grossly disorganized or catatonic behaviour

(5) negative symptoms, i.e., affective flattening, alogia, or avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the persons behaviour or thoughts, or two or more voices conversing with each other.

B. Social/ occupational dysfunction: For a significant portion of time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self care are markedly below the level achieved prior to the onset (or when the onset in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. Duration: Continuous signs of the disturbance for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A, present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizo-affective and Mood Disorder exclusion: Schizo-affective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood symptoms have occurred during active- phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. Substance/ general medical condition exclusion: The condition is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. Relationship to a Pervasive Developmental Disorder: If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is only made if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

1.3.2. Diagnostic Criteria - ICD-10:

The ICD-10 classification states that it is useful to divide the symptoms into groups that have special importance for the diagnosis and often occur together, such as:

(a) thought echo, thought insertion or withdrawal, and thought broadcasting;

(b) delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception;

(c) hallucinatory voices giving a running commentary on the patients behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body;

(d) persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world);

(e) persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end;

(f) breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms;

(g) catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor;

(h) negative symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance - it must be clear that these are not due to depression or to neuroleptic medication;

(i) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self absorbed attitude, and social withdrawal.

The ICD-10 gives clear guidelines with regard to the number of symptoms and necessary duration, in order for the diagnosis to be met. "The normal requirement for a diagnosis of Schizophrenia is that a minimum of one very clear symptom (and usually two or more if less clear-cut) belonging to any one of the groups listed as (a) to (d) above, or symptoms from at least two of the groups referred to as (e) to (h), should have been clearly present for most of the time during a period of 1 month or more. Conditions meeting such symptomatic requirements but of duration less than one month (whether treated or not) should be diagnosed in the first instance as acute Schizophrenia - like a psychotic disorder - and reclassified as Schizophrenia, if the symptoms persist for longer periods" (World Health Organisation, 1992).

There are also exclusion criteria, with regard to the presence of extensive depressive or manic symptoms. The diagnosis of Schizophrenia should not be made in the presence of overt brain disease or during stages of drug intoxication or withdrawal.

1.4. Diagnostic Issues:

Both the DSM-IV and ICD-10 have subtypes within the Schizophrenia diagnosis, which are defined by the predominant symptomatology at the time of evaluation (American Psychiatric Association, 1994; World Health Organisation, 1992). These are: the Paranoid Type, Disorganized Type (Hebephrenic in ICD-10), Catatonic Type, Undifferentiated Type and Residual Type. These subtypes have generally not been used in the literature on children, except by Werry et al. (1991) and Remschmidt et al. (1994).

It is possible that the use of sub-classification in children with Schizophrenia has not occurred, because there has been a general lack of conclusion, regarding the recognition of Schizophrenia as an independent category in children (as previously discussed). Furthermore, in those studies where a valid classification system was used, it may not have been possible to neatly subdivide the symptoms into the sub-categories. It could also be that sub-classification is related in some way to the age and developmental level of the child, and may shift with development. Further research is needed to clarify this.

In contrast to the specific duration of 6 months needed to diagnose Schizophrenia in DSM-IV, the ICD-10 requires that symptoms be present for a period of one month or more. This discrepancy may present problems when comparing studies where different classification systems are used, because the DSM-IV uses the diagnosis of Schizophreniform Disorder, where the essential features of Schizophrenia are present, except that the disorder does not last for 6 months.

The research using ICD-10 would therefore include both the categories of Schizophrenia and Schizophreniform disorder, and thus have larger samples that are not homogeneous. This will influence the outcome data, particularly as the prognosis is better for Schizophreniform psychosis than Schizophrenia. Outcome research using ICD-10 criteria may thus have slightly more favourable findings.

In addition, the ICD-10 makes no provision for the modification of criteria for use in children at varying developmental levels. The DSM-IV does highlight the fact that delusions and hallucinations may be less elaborated than those observed in adults. An addition to the DSM-IV impairment of function criterion is, "when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement" (American Psychiatric Association, 1994). This is at least some concession to the potential expression of the illness in children, although it could be argued that more research in this area is needed, to inform DSM-V and ICD-11.

CHAPTER TWO

THE PHENOMENOLOGY OF CHILDHOOD SCHIZOPHRENIA

2.1. Introduction:

The diagnosis of Schizophrenia should not just involve a mechanical counting of criteria, but an elicitation and description of symptomatology. The seminal study by Kolvin et al. (1971a), not only differentiated Schizophrenia from infantile psychosis (autism), but also described the clinical symptoms specific to each group. Disorder of the form and disorder of stream of thought were present in 60% of the group with Schizophrenia. Also present were delusions (disorder of content of thought) of persecution, grandeur, hypochondriacal and fantastic delusions. In addition it was noted that 81% of the sample had auditory hallucinations. Other hallucinations documented were bodily (36%) and visual (30%).[2]

The features described by Kolvin et al. (1971b) are central to the diagnosis of Schizophrenia in children. Subsequent research, using DSM III criteria and structured diagnostic interviews, have produced similar results and validated the diagnosis of Schizophrenia in children. The research in this area - since the publication of the DSM III - has generally adhered to the diagnostic criteria, with its strict inclusion and exclusion criteria. There has thus been a marked shift in diagnostic rigour and classification, in an attempt to identify a homogenous group.

[2] Karl Jaspers (1968) gives an interesting account of the distinction between imagery and hallucination, at a phenomenological level. (p.1321)

2.2. Hallucinations:

These are defined as "perceptions occurring in the absence of any or sufficient sensory stimulus and, as a consequence not observed by anyone else present at the same time"(Rutter, Taylor and Hersov, 1994). Russell et al. (1989), reported that auditory hallucinations were present in 80% of their sample of children with Schizophrenia (mean age 9.54 years). Green et.al. (1992), found that 84.2% of their sample had auditory hallucinations of various types.

Other studies showed a range from 57% (Werry et al. 1991) to 100% (Spencer and Campbell 1994). (The most likely reason for the high rate of 100% in the Spencer and Campbell study is because of the small sample size resulting in a rapid 'ceiling' effect, i.e. measurement artifact).

The types of auditory hallucinations varied. Some were unrelated to depression or elation e.g. a girl reported the voice of a dead baby brother saying 'I love you sister, sister I am going to miss you' (Russell et.al., 1989; Russell 1994). Yet others reported were command hallucinations, religious hallucinations, conversing voices, persecutory hallucinations and commenting voices (Russell et al. 1989).

Researchers generally (except Kolvin et al., 1971b; Russell et al. 1992; McKenna et al.; 1994) have not reported on the detailed analysis of *types* of auditory hallucinations, but have only looked at the broad category, for the purpose of general diagnosis.

Visual hallucinations were consistently reported by different researchers (Kolvin et al. 1971b; Russell et al.1989; Green et al.1992; Spencer and Campbell, 1994), with the incidence varying from 30% (Kolvin et al. 1971b) to 47.4% (Green et al. 1992). Examples of these were: one child saw the devil, and another saw the Martians who talked to him (Green et al. 1992).

Other hallucinations reported were tactile, (Russell et al. 1989; Green et al. 1992, Spencer and Campbell, 1994), and somatic and olfactory (Russell et al. 1989). It is important diagnostically to note that non-auditory hallucinations were never reported without accompanying auditory hallucinations, and one child often exhibited several types of auditory and other hallucinations (Russell et al. 1989; Spencer and Campbell, 1994).

Andreasen (1987), in her assessment of adult schizophrenic patients, reported that 75% of the sample had auditory hallucinations. Somatic-tactile, olfactory and visual hallucinations were less common. The rate and type of hallucinations appear to be similar in children and adults.

Hallucinations in children are not necessarily pathognomonic of Schizophrenia. This was demonstrated by Garralda (1984b), in a retrospective study of children with emotional or conduct disorders, who also had hallucinations. In this sample precipitants of illness were present in the histories of most of the children. When these children were followed up (mean of 7 years) there was no increased risk for psychosis, depressive illness, organic brain damage or other psychiatric disorders (Garralda 1984c).

A recent study by Altman, Collins and Mundy (1997), examining non psychotic adolescents from a residential and day treatment centre, found that 33% of the participants reported having experienced auditory hallucinations. There was a strong association between auditory hallucinations and dissociation. (Dissociation will be further discussed in the differential diagnosis). These findings are therefore in keeping with that of Garralda (1984a), and underlines the importance of careful differential diagnosis, and obtaining a comprehensive list of symptoms.

2.3. Delusions:

These are fixed, false beliefs inappropriate to the person's culture, peer group or developmental level, that do not respond to reasonable explanations to the contrary (Rutter, Taylor and Hersov, 1994, p.596). Kolvin et al. (1971b), noted that "disorder of content or possession of thought, incurred relatively infrequently in the late-onset psychosis group, but never in the infantile psychosis group."

In his study, the most frequent delusion (disorder of content of thought) was : delusions of persecution (42%), followed by fantastic delusions (39%). Hypochondriacal delusions and delusions of grandeur were less frequent, with rates of 12% and 9% respectively.

Other reports have subsequently shown a range from 100% (Spencer and Campbell, 1994) to 55.3% (Green et al.1992). This variation could possibly be due to a referral bias or measurement artifact (small sample size).

In the papers reviewed, there were differences in the type of delusions, with McKenna et al. (1994) reporting that 94.7% of their sample had paranoid delusions and 78.9% had bizarre delusions. This is in contrast to the papers by Russell et al. (1989); Green et al. (1992) and Spencer and Campbell, (1994) where no particular type of delusion predominated. In addition to the persecutory and bizarre delusions, the others reported were :

somatic delusions

delusions of reference

grandiose delusions

delusions of thought insertion

delusions of control / influence

delusions regarding mind reading

delusions regarding thought broadcasting

delusions regarding thought control

religious delusions.

As with hallucinations, it was common for one child to describe several different delusional beliefs (Russell et al.1989). Spencer and Campbell (1994) and Russell (1994) highlight the fact that the delusions were simple rather than complex, with some older children showing some degrees of elaboration. Childhood themes involving monsters or animals were common. The rates of delusions in children are similar to that in adults, with several different delusional beliefs described by each adult in Andreasen's study (1987).

Hafner et al. (1993) claim, however, that there is a tendency for delusions in childhood and adolescence to be relatively non-specific and undifferentiated. They argue that systematized delusions (for example, of persecution) are more common in later adulthood, possibly reflecting the impact of cognitive development or rational and projective coping strategies with pathological experiences, during the course of the disease.

2.4. Formal Thought Disorder (e.g. incoherence, illogicality and loosening of associations): Prior to the publication of the DSM III, the definition of what constitutes formal thought disorder varied.

Kolvin et al. (1971b), quotes a definition from Bleuler, "in formal thought disorder, there is fundamentally a weakness of association, which leads to an increase of autistic and dereistic thinking (i.e. fantasy thinking which is entangled with private fantasy, and is not therefore goal directed)."

This definition was *very* broad and was open to a wide range of interpretations. Both clinicians and researchers were therefore without a clearly defined standard, and uniformly agreed on, definition in adult psychiatry.

Andreasen (1979a), in an attempt to redress the problem, presented a set of definitions that "takes a *relatively* broad approach to the concept of thought disorder." These definitions were based on clinical reports, tested empirically, and conceptualized thought disorder as consisting of a variety of subtypes. These definitions were used in the glossary of the DSM-III, so that they would become standard for American psychiatrists.

In addition to providing a set of consistent definitions, Andreasen (1979b) also developed a scale for the assessment of thought disorder called Scale for the Assessment of Thought Language, and Communication (TLC) for use in adults.

Advances with regard to the definition of thought disorder and the use of an assessment scale were made in adult psychiatry, but this was not immediately paralleled in child psychiatry. The work of Kolvin et al. (1971a-f) was a major improvement, but there was no uniformity about the definition and assessment of thought disorder in children. In the DSM-III, even without supportive empirical data for children, the definitions were assumed to be appropriate.

Subsequent empirical studies found varying rates of thought disorder. In Kolvin et al. (1971a), the frequency in "late-onset"[3] (pre-pubertal) psychosis was 60% for disorder of association, 45% had derailment of thought, and 51% had talking past the point. Russell et al. (1989), using the Interview for Childhood Disorders and Schizophrenia (designed by the authors), made global clinical ratings of the DSM-III criteria of formal thought disorder. They found incoherence or marked loosening of associations, illogical thinking or poverty of speech content in 40% of their sample.

The assessment of thought disorder in children with developmental language disorders can be problematic. The DSM-IV attempts to solve this by focusing on disorganized speech (frequent derailment or incoherence), rather than the underlying thought disorder.

The first researchers to use a psychological instrument to assess formal thought disorder in children were Arboleda and Holzman (1985). They used the Thought Disorder Index (TDI) to code the frequency and severity of 20 categories of verbal responses to standard Rorschach cards that have been grouped into four broad categories of thought disorder: associative, combinatory, disorganized, and unconventional verbalizations.

Arboleda and Holzman (1985) reported that children with psychosis, psychotic spectrum disorders, and children at risk for Schizophrenia and Affective Disorder, had more severe TDI scores than children with non-psychotic psychiatric diagnoses and normal children. Caplan et al. (1989), used an alternative approach, in the study of formal thought disorder in childhood.

They developed an indirect interview technique called the Story Game, which elicits speech samples, adequate for rating formal thought disorder in children. Furthermore, they also developed the Kiddie Formal Thought Disorder Scale (Caplan et al.1989), to rate the level of observed thought disorder (based on Andreasen's (1979b) Thought, Language and Communication Scale).

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[3] This is an example of classification anomalies: Kolvin's 'late onset' refers to children between 5 and 15 years of age, and is contrasted with 'infantile psychosis' (autism) with an onset before 3 years of age.

A trained clinician administers the three parts of the Story Game to the child. In the first and last part, the child hears an audio-taped story about a dream about a friendly ghost and an ostracized boy respectively. The child retells the tale and answers standardized, open-ended questions on each story. In the second part of the Story Game, the child makes up a story chosen from five topics (the Incredible Hulk, a witch, a good or bad child, an unhappy child). The Kiddie Formal Thought Scale then provides systematic guidelines for rating illogical thinking, loose associations, incoherence and poverty of content of speech in children.

Subsequent research using the Kiddie Formal Thought Disorder Story Game and assessment scale demonstrated that children with Schizophrenia and children with Schizotypal Personality Disorders could be distinguished from age-matched normal controls, based on illogical thinking and loose association scores (Caplan et al.1990).

Caplan et al. (1989, 1990) highlighted the importance of a developmental perspective, when they showed that illogical thinking and loose associations were normal in children under seven. These authors hypothesized that "the more severe illogical thinking and loose associations in the younger children with Schizophrenia spectrum disorder might imply that the onset of this disorder in middle childhood might impair maturation of cognitive skills that children use to present their thoughts to the listener in a logical and cohesive manner." Onset of Schizophrenia spectrum disorder in late childhood, however, might spare the maturation of these skills. Further research is needed to test this hypothesis.

Andreasen and Grove (1986) investigated thought, language and communication in adults with Schizophrenia, Schizo-affective Disorder, and Mania using the Thought Language and Communication Scale. They found that patients with Mania and Schizo-affective Disorder also display prominent abnormalities in thought, language and communication. They reported that "the global concept of thought disorder should not be considered to be pathognomonic of Schizophrenia or diagnostic of it." Again, as with hallucinations, caution should be exercised in not rushing to a diagnosis.

As far as I am aware, a longitudinal study (using a reliable assessment scale), to determine the significance of thought disorder in different psychiatric conditions in children, has not been done. Further research is needed to assess thought disorder in psychiatric disorders in children - a longitudinal study would help to determine the prognostic significance of thought disorder in children.

In addition, the issue of language impairments impinging on psychiatric assessment needs to be considered. Language difficulties could potentially be misconstrued as thought disorders. Cantwell et al. (1979) demonstrated that a significant number of children with developmental language disorder, had psychiatric problems. The most common diagnosis was Attention Deficit Disorder, followed by Oppositional Disorder. The remainder had a variety of anxiety disorders, although there was no diagnosis of Schizophrenia or Bipolar Disorder. However, there sample was small and the condition is rare. Generally, research into language difficulties in Schizophrenia have focused on adult rather than children (e.g. Sims, 1995).

2.5. Positive and Negative Symptoms:

Positive symptoms of Schizophrenia refer to the hallucinations, delusions and thought disorder, whereas negative symptoms are those of deficits - e.g. flat affect, a-sociality, anergy, and paucity of speech and thought (Andreasen et al. 1990). They demonstrated that negative symptoms have been associated with chronicity, poor pre-morbid adjustment, impaired cognitive functioning and brain injury. Positive symptoms have been associated with better pre-morbid functioning, and higher overall level of functioning.

The research was based on adults with Schizophrenia. There have not been many studies applying this differentiation to children; (Bettes and Walker, 1987; Remschmidt et al.1991; Maziade et al. 1996b).

McKenna et. al, (1994) used the scales developed by Andreasen (1979a,b) - the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms. They reported that those children diagnosed as schizophrenic, generally resembled schizophrenic adults, in having flat or inappropriate affect, deterioration of function, prominent hallucinations and delusions, avolition and alogia. Unfortunately, they do not report on the proportions of children with positive symptoms, negative symptoms or both. It would have been interesting to see if these children showed any resemblance to the associations with positive and negative symptoms, as seen in the adults.

Further research is required to assess the reliability in children of the Scale for the Assessment of Positive Symptoms and the Scale for the Assessment of Negative Symptoms.

In addition longitudinal research will help to demonstrate whether the associations of the positive and negative symptoms present in adults are valid in children with Schizophrenia. Some preliminary results from Maziade et al. (1996b), seem to indicate that this may be so.

Using the Scales for the Assessment for Positive and Negative Symptoms, they undertook a factor analysis, within a longitudinal framework. Their findings confirmed the independence of these two clusters in Childhood Schizophrenia as well. Maziade et al. (1996a) also found a high stability of diagnosis in their 15 year follow up study, although the presentation of positive or negative symptoms were less stable. Taken together, however, these findings provide additional support for the notion of continuity between child and adult onset Schizophrenia.

In summary, the research documenting the phenomenology of Schizophrenia in childhood generally concurs that the diagnosis of Schizophrenia *can* be reliably made in children, while taking into consideration the age and developmental level of the child. The diagnosis is therefore based on a clinical assessment using the traditional methods of assessment, i.e., a thorough history, mental state examination, physical examination, and any special investigations necessary. In those situations where the clinical picture is not clear, an ongoing longitudinal assessment should help to clarify the diagnosis (King et al. 1997).

CHAPTER THREE

EPIDEMIOLOGY AND COURSE

3.1. Prevalence:

Prevalence refers to the proportion of a population affected by a specific condition. Whilst adult Schizophrenia has been fairly extensively researched, with a prevalence estimate of between 0.5% and 1% (American Psychiatric Association, 1994; Eaton et al. 1995), there are very few epidemiological studies looking at the incidence and prevalence of Schizophrenia in children.

Part of the difficulty has been changing diagnostic clarity, with a distinction between Autism and Childhood Schizophrenia only emerging after the publication of DSM-III (Hafner and Nowotny, 1995). Some earlier studies thus have misleading rates, based on a heterogeneous group of 'childhood psychoses' (Thomsen, 1996).

In addition, the numbers of pre-pubertal cases are extremely rare, making prevalence assessment a matter of estimation. Extrapolating from their data, Burd and Kerbeshian (1987) maintain, on the basis of their survey in North Dakota, the rate of Childhood Schizophrenia up to 12 years of age is 0,19 per 10 000. For boys in this age group, the rate is 0,35 per 10 000, indicating the incidence of 'Very Early Onset Schizophrenia' (VEOS)[4], is considerably higher amongst boys than girls (p.348).

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[4] Werry(1992), stressed the importance of distinguishing between early- onset Schizophrenia (EOS) and Very Early Onset Schizophrenia(VEOS) which develops before 13 years. The main reason for this differentiation was to move away from the pubertal/ pre-pubertal dichotomy as, in most studies, it was often difficult to be specific about the onset of puberty (Jacobsen and Rapoport, 1998).

The rates increase markedly during adolescence, especially during later adolescence. Thus even at 15 years and younger, the prevalence is still just 0,14 per 1000, roughly approximating almost 50 times less than their probands between 16 and 54 years (Thomsen, 1996).

Remschmidt et al. (1994), in their study of psychotic disorders in a clinical population of children and adolescents, also found that Schizophrenia was extremely rare up to the age of 12 years. They similarly found a dramatic increase in the occurrence of Schizophrenia after age 13, which reached maximum incidence in late adolescence and early adulthood (Volkmar, 1996; Thomsen, 1996; Hafner and Nowotny, 1995).

In a population-based survey in Goteberg, Sweden, the prevalence for general psychosis amongst teenagers was 0,54% (Gillberg, Wahlstrom, Forsman, Hellgren and Gillberg, 1986). The most common diagnosis was Schizophrenic Disorder (41%), followed by Major Affective Disorder (21.3%), Substance Induced Disorder (21.3%) and Atypical Psychosis (9.8%). In childhood, under the age of 13 years, only 2 cases of diagnosed Schizophrenia occurred (corresponding to a prevalence rate of 1.8/10000). These authors suggest that the problem of teenage psychosis is at least ten times more common than childhood psychosis.

Again, earlier onset appears to be more common amongst boys, who may be proportionately over-represented by ratios of up to 3 or 4 to 1 (Eaton et al. 1995; Green et al.1992; Hollis, 1995; Kolvin et al. 1971a; Remschmidt et al.1994; Russell, 1994; Russell et al.1989; Spencer and Campbell, 1994; Thomsen, 1996; Werry, 1992).

As the age of onset increases, so does the proportional representation of girls, such that over 45 years of age, women tend to predominate. (Major risk ages for boys appear to be between 15 and 24, for girls, 25 and over: Eaton et al. 1995).

However, Wahl and Hunter (1992) have claimed that there is also a bias towards male selection in analyzing Childhood Schizophrenia samples. Although younger males are more accessible in terms of their greater prevalence (and more frequent and longer hospitalizations), they maintain that they are still disproportionately over-represented, stating that this may possibly reflect wider societal bias (p.316).

Although the epidemiological research on Schizophrenia in children is sparse (and the literature reported is only from developed countries), the situation is different with regard to Schizophrenia in adults, where data is far more readily available (Jablensky, 1995; Eaton et al. 1995). Due to the low incidence rate of VEOS, it has been suggested that follow up studies of children diagnosed as Schizophrenic, should help to establish the continuity with adult pathology, and hopefully a clearer sense of the course of the illness (Hafner and Nowotny, 1995). Whilst this is labour intensive and prone to sample attrition, it may be useful in validating the diagnostic entity of Childhood Schizophrenia, and gaining a developmental perspective on the course of the illness.

3.2. Incidence:

Incidence refers to the rate at which new cases occur. Again, owing to its rarity, no reliable figures exist for Childhood Schizophrenia. Some tentative evidence suggests that there might be a decline in the incidence of adult onset Schizophrenia.

However, it is not clear whether this stems from tightening diagnostic criteria, rather than improved interventions (Eaton et al. 1995).

3.3. Course and Outcome:

3.3.1. Onset:

The onset of Schizophrenia in children is usually considered to be either acute or insidious. However, Kolvin et al. (1971b), highlighted the difficulty in trying to pinpoint the exact onset of clear-cut psychotic features, when the onset of Schizophrenia is insidious. In children younger than 14 years, the onset is predominantly insidious (Alaghband-Rad et al. 1995; Hollis, 1995; Asarnow, 1994; Russell, 1994; Green et al. 1992; Werry, 1992; Kolvin et al. 1971b), with an acute onset in about 25% of cases. Insidious onsets have been more linked to negative outcomes than acute onset (Eggers and Bunk, 1997).

3.3.2. Pre-morbid Functioning:

It is important to try and distinguish pre-morbid functioning from the 'prodromal' phase of the illness - a practice not easily accomplished, as there may be an overlap in presentation (Amminger et al. 1997). McGorry et al. (1995) argues that the notion of 'prodrome' lacks specificity and is easily over-estimated, especially in retrospective designs, or with ambiguous data collection. It can often only be discerned retrospectively, as part of an insidious onset (World Health Organisation, 1992, p.88). Attempts to predict those individuals 'about to become psychotic,' on the basis of current knowledge, appears unreliable (Yung, et al. 1996).

With respect to pre-morbid functioning in children with Schizophrenia, however, there have been many studies conducted, which show its importance. Although the methodologies have varied, the results have been consistent.

The reports by Hollis (1995) and Alaghband-Rad et al. (1995), have both shown a greater delay in language development and more pre-morbid speech and language disorders, in children with onset of Schizophrenia before age 13.

Further, the other pre-morbid variables shown to be present in this age group are: pre-morbid personality characterized by shyness, introversion and withdrawal (Remschmidt et al.1994; Werry et al. 1991; Kolvin et al. 1971c). In addition, there is generally poorer pre-morbid adjustment and chronic patterns of dysfunction (Asarnow and Ben-Meir, 1988), with developmental abnormalities seen in children with pervasive developmental disorder (Alaghband-Rad et al. 1995; Russell et al.1989).

The significance of the pre-morbid abnormalities and developmental delays may represent the early neuro-pathological manifestations of the disorder, which could support the hypothesis that Schizophrenia may be a neuro-developmental disorder with early central nervous system lesions affecting normal maturational processes (McClellan and Werry, 1994; Murray, 1994; Fish et al.1992).

However, these features are not necessarily present in all cases of Childhood Schizophrenia. Neumann et al. (1995) have noted that there are a broad range of potential behavioural precursors to Childhood Schizophrenia, and that children vary in terms of the extent and variety of pre-morbid difficulties they exhibit. They attempted to examine these, with the hope of possibly uncovering 'behavioural subtypes' of Schizophrenia, given the heterogeneity of behavioural precursors. (Maziade et al. (1996a), has also argued that this might be a fruitful line of research, in terms of possibly identifying more specific subtypes).

They found that behavioural abnormalities increase with age, but cluster analysis indicated an early onset deviating sub-group, characterized by greater behavioural problems and associated neuro-motor difficulties. They postulated that this sub-group may possibly reflect a neuro-developmental sub-type of Schizophrenia, involving significant and progressive impairment. However, they were uncertain as to whether this cluster was a clinically distinctive entity, or else possibly a statistical artifact. If an artifact, this could potentially be obscuring an underlying continuum with other cases of later onset and less severe (or absent) pre-morbid difficulties.

Notwithstanding this, it appears quite clear that Childhood Schizophrenia accompanied by earlier onset and greater pre-morbid problems, generally exhibits poorer outcome results (Amminger et al. 1997; Maziade et al. 1996a; Neumann et al. 1995). (Maziade et al. (1996a) has referred to these pre-morbid behavioral difficulties as 'NPBD,' i.e. non-psychotic behavioural disturbances).

Given that these children tend to be predominantly male, it has been argued that the prognosis for females is better (Johnstone et al. 1995). The evidence for this is not necessarily so clear cut, however, several studies noting that pre-morbid functioning is almost unequivocal as a prognostic indicator, gender less so (Amminger et al. 1997; Harding et al. 1987; Hafner and Nowotny, 1995).

3.3.3. Course:

The long- term course appears to be similar to that of Schizophrenia beginning in adult life, i.e. a fluctuating course, with each episode marked by pro-dromal, active and recuperative phases, followed by quiescent or residual deficit periods (Rutter, 1995).

This relapsing and remitting course could therefore have a marked impact on the various developmental milestones - especially with regard to cognitive, social and emotional development. Some researchers thus feel its course might be more unremitting and potentially damaging than adult onset Schizophrenia. Schmidt et al. (1995) describes Childhood Schizophrenia as "a chronic and relapsing disorder, accompanied by considerable disability and significant deterioration in adaptive functioning, from often already impaired pre-morbid levels" (p.94). We thus need to look closely at outcome studies.

3.3.4. Outcome:

Ciompi (1980) has argued that there is an enormous variety of possible evolution of development in Schizophrenia, suggesting there is "no such thing as a specific course of Schizophrenia, and the potential for improvement has long been under estimated." (p.420)

Unfortunately, however, this appears to refer to adult onset Schizophrenia. Despite identical diagnostic criteria and similarities in phenomenology, child onset Schizophrenia appears to have a more pessimistic prognostic outlook. There are few outcome studies using DSM III criteria, but they are generally in agreement.

Werry et al. (1991) (with a follow-up of 1-16 years (mean, 5 years)), reported that only 17% of children and adolescents with Schizophrenia were well at follow-up. Eggers (1978) had stated that, in his sample of children with follow-up of an average of 15 years, 20% had recovered completely, 30% had reached relatively good social adjustment, and 50% had moderate or poor remission. It is not clear however, which diagnostic criteria were used, and what measures were used in determining the level of adjustment.

In a later and longer follow up study, Eggers and Bunk (1997) again emphasized the finding that the earlier the age of onset, the poorer the prognosis. Despite their differences in methodology and small sample sizes, both Werry et al. (1991) and Eggers and Bunk (1997) suggested that those children with an early onset of psychosis had a poor outcome.

Remschmidt et al. (1994), in their prospective study, also found that those patients with onset of schizophrenic psychosis before age 14, have a poor prognosis. Werry et al. (1994), further independently supported an association between pre-morbid clinical features and prognosis, noted above. Both Werry et al. (1994) and Remschmidt et al. (1994) mentioned that outcome was also predicted by pre-morbid personality and cognitive functioning - i.e. "patients who were cognitively impaired, shy, introverted and withdrawn before the beginning of their psychotic state, have a poorer prognosis" (Remschmidt et al. 1994).

It thus appears that an early, insidious onset, combined with pre-morbid difficulties, might be a particularly pernicious combination of factors for outcome. Werry and Taylor (1994) succinctly highlighted the clinical implications of Schizophrenia in childhood. According to them, it had to be regarded as a serious, episodic, but ultimately usually chronic progressive disorder. This produces considerable disability, and requires continued psychiatric supervision.

Possible explanations for this have been provided at both the biological and social levels. Thus Eggers and Bunk (1997) argued that the early onset of Schizophrenia potentially impacts on the immaturity of the central nervous system, "especially dysfunctions of the cortico - sub cortical pathways, like the dorsolateral prefrontal cortex, and connections with mesolimbic structures" (p.113).

This and other potential biological explanations will be examined in a little more detail in the next section, looking at 'neuro-developmental hypotheses'. (Etiology: Chapter 4).

A social-psychological explanation posited by Schmidt et al. (1995), was that children and adolescents tend to be primarily environmentally sensitive and dependent, unlike adults. Early developmental difficulties could potentially act as a negative 'domino effect' for subsequent developmental tasks, rapidly accruing impairment. Familial adversities (for example, disengaged, distant or else high 'EE'[5] families), and disrupted schooling, may only tend to compound this. Needless to say, these two levels of explanation are potentially compatible (rather than competing), and further multi-layered studies are needed, to address the issue of improving the prognosis in Childhood Schizophrenia.

As Jones et al. (1994) have stated: "The view of attenuated development, even before the clinical syndrome of Schizophrenia appears, is quite compatible with etiological heterogeneity" (p.1401). Further attempts to uncover more clearly the exact etiology of Schizophrenia will be discussed in the following chapter.

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[5] Expressed Emotion: A reference to critical and over involved emotional attitudes by key relatives (e.g. parents). This has been seen as one predictor of outcome in adult schizophrenic studies. More studies are needed in Childhood Schizophrenia (e.g. Asarnow et al. 1994; Tompson et al. 1997).

CHAPTER FOUR

ETIOLOGY

4.1. Introduction:

The emphasis of research into causes for the onset of Childhood Schizophrenia has moved away from psycho-social to biological ones. Although there are some interesting and plausible neuro-developmental hypotheses, the actual definitive pathogenic base remains unknown. Bleuler's view that the disorder was biogenic, but symptomatology and outcome were largely shaped by psycho-social factors, appears to be pertinent to current findings (Werry, 1990).

Most research into the etiology of Schizophrenia has been focused in the area of adults. Despite the recent profusion of this work, which has uncovered evidence on the importance of genetic factors, changes in brain structures and neuro-chemical pathways, there is still no solid understanding of the pathogenesis of the disease.

Even more recently, there has been an increased interest in the area of childhood-onset Schizophrenia, with findings that support the continuity between child and adult onset Schizophrenia. There has been a renewed focus on trying to uncover neuro-biological factors, but this time looking more specifically at children. The research findings will be discussed in the following areas:

4.2. Genetics:

Although most of the extensive genetic research into Schizophrenia has been focused on adult patients, due to the continuity of the illness with child onset forms of Schizophrenia, it seems reasonable to assume many of the findings may extrapolate there. However, there is a need for more careful genetic research to be made specifically into Childhood-Onset Schizophrenia, such as have begun at NIMH (Jacobsen and Rapoport, 1998).

The recognition that Schizophrenia runs in families has long been present in the research literature. This has been based on the compelling evidence from family, twin, and adoption studies, that inherited factors are potentially important in the transmission of the illness (Gottesman et al. 1987).

Gottesman and Shields (1982) summarized the results of the main genetic studies (before the use of operational diagnostic criteria), looking at the frequency of the disorder among various classes of relatives (See Table 1 below). These figures clearly demonstrated that the risk of developing Schizophrenia in schizophrenic probands is markedly increased relative to the general population.

A more recent study by Kendler et al. (1985), using standardized methods of assessment and explicit diagnostic criteria in blind controlled samples, has shown that the lifetime risks for Schizophrenia amongst first degree relatives was 3,7% (DSM-III criteria). This was opposed to a lifetime risk in the control samples of 0,2%.

Table 1. Relationship and Risk to Develop Schizophrenia.

Relationship	Percentage 'Schizophrenic Risk'
General population	1
Spouses of patients	2
Third degree relatives (e.g. first cousins)	2
Second degree relatives (e.g Uncles/ aunts)	2
Nephews/nieces	4
Grandchildren	5
Half siblings	6
First degree relatives (e.g. Parents)	6
Siblings	9
Siblings with 1 schizophrenic parent	17
Di-zygotic twins	17
Children with 2 schizophrenic parents	46
Mono-zygotic twins	48

Current NIMH studies indicate that there might be even higher rates of Schizophrenia and Schizophrenia spectrum disorders observed among first degree relatives of the UCLA Childhood-Onset Schizophrenia group, than seen among first-degree relatives of patients with adult onset Schizophrenia (Jacobsen and Rapoport, 1998).

The studies on genetics have shown that Schizophrenia tends to cluster in families. However, families share environmental experiences as well as genes. What has not been demonstrated are the relative contributions of genetic and environmental factors.

Therefore, the classical genetic approaches, utilizing twin and adoption studies, need to be examined (Plomin and McCleam, 1995; Rutter and Plomin, 1997).

4.2.1. Twin Studies:

In twin studies, the main strategy is to compare the concordance for the disease between members of mono-zygotic twin pairs (MZ) and members of dizygotic twin pairs (DZ). MZ twins are identical and share 100% of their genes - in contrast, DZ twins share an average of 50% of their genetic material. Greater MZ than DZ concordance will thus reflect genetic influence - on the condition that both sets of twins environmental experiences are roughly approximate.

The concordance rate for MZ versus DZ twins in Schizophrenia are 46% to 14% (Gottesman, 1995). Other studies have reported MZ concordance rates are approximately about three times higher than DZ concordance rates. However, a number of these were not based on strict diagnostic operational criteria, and are thus open to the criticism of diagnostic unreliability. Onstad, Skre, Torgosen and Kringlen (1991), using blind structured interviews and DSM-III-R criteria, found concordance rates to be 48% versus 4%, again strongly supporting the notion of genetic influence.

A study by Gottesman and Bertelsen (1989) looked at the offspring of discordant mono-zygotic twins, in comparison to dizygotic twins. They found no difference between the prevalence of Schizophrenia in the children of the sick twin (16,8%) and in the offspring of the twin who remained healthy. By contrast, discordant DZ twins show a marked difference in the risk of Schizophrenia developing amongst their offspring.

This therefore argues strongly for the principal that non-genetic forms of the disorder ('phenocopies') - if they exist - are relatively uncommon. In addition, genotypes that give susceptibility to Schizophrenia may not always be expressed.

4.2.2. Adoption studies:

Adoption studies have also been important in helping to distinguish inherited from non-inherited factors. One of the best known adoption studies in Schizophrenia has been that of Rosenthal et al. (1971), called the 'Danish American' adoption study.

The researchers obtained subjects from Danish adoption registers. Most of the parents on the register had given up their children for adoption before their first psychiatric admission. They found that Schizophrenia and the schizophrenic spectrum disorders were more common amongst adopted children with schizophrenic biological mothers (or other biological relatives), than in control groups consisting of other adoptive children.

These findings have been criticized by other researchers, on methodological grounds, especially as the family environment of the adoptive children were not studied (Kety et al. 1994).

The largest, most recent adoption study was described by Tienari et al. (1993). A national Finnish sample of schizophrenics' offspring given up for adoption was compared broadly with matched controls, i.e. adopted away offspring of non-psychotic biological parents. Both adoptive and biological parents were interviewed and tested.

They found that the percentage of both psychoses and other severe disorders ('Borderline' syndrome and severe Personality Disorders), was significantly higher (30%) than in matched control adoptees (15%). However, clear differences between the two groups emerged only in adopted families who were independently rated as disturbed.

Thus the psychological factors connected with the rearing environment - especially disordered communication, lack of empathy and conflicts between parents and offspring - played an even greater role than genetic factors in the onset of serious disorder in these adoptees. Disturbed behaviour thus appeared to act as a dependent variable, whereas familial dysfunction interacted with genetics to influence its expression. These findings also demonstrated that a healthy family environment can protect from disturbance even children whose biological mothers have had Schizophrenia.

From the above discussion on the genetics of Schizophrenia, it can safely be concluded that there is a genetic component in the etiology of the illness. This appears to be particularly so in cases of Childhood-Onset Schizophrenia (Werry, 1992).

However, Gottesman (1995) places this in context by pointing out that 89% of patients will have parents who are not schizophrenic, 81% will have no affected first degree relatives, and 63% will show no family history of the disorder at all. Furthermore, although the predisposition to develop Schizophrenia can be inherited, family environment may potentially act as a trigger or a buffer. The lack of a 100% concordance rate in MZ twins highlights the involvement of additional factors.

4.3. Neuro-physiology:

The bulk of studies in the neuro-physiology of Childhood-Onset Schizophrenia, has focused in the areas of eye tracking studies and autonomic functions (Rapoport, 1998). We will thus look specifically at these areas.

4.3.1. Eye-tracking studies:

Many studies in the area of adult schizophrenics have documented that 50 to 85% of adults with Schizophrenia (even in remission), compared to 8% of 'normals,' have abnormalities in smooth pursuit eye movements (Gordon et al. 1994; Holzman, 1989). The use of infra-red oculography has demonstrated that the developmental sequence for smooth pursuit tracking abilities parallels that of other frontal lobe functions. Age has been positively correlated with smooth pursuit system performance in 8 to 15 year old subjects - this performance reaches adult level peaks by about the age of 14. Accurate fixation, on the other hand, reaches an adult pattern much earlier, round about 7 years of age (Ross et al. 1993).

One study which examined eye tracking in Childhood-Onset Schizophrenia, had two comparison groups: children with ADHD and age matched healthy controls. The children with Schizophrenia exhibited greater eye tracking impairments than did the 'normal' or ADHD subjects (Jacobsen et al. 1996b). This finding corroborates an earlier study by Gordon et al. (1994) - also at the NIMH, Bethesda - comparing the eye movements in 10 Childhood-Onset Schizophrenic patients, with 12 normal control subjects. They also found a greater degree of impairment of smooth pursuit eye movements in the Childhood-Onset Schizophrenia group than with the 12 normal control subjects.

Furthermore, Gordon et al. (1994) found that there was a greater degree of impairment in smooth pursuit eye movement amongst childhood onset - as opposed to adult onset - Schizophrenia. However, the impairments were qualitatively similar, supporting the notion of continuity between the disorders. Despite this, it does not implicate a *specific* lesion, as lesions in a variety of areas in the brain can produce these abnormalities (Leigh and Zee, 1991). This may imply that there is unlikely to be one specific lesion consistently involved.

4.3.2. Autonomic Functions:

There have been consistent abnormalities reported in perceptual measures of autonomic reactivity, including skin conductivity, and heart rate in adult Schizophrenia. Once again the NIMH, Bethesda, has been the only centre so far to compare the autonomic functioning of Childhood-Onset Schizophrenia with age matched controls.

Gordon et al. (1994) assessed the electro-dermal activity (as indexed by skin conductance) and heart rate, in a protocol that included a 3 minute rest period, a series of 10 minute signal tones, and a simple warned reaction time task.

The Childhood-Onset Schizophrenic patients had high baseline autonomic activity, slow habituation and adaptation, and impaired autonomic responses to the novel, significant stimuli of the experimental protocol. (These findings had diagnostic specificity, as they were not found in children with disruptive behaviour disorders or obsessive compulsive disorder). They also tended to support findings detailing attentional difficulties in adults as well as Childhood-Onset Schizophrenia (Zahn et al. 1998).

This general pattern of autonomic dysfunction has also been uncovered in adults - but generally those with poor and chronic outcome Schizophrenia (Zahn et al. 1997). These findings thus suggest that Childhood-Onset Schizophrenia may possibly represent a more severe variation of the illness (Gordon et al. 1994) .

4.4. Neuro-psychology:

Neuro-psychological and/or experimental tasks have been used to link behavioral findings to putative CNS dysfunctions, in an attempt to clarify the exact nature of the dysfunction. The main pioneers in this area have been Asarnow and colleagues.

A strong finding that has emerged with schizophrenic children, is that they show similar difficulties with attention and information processing, that have been demonstrated in adult schizophrenics. The key characteristic of the tasks that elicit impaired performance in children with Schizophrenia, is that the task makes extensive demands on processing resources. This suggests that these children have limited information processing capacity (Asarnow et al. 1994).

Asarnow et al. (1995) also demonstrated that children with Schizophrenia show impairments on the span of apprehension task - a task that requires a child to identify a target stimulus when shown briefly (for 50 m.sec) on a screen, embedded in an array of other letters. When required to process larger arrays of visual information (five and ten letters, versus one and three), these children performed more poorly than children with Attention Deficit Disorder, and age and I.Q. matched normal controls. The performance of the children with Schizophrenia was markedly impaired by increasing the amount of information required to be processed.

Event related potential (ERP) data was also recorded during the performance of the span of apprehension task. This also showed similar patterns for child and adult onset schizophrenics. When compared with age matched normal controls, both child and adult onset schizophrenics produced endogenous negative activity. This appears to reflect limitations on the amount of processing resources available to carrying out cognitive tasks, and provides convergent supportive data for this phenomenon.

In summary, not only do schizophrenic children show an attention information processing deficit that has been shown to characterize schizophrenic adults, this deficit also shows some specificity to Childhood-Onset Schizophrenia, when compared to a number of other child psychiatric disorders. These findings further support the notion of a similar disease process and neuro-psychological dysfunctions in child and adult onset Schizophrenia (Asarnow et al., 1995; Strandburg et al. 1994; Zahn et al. 1998).

Jacobsen and Rappoport (1998), also reported from their unpublished data, that the IQ in 10 patients from their Childhood-Onset Schizophrenia group showed a significant deterioration in intellectual functioning during the time interval between the pre-morbid period and after the onset of psychosis. However, unlike adults with Schizophrenia, intellectual functioning continued to decline 1 to 2 years after the onset of psychosis. If this pattern of intellectual deterioration continues, then there is the implication of a pathological process that is continuous rather than static. This would certainly challenge the current neuro-developmental hypothesis.

4.5. Neuro-anatomic and functional imaging:

(a) Neuro-anatomy:

Neuro-imaging studies have contributed greatly to the understanding of the neurobiology of Schizophrenia The computerised tomography (CT) studies of adults with Schizophrenia in the early 1980`s and late 1970`s were, along with the efficacy of chlorpromazine, a major landmark in establishing the biological basis of the disorder. With the advent of magnetic resonance imaging (MRI) of the brain, improved studies of brain morphology emerged.

There have been numerous studies, along with many abnormalities of brain structure reported. The findings most consistently replicated in adults have been: reduced volume of the medial temporal lobe structures, decreased grey matter volume, increased ventricular volume and decreased grey matter volume (Rapoport 1997, Kaplan and Sadock, 1995, Petersen, 1995).

Neuro-imaging studies of individuals with early onset Schizophrenia provide an important opportunity to examine the continuity between various forms of the illness and to further study the neuro-developmental hypothesis of Schizophrenia.
Unfortunately, there has been a paucity of imaging studies and those done have been on small sample sizes. The NIMH Childhood-Onset Schizophrenia project has been the source for most of the research in this population. Jacobsen and Rapaport (1998), members of the NIMH team, reviewed the literature and only a summary will therefore be presented.

In a group of 28 patients with Childhood-Onset Schizophrenia, when compared with age matched normal controls, the Schizophrenia group had "significantly reduced total cerebral volume."

The lateral ventricles in children were increased in size - as had been found similarly in adults (Frazier et al. 1996b).

The midsagittal thalamic area is significantly decreased - as in adults. Petersen (1995) suggested that the thalamus may have an important role in the patho-physiology of Schizophrenia, producing a loss of appropriate gating of sensory information with a consequent flooding of cortical centres by sensory stimuli and a fragmentation of thought processes.

They also found larger total, anterior and posterior corpus callosum areas emerged after adjusting for the small cerebral volume. This suggested a relative sparing of the white matter. Further research analyzing white to grey matter densities is awaited.

In a previous report from the same centre (when correlating clinical symptoms with Magnetic Resonance Imaging), a significant negative correlation was found between the score on the scale for the assessment of negative symptoms, and the total cerebral volume (Alaghband et al. 1997). This finding has also been seen in adults with Schizophrenia.

Frazier et al. (1996b), found an increase in the size of the globus pallidis in the childhood onset group. This correlated with neuroleptic exposure and with age of onset of psychosis.

In a sub-sample, 8 adolescent patients with onset of Schizophrenia before age 12 were matched with 8 comparison subjects. They had an initial and 2 year follow-up brain MRI scans, measuring basal ganglia and lateral ventricle volumes. The patients were being treated with Clozapine during this 2 year period.

The caudate volume was larger in the patients initially – decreased between scans – but did not differ from the controls at the second scanning. The caudate enlargement in patients with Childhood-Onset Schizophrenia appears to be secondary to medication exposure.

In a recent publication of a longitudinal study involving the re-scan after 2 years of 16 patients with Childhood-Onset Schizophrenia and 24 matched controls, results indicated that the mid sagittal thalamic areas decreased significantly in schizophrenics, but not controls. The ventricular volume was also shown to be increasing at a more rapid rate than the control group (Rapoport, et al. 1997).

These longitudinal studies indicate that the brain MRI investigations will be of vital importance in helping to understand the pathology and pathogenesis in Schizophrenia. The findings to date indicate that many of the replicated brain abnormalities in adult schizophrenics have been found to be present in Childhood-Onset Schizophrenia.
What has not been demonstrated is whether the abnormalities are more severe. Some of these abnormalities change over time, and further longitudinal research will contribute significantly to exploring this more carefully.

(b) Functional brain imaging:

Studies in adults with Schizophrenia have demonstrated by measuring cerebral blood flow and glucose metabolism, that there is abnormal frontal blood flow and metabolism (Petersen, 1995).

Jacobsen and Rapoport (1998) describe results from their NIMH Childhood-Onset Schizophrenia group. Using positron emission tomography (PET) and F-flurodeoxyglucose subjects (FDG), Childhood-Onset Schizophrenic patients and 26 healthy adolescents were matched for age, sex and handedness.

The subjects all performed an auditory continuous performance task during FDG uptake. There were no significant group differences in global cerebral glucose metabolism. There was, however, an increased metabolic rate in the supra-marginal gyrus and inferior frontal gyrus/insula, and decreased metabolic rate in the middle frontal gyrus and superior frontal gyrus, in schizophrenics. There was a bilaterally increased cerebellar metabolism.

The authors conclude that these findings suggest "abnormal neural circuitry in Schizophrenia, that includes the cerebellum." These results will clearly need to be replicated in larger samples and with stronger statistical certitude and generalizability. If they hold true, the significance for possible interventional approaches need to be evaluated.

4.6. Neurochemistry:

Although much research has been done on measuring the cerebrospinal fluid (CSF) metabolites in adults with Schizophrenia, there have been no consistent results replicated. Jacobsen et al. (1997), have published the only study of CSF monoamines in Childhood-Onset Schizophrenia.

They measured CSF homovanillic acid (HVA) (dopamine metabolite), 5-hydroxyindoleacetic acid (5-HIAA) (serotonin metabolite), 3-methyxy-4-hydroxyphenylglycol (MHPG) (noradrenalin metabolite) and serum prolactin during drug free and antipsychotic medication (Haloperidol and Clozapine) in 18 patients who had onset of Schizophrenia by age 12. The relationships between changes in CSF monoamines and serum prolactin and clinical outcome were examined. In addition, the degree of change in CSF monoamines in response to Clozapine treatment was compared to that for 16 patients with later onset Schizophrenia.

There was no significant change in the CSF monoamine concentration. The ratio of HVA/5IAA and HVA/MHPG did not significantly change with either Haloperidol or Clozapine treatment, despite the patients significant clinical improvement. The serum prolactin levels increased during Haloperidol treatment. This study did not have a control group from a healthy control paedriatic population and therefor the findings can only be seen as preliminary.

One explanation offered for the findings is that there was a tolerance pattern of neuro-chemical response. Alternatively, there may be other metabolic correlates of clinical symptoms and treatment response.

This highlights the complexity of the biochemical events which mediate clinical changes. Future research may hopefully identify the biological markers correlating with clinical symptoms and treatment response.

4.7. High Risk Research

High-risk research refers to the study of individuals who are considered to have a higher statistical risk of developing Schizophrenia than do individuals in the general population. The definition of risk most widely selected has been genetic relatedness, with the study population being the offspring of schizophrenic parents. The rationale has been based on the well established familial rates of Schizophrenia. (This was discussed in 4.1).

The goals of the prospective high-risk research have been to study the unfolding of the illness and to identify the critical neuro-biological and environmental risk factors. As a result, subjects have been followed for as long as 25 to 30 years, involving much time effort and expense.

Barbara Fish was the pioneer of prospective longitudinal high-risk research and launched the New York Infant High Risk Study in the early 1950s. She proposed that an index known as pandysmaturation (a measure of disorganized motor and sensori-motor development) reflected a genetically determined neuro-integrative defect . This defect manifested during the first 2 years of life and could serve as an early marker (Fish, 1987; Fish et al.1992).

A number of other studies followed, and in 1987, a full issue of Schizophrenia Bulletin (Volume 13, Number 3) was devoted to the first generation of high-risk studies.

Cornblatt and Obuchowski (1997) have clearly summarized the major findings through to 1997: "A number of environmental risk factors were examined in the first generation of high risk studies, including pregnancy and birth complications, life events and family characteristics. Overall, the results were non-conclusive. No solid evidence was yet available to link any of the environmental risk factors with specific behavioural outcomes."

Similarly, it was concluded that the findings of neuro-motor abnormalities were inconsistent across high-risk studies, and the specificity to Schizophrenia was not clearly established. With the exception of Fish's early work, there was no indication that neuro-motor dysfunctions were predictive of later clinical outcome (Cornblatt and Obuchowski, 1997).

The current consensus about the risk factors and bio-behavioural markers can be summarized as follows: (Cornblatt and Obuchowski.,1997; Fish et al.1992, Marcus et al.1981, Mirsky et al. 1995, Nagler et al.1985b, Sohlberg,1985a, Walker,1994a, Walker et al.1994).

A: Environmental Risk Factors:

The role of environmental stresses have not been conclusively identified. Similarly, in pregnancy and birth complications, the findings have been inconsistent.

B: Biobehaviour markers

Neuro-motor abnormalities: Motor abnormalities during the first 2 years of life could serve as a potential marker for later development of Schizophrenia.

Attention: Impaired attention is one of the strongest candidate markers of a biological susceptibility to Schizophrenia.

C: Neuro-cognitive dysfunctions:

The first generation high-risk studies did not incorporate neuro-psychology (verbal learning and executive functioning). The results of prospective research are awaited.

D: Eye movement dysfunctions (EMDs).

Eye movement dysfunctions are also a strong contender for candidate markers. Evidence from research in adult first degree relatives demonstrated that EMD's are biologically based, genetically determined and specific to Schizophrenia. However, this has not been studied in at-risk children longitudinally. The results of prospective research is awaited

E: Psycho-physiological variables:

There has been an interest in electrodermal markers following Cannon et al. (1998) reanalyzing the Copenhagen high-risk project data when the subjects were at a mean age of 15 years. They found that electrodermal non-responsiveness interacted with genetic risk and birth complications to predict negative symptoms in affected adults. In contrast, heightened electrodermal responsiveness interacted with genetic risk and stress from unstable family rearing environment to predict adult illness with predominantly positive features. Although very appealing, this was based on a very small sample and requires replication.

The information provided by the high-risk research has made a significant impact on the understanding of the predictors of illness and potential markers of adult onset Schizophrenia. However, the research on the high-risk samples has not had any subjects developing Schizophrenia before the age of 13.

There is some overlap between the potential biological markers for adult onset Schizophrenia and the neuro-physiological abnormalities as manifest in Childhood-Onset Schizophrenia. It is accepted that Childhood-Onset Schizophrenia can be diagnosed using the same criteria as in adults and is not a separate illness from adult Schizophrenia. The theory that takes into account the early onset, biological abnormalities and poor prognosis is the neuro-developmental hypothesis. This is discussed further under section 4.8.

4.8 Neuro-developmental Hypothesis:

There has been great interest in the neuro-developmental hypothesis. The most influential contributions have been made by Murray (1994), Murray et al. (1992), and Weinburger (1987).

According to Weinberger's (1987) highly influential conceptualization:
Schizophrenia is a neuro-developmental disorder, in which the primary cerebral insult or pathological process occurs during brain development, long before the illness is clinically manifest. This early lesion interacts with certain normal maturational events that occur much later. The lesion itself is static, but its effects on neurological function change - if a lesion affects a brain structure or region that is yet to mature functionally, the effects of the lesion may remain silent until that structure or system matures (page 660).

Murray et al. (1992) similarly proposes that an abnormality is present, although not recognizable, at birth. They postulate that congenital Schizophrenia (Childhood-Onset Schizophrenia), may arise as a consequence of a genetic defect, that results in the neuro-imaging defects seen.

They suggest further that a similar clinical and neuro-pathologic picture may also result from early environmental hazard or combinations of genetic predisposition and environmental hazard. These children are more likely to have pre-morbid abnormalities and present early to psychiatric services.

This hypothesis is indeed very plausible and integrates most of the various research findings. However, it will remain a hypothesis until the research is able to conclusively identify the aetiological factors and their mode of interaction.

Already some findings - ongoing intellectual decline and increasing ventricular volume in children with Schizophrenia - have emerged, that indicate the presence of a pathologic process eroding brain function, rather than a fixed static lesion. Further longitudinal studies are needed to replicate these findings.

CHAPTER SIX

CULTURAL DIMENSIONS

6.1. Cross-cultural Psycho-pathology:

There are two major theoretical orientations regarding psycho-pathology in a cross-cultural context. These are: (a) etic, and (b) emic (Marsella, Tharp and Cibrowski, 1979: Marsella and Pederson, 1980). Etic refers to the perspective that experience is universal and 'trans-cultural' and is therefore not qualitatively distinct across cultures.

Within this perspective, Schizophrenia, for example, will manifest similarly in different cultures. Thus, there are some systematic studies (which have used standardized methods of assessment), which have indicated similarities in the clinical symptoms of Schizophrenia in different cultures (Jablensky et al. 1992; Katz et al. 1988; Sartorius, et al. 1986).. However, it was noted that some symptoms (e.g. visual hallucinations) tend to be more frequent among patients in developing countries, while others (e.g. primary delusions) are more often diagnosed in patients in developed countries.

Some criticisms of the 'etic' approach are that it involves a form of 'cultural imperialism' (for example, importing 'Western' notions of mental illness and nomenclature), whilst ignoring cultural differences and the influence of cultural variables (Hall and Malony, 1983). The 'emic' perspective accordingly attempts to explain phenomena in terms of categories that are meaningful *within* various cultures.

Description is therefore culturally idiographic and relative, in contrast to the universalist etic method. Within this view, culture uniquely shapes the expression of various things (for example, 'mental illness'), essentially ruling out the superimposition of labels from one culture to another.

Given that Schizophrenia in childhood can be reliably diagnosed in children (taking into account age and developmental level), the presentation in different cultures should therefore be very carefully evaluated. In addition, researchers have noted that different cultures exhibit local patterns of behaviour, which may not fit easily into Western classification systems.

These have been referred to as variously 'culture bound' or 'culture specific'[6] syndromes (Littlewood, 1990). In South Africa, Robertson and Kottler (1993), highlighted different culture- specific syndromes in children and adolescents seen by 4 traditional healers.

They noted that the term 'ukuphambana' was used nonspecifically and pejoratively to denote psychotic behaviour. "Ukuphaphazela may describe panic disorder and amafufunyane in adults has been said to resemble hysterical psychosis. Umoya sounds like a primarily physical disorder which occurs in young children; in some cases this may include an organic mental syndrome such as could be associated, for instance with a congenital abnormality of the brain. Ukuthwasa seems to be a form of existential anxiety which does not appear to correspond to any of the anxiety disorders" (Robertson and Kottler, 1993).

[6] The use of 'culture bound' or 'culture specific' syndromes have been argued by some to be redundant, as all behaviour is to some extent culturally influenced. Anorexia nervosa, for example, could be considered a Western 'culture bound syndrome (Dein, 1997).

(Buhrmann (1977) posited that the experience of 'ukuthwasa' constituted a form of 'calling' to become a traditional healer).

The report by Robertson and Kottler (1993), highlights the different culture - specific syndromes treated by Xhosa speaking traditional healers in Guguletu, Cape Town. Other studies have identified similar 'culture-bound' syndromes amongst Zulu speaking people. Edwards et al. (1982), for example, state that for Zulu speaking people, culture-bound syndromes are believed to be "unique or peculiar to their people in the sense that their etiology, diagnosis and treatment are all inextricably bound up with the traditional Zulu and African views of sickness and health" (p.82).

The issue of culture specific/bound syndromes and their interpretation is thus one potentially fraught with difficulties - to 'reduce' these without negotiation to traditional Western labels, might be considered a form of 'cultural imperialism' and invoke resistance from patients. The resilience of traditional beliefs, even amongst an urbanized Black population, has been noticed by some researchers, especially when stress and illness are present (Lambo, 1974: Manganyi, 1973).

What is regarded as disease by Western medicine, may carry different meanings for other communities, relating to cosmological, moral or kinship disturbances (Dein, 1997; Littlewood, 1990; Milne and Robertson, 1998). It is thus important that psychiatric assessments should take these into consideration, because the therapeutic benefits could potentially be enormous, if these beliefs could be harnessed into a holistic treatment programme.

Having access to the cultural meanings of some symptoms (e.g. by the presence of a knowledgeable representative of the culture), may also mitigate against the mistake of a pathologising medical reductionism, for example, by labeling a culturally appropriate belief as a 'delusion' (Dein, 1997).

Such an integration of 'Western' and 'indigenous' approaches requires combining the dichotomous models of 'etic' and 'emic'. It seems that neither an exclusively 'etic' or 'emic' approach is entirely satisfactory. Criticisms of the emic perspective include the notion that it prevents cross cultural comparisons, and is too 'relative' and subjective to provide meaningful analytical data (Hall and Malony, 1983). A model perhaps closer to the complexities of 'reality,' could involve a synergistic combination of the two approaches.

Within the realm of 'depression' for example, some early myths concerning Africans was a belief that it was absent in their population (Marsella et al. 1979). However, some studies noted that depression may be manifest in a 'masked' form, frequently through the use of somatisation (Ebie, 1972). This is a contentious finding, Marsella et al. (1979), for example, mentions that - contrary to early myths - depression is common in Africa, and may present similarly to the Western pattern, especially amongst urban Blacks.

However, even if it *is* expressed in a culturally specific way (emic), the nature of the underlying disorder (e.g. depression), is assumed to be universal (etic). Thus, with regard to Schizophrenia, although its *form* remains relatively constant, culture determines the *content* of the illness and the way it is expressed. Thus, it has been noted that the incidence of delusions and hallucinations vary cross culturally (Jablensky et al. 1992), and the content and symbolism of the delusions and hallucinations vary too (Dein, 1997).

However, the correlation between culture - specific syndromes and the DSM IV classification system is not clear and further research is needed (Dein, 1997).

Just as developmental phase may influence the presentation of symptoms in children with diagnosed Early Onset Schizophrenia, so to it seems reasonable to suggest, will cultural factors and beliefs. These need to be incorporated into any holistic treatment approach. We will thus look more closely at culture and illness outcome.

6.2. Culture and Outcome:

One of the contentious findings of the World Health Organization's (W.H.O.) 'Determinants of Outcome of Severe Mental Disorder' (DOMSD) study was not the core uniformity of a schizophrenic syndrome across cultures, but the finding that better prognostic predictors included acute onset and *developing* country locality (Jablensky, 1995: Jablensky et al. 1992). It was argued that improved prognostic indicators in developing countries may reflect the contribution of cultural factors (Jablensky et al. 1992).

This finding has been disputed, most vehemently by Cohen (1992a,b) and Edgerton and Cohen (1994). They argue that the evidence is inconclusive, on the basis that there are widely discrepant attrition rates between developing and developed countries. With a far higher attrition rate amongst patients in developed countries, they claimed that these might be people who have had a better outcome, but are not identified as such, because of 'dropping out'.

They maintain that differing attrition rates would lead to biased comparisons (Edgerton and Cohen, 1994, p.226). While this argument may be valid, it could also be that 'drop outs' alternatively reflected non-compliance amongst people who may have been getting increasingly ill. In the absence of follow-up data, it is impossible to be certain.

Edgerton and Cohen (1994) also argued that better outcomes in developing countries may not necessarily reflect better societal or treatment practices there, but more pernicious environmental effects in developed countries. (Of course, both factors may be at play). They go on to state that although they have criticized the W.H.O. DOMSD findings, it "sounds plausible that some 'cultural' factors such as the conditions imposed by hospitalization and social isolation contribute to a less favourable course in developed societies, just as other factors such as tolerant families and social acceptance may lead to more favourable outcomes in developing countries"(p.227).

Craig et al. (1997) re-analyzed the W.H.O. DOMSD data, and generally confirmed the findings of the original data. However, they argued that there were insufficient details on cultural factors, to draw meaningful conclusions about the possible contributions of these.

More detailed cultural information (e.g. the use of local and anthropological information) was cited as essential to facilitating clarity on the findings. This call had already been made by Hopper (1992), in response to Cohen's (1992a,b) criticisms of a naïve labeling of 'culture' as a holistic variable. Even Edgerton (1980), in response to the International Pilot Study of Schizophrenia's (IPSS) similar finding of better outcome in developing nations, felt that the integration of cultural practices with Western approaches may be responsible for improved outcome.

However, since the decade and a half of the DOMSD study, there have been major shifts in the cultural settings, including migration, industrialization, and health care changes. These also need to be considered, and this will apparently be included in a follow-up W.H.O. DOMSD study planned (Craig et al. 1997).

Edgerton and Cohen (1994) concluded that it is important to specify interventions made during the course of illness, which include environmental (including cultural) factors, combined with biomedical factors, in prospective, longitudinal designs. The impact of treatments on outcome obviously needs to be carefully analyzed. It is to the issue of therapeutic intervention we will thus focus next.

CHAPTER SEVEN

TREATMENT

7.1. Introduction:

The literature on the treatment of children with Schizophrenia (under 14 years), is scant. Treatment will depend on the characteristics of the individual, the stage of the illness, and the developmental level of the child (Volkmar, 1996). McClellan and Werry (1994) and McClellan et al. (1997) have outlined the practice parameters for the assessment and treatment of children and adolescents with Schizophrenia.

With such a serious illness, in order to minimize the impact on social, cognitive and occupational functioning, multiple treatment modalities are needed including pharmacotherapy, educational and family interventions, and supportive psychotherapy (Volkmar, 1996; McClellan and Werry, 1994; Remschmidt et al. 1994).

7.2. Environmental Interventions:

The importance of early detection and intervention has been emphasized in a number of papers, which have uncovered this as a potentially crucial factor, in possibly influencing a more positive prognostic illness course (Birchwood, McGorry, & Jackson 1997; Johnstone, 1998; Johnstone et al. 1995).

7.2.1. Early Intervention:

There has been some pilot research on early interventions in young people (e.g. Yung, McGorry, McFarlane, Jackson, Patton, and Rakkar, 1996) and adults (McGlashan, 1996) at incipient risk of psychosis. These researchers are in the process of defining their measures of early phases and case criteria. They plan a longitudinal follow-up using, amongst others, a number of neuro-biological markers such as increased ventricular brain ratio and ventricular enlargement, neuro-chemical markers, such as reduced dopamine uptake by platelets. The psycho-pathological features of the illness were also examined. The predictive power of the neuro-biological markers and the psycho-pathological will be examined over a period of time.

The other research component that was examined, was the assessment of the current disability afforded by the prodromal states, as well as the process of transition from at risk mental state to psychosis - with the focus on factors that favour it (risk /vulnerability factors) and inhibit it (resilience). The results of this study would potentially make a positive contribution to the research on early intervention in psychosis and may help in designing early intervention programmes for children - even potentially those exhibiting pre-psychotic symptomatology.

However, the problem of 'false positives' (cases that do not develop into Schizophrenia, despite high risk factors), and the difficulty of ascertaining 'prodromal' states, makes it an ambitious project, fraught with potential difficulties.

Birchwood et al. (1997) mentions that the mean period between onset of 'frank psychotic symptoms' and treatment is approximately a year - the many cases of 'insidious' onset in Childhood-Onset Schizophrenia appear to delay intervention.

Those cases which involved lags longer than a year showed a threefold increase in relapse rates over the following two years, compared to those with a briefer duration of untreated illness. Help seeking behaviour was impeded by negative social attitudes around mental illness.

Early intervention thus appears to need community re-education around stigma and symptoms, alerting people and 'normalizing' the illness. The training of GP's to recognize psychotic symptoms (like many have been successfully trained to recognize depression), may also assist with early detection. As Clark and Lewis (1998) state: "The likely longer-term benefits of early and appropriate treatment must increasingly be seen to outweigh traditional clinical reluctance to apply the diagnosis of Schizophrenia for a first psychotic episode in a child" (p.1074).

7.2.2. Acute phase:

In the acute phase, with disordered and psychotic behaviour, in-patient treatment in a children's unit may be needed. This does not present a problem in developed countries where such treatment facilities are available. However, in South Africa, where resources are scarce, many children would either be managed in a general paediatric ward or in an adult psychiatric unit. In many situations then, in-patient treatment may be a last resort if the child could not be managed at home.

The type of in-patient unit was not specified in the literature, nor the therapeutic programmes likely to be beneficial in children with Schizophrenia. This is again most likely due to the rarity of the disorder and the lack of certitude around this issue. However, as regards the unit itself, it is felt that ideally this would be staffed with a full multi-disciplinary team, including educational professionals (Clark and Lewis, 1998).

Inpatient care is most likely needed to "be necessary during the first episode, because of the need for a thorough diagnostic assessment and institution of acute treatments" (ibid, p.1074).

McClellan and Werry (1994), when reviewing the efficacy of treatment interventions in adults with Schizophrenia, do suggest that the findings from the adult literature have shown that the combination of social skills training, family psycho-educational treatment, and medicinal intervention have been shown to decrease relapse rates.

They stated that patients with early onset Schizophrenia "should benefit from the combination of individual, family and/or group therapies as adjuncts to medication therapy. Such treatment should be developed in accordance with the developmental level of the child and should focus on psycho-educational information regarding the symptomatology, etiological factors, prognosis, and treatment factors for Schizophrenia. In addition, cognitive-behavioural strategies, such as social skills, problem solving strategies, self help skills, and therapies directed at family function, should be incorporated into the treatment plan."

How these therapeutic interventions are incorporated into the in-patient setting is not clear. One assumes that good clinical practice would dictate that the various therapies are introduced at a rate that both the patient and the family can tolerate - initially starting in the in-patient unit, and then the bulk of therapy being done on an out-patient basis, as the child's ego strength and external supports increase.

The goals of therapy would need to be constantly monitored according to the developmental level of the child, and in conjunction with any changes within the family. Family interventions would be focused around educating them on the illness and removing 'scape-goating' or 'high EE' (overly intrusive and critical) behaviour (McClellan et al. 1997).

McClellan and Werry (1994) do highlight the importance of maintaining a stable, consistent therapeutic relationship which 'serves to better monitor relapse and noncompliance, while also focusing on more disabling negative symptoms of the disorder'.

In addition, other services that may be needed are crisis intervention and family support programmes, in-home services, and a parent advocacy group. Furthermore, given impaired social functioning, social skills training may be helpful.

As many children with 'Very Early Onset Schizophrenia' also have scholastic problems, appropriate special education services, may also form an important part of a holistic treatment programme. Where specialized classrooms are available, these children would benefit from an individually designed curriculum, intended to meet their specific needs (McClellan and Werry, 1994).

Generally, insight oriented therapies are not beneficial - and may even be harmful in some cases (McClellan et al. 1997). CBT (Cognitive Behaviour Therapy) may be helpful to reduce the intensity of belief and pre-occupations with delusions, as well as raising problem solving strategies and coping resources (Enright, 1997).

All the psychotherapeutic and psycho-educational interventions make huge demands on the health and education budget, which developed countries can generally afford. The implications for a developing third world country like South Africa, however, are potentially enormous. There is some rudimentary community psychiatric infrastructure provided for adults. The services for children - especially black children, because of the gross inequalities from the apartheid system - are virtually non-existent (Robertson and Berger, 1994).

An intensive, interventionist model as proposed by McClellan and Werry (1994) may not be feasible. In addition, there are only 15 practicing Child Psychiatrists in South Africa. The number of psychiatrists and psychologists working in the African community is also limited (Robertson and Berger, 1994; Milne and Robertson, 1998).

Much work is required to develop an intervention strategy that combines great vigilance in monitoring at risk groups, with good clinical practice and appropriate psycho-educational and community intervention, in order to meet the South African need. It is highly probable that there will have to be a departure from the traditional medical model, and a move to incorporate indigenous healers and herbalists, into the management team.

7.3. Psycho-pharmacology of Schizophrenia:

7.3.1. Introduction:

The introduction of neuroleptics has produced a radical change in the medical and social prognosis of the psychotic disorders, especially Schizophrenia. Thus, for adults, the efficacy of the neuroleptics in treating Schizophrenia, has been well established (Masi, 1997).

The medication possibilities for Childhood-Onset Schizophrenia has been less extensively researched (Kumra et al. 1998c).

7.3.2. Anti-psychotic classifications:

It must be borne in mind that anti-psychotic medications are not homogenous, and it is important to be aware of the major distinctions between them. The British Medical Association (B.M.A). and the Royal Pharmaceutical Society of Great Britain (R.P.S.G.B). have derived a typology of anti-psychotic medication:

Group 1: Chlorpromazine, Methotrimiprazine, and Promazine, generally characterized by pronounced sedative effects, and moderate anti-muscarinic and extrapyrimidal side effects.

Group 2: Pericyazine, Pipothiazine, and Thioridazine, generally characterized by moderate sedative effects, marked anti-muscarinic effects, but fewer extrapyrimidal side effects than for Groups 1 and 3.

Group 3: Fluphenazine, Perphenazine, Prochlorperazine, and Trifluoperazine, generally characterized by fewer sedative effects, fewer anti-muscarinic effects, but more pronounced extrapyrimidal side effects than Groups 1 and 2.

Drugs of other chemical groups tend to resemble the phenothiazines of Group 3. These include the butyrophenones (Benperidol, Droperidol, and Haloperidol), thioxanthines (Flupenthixol, Zuclopenthixol and Loxapine, amongst others). Clozapine differs, in that it is a sedative, with fewer extrapyrimidal side effects.

The neuroleptics generally have well documented side-effects. These range from extra-pyramidal side-effects to tardive dyskinesia and neuroleptic malignant syndrome (Popper, 1995).

7.3.3. Modes of action:

The classic neuroleptics act on the post-synaptic dopaminergic receptors, especially the D2 receptors.[7] The anti-psychotic effect of the classic neuroleptics is believed to be based prevalently on the blockade of dopaminergic transmission in the meso-limbic and meso-cortical systems. (Many had noted extrapyrimidal and endocrine side effects, however).

More recently other neurotransmitters probably involved in Schizophrenia were explored, particularly serotonin. Drugs blocking serotoninergic receptors in CNS (Olanzapine), were reported to have the tolerance effect of standard neuroleptics on negative symptoms, but with a reduced incidence of extrapyrimidal side effects (Masi, 1997).

Therefore, drugs that block the dopaminergic receptors, but which also have a serotonin blocking activity, should be clinically more effective, with a lower incidence of extrapyrimidal side effects. The more recently synthesized neuroleptics, with combined action on dopamine and serotonin receptors, have been called atypical neuroleptics. The atypical neuroleptics currently used in clinical practice are Clozapine and Risperidone (Masi, 1997). These have been found to be useful in adults with Schizophrenia - the research with children has been less extensive and clear-cut.

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[7] 5 types of dopaminergic receptors are currently known, situated in various areas of the Central Nervous System (Masi, 1997).

7.3.4. Developmental pharmaco-kinetics:

The use of neuroleptics in Childhood-Onset Schizophrenia is a particularly complex problem. The illness has a poor prognosis - it is difficult to determine whether this reflects a more virulent version of the illness, or if the neuroleptics are less effective in this phase.

The protocols of dosage levels in children needs to be carefully evaluated, with the major factors being body size (mg/kg calculated dosage) and hepatic drug metabolism (Popper, 1995). The rapid drug metabolism and renal clearance in youths lead to a shorter drug half-life than in adults. This implies a shorter duration of drug effect - for this reason, it is often essential to administer doses more frequently than expected (based on adult psycho-phramacology).

However, quantitative estimates of those differences in clearance and related kinetic variables, are generally not yet available for children or adolescents. Empirical dosing of individual patients may be required to optimize treatment (Popper, 1995).

7.3.5. Psycho-pharmacology in Childhood-Onset Schizophrenia:

There have been very few trials to assess the efficacy of pharmacological treatment of Schizophrenia in childhood, (using post DSM III diagnostic criteria, and with a double-blind crossover methodology). There have been mixed reports on the efficacy of the major tranquilizers.

Spencer and Campbell (1994), in a double-blind placebo-controlled trial in children with Schizophrenia (age range 5,5 to 11.75 years) showed that Haloperidol (a classic neuroleptic, in dosages ranging from 0,5 to 3.5mg/day), improved psychotic symptoms in a short term in-patient setting. Green et al. (1992), however, reported a poorer therapeutic response to Thioridazine, Haloperidol, Chlorpromazine and Trifluoperazine, with no child achieving symptom remission.

Gordon et al. (1994) had compared the efficacy of Haloperidol and Clozapine[8], in a double blind trial over six weeks, in adolescents who had not responded to typical neuroleptics. They found that these adolescents showed greater improvement in psychotic symptoms on Clozapine. Remschmidt et al. (1994) in an open study of adolescents with Schizophrenia, found that 75% of children on Clozapine had shown 'remarkable improvement of schizophrenic symptoms'. In addition, there have been case reports on the efficacy of Clozapine in children with Schizophrenia, who have been unresponsive to the typical neuroleptics (Mozes et al. 1994; Towbin et al. 1994).

Kumra et al. (1996), in a double-blind study, found that Clozapine was superior to Haloperidol on all measures of psychosis - positive and negative. However, the side - effects of neutropaenia and seizures were major concerns, and one third of the group had discontinued using Clozapine.

[8] Clozapine is a dibenzodiazipine, with a strong affinity for serotonin receptors and a greater affinity for D1 and D4 receptors (Masi, 1997).

The long term effects of Clozapine are not known in children (the only double - blind trial mentioned previously lasted 6 weeks), and McClellan and Werry (1994) advise that Clozapine should only be "considered in adolescents who have not responded to standard neuroleptic therapy." They do not mention children - but, given the same situation in children, Clozapine could also be considered.

The side-effect profile of Clozapine does potentially include recurrent neutropenia, weight gain and recurrent seizures (Campbell and Cueva, 1995a,b).There is at present, not enough information on the long term effect of Clozapine use in children, and thus the outcome of further research is awaited.

It is important to note that "the onset of therapeutic effect may not be apparent for some time after treatment is initiated" (Volkmar, 1996), and trials are needed for at least four to six weeks at adequate dosages (McClellan and Werry, 1994).

Another promising drug used successfully in adults with Schizophrenia, is Risperidone. It has the advantage of being a very potent serotonergic and dopamine blocker, with relative freedom from extra pyramidal symptoms or agranulocytosis. In a case study of children and adolescents with Schizophrenia, Quintana and Keshavan (1995), found that three out of four patients had substantial improvement in their negative symptoms, without side effects.

In a recent open pilot study in adolescents with Schizophrenia, Risperidone was found to produce clinically and statistically significant improvement on the Positive and Negative Syndrome Scale for Schizophrenia, Brief Psychiatric Rating Scale, and Clinical Global Impression Scale (Armenteros, Whitaker, Welikson, Stedge and Gorman, 1997). There were no adverse reactions with Risperidone use in the dosage range from 4 mg/day to 10 mg/day. This is a relatively new drug, which extends the treatment options in Schizophrenia in children, who may be unresponsive to the first line major tranquilizers. The long term effects are not known however, and further trials are awaited.

Another atypical neuroleptic that has become available for adults with Schizophrenia, is Olanzapine (a potent serotonin 5-HT 2a/2c and dopamine D1D2D4 antagonist). There is one case report in the literature supporting the efficacy of Olanzapine in some (treatment resistant) children and adolescents. However, as with Risperidone, this is a new drug, and the results of additional double-blind controlled trials are awaited (Kumra et al. 1998c).

McClellan et al. (1997), in their detailed protocol for the treatment of children and adolescents with Schizophrenia, specified the importance of informed consent (from both the youth and the parents/guardians). Furthermore, they stated the need for a thorough psychiatric evaluation (paying particular attention to any abnormal movements), before commencing pharmacological therapy. In this way, a baseline is obtained, so that pre-existing abnormal movements are not mistaken for side-effects.

7.3.6. Electro-convulsive therapy (ECT) and programmes:

The role of electroconvulsive therapy (ECT) in children is controversial. McClellan and Werry (1994) suggest that it be a carefully considered decision, taking into account the severity of the illness, the relative risks and benefits of the treatment, the attitudes of the patient and family, and the experience of the clinician using ECT. Tolbert (1996) suggested that, given the adverse effects of drugs are often more significant than those encountered with ECT, it may be more cost-effective to begin ECT within a few days of hospitalization, for the first psychotic episode.

Thereafter, Tolbert (ibid) suggests that after a short length of in-patient stay, there should be a move to outpatient treatment. This stance is a radical shift from a more conservative approach - but as there are no empirical studies on detailed treatment programmes for Childhood-Onset Schizophrenia to support Tolbert's suggestion, the protocol by McClellan and Werry (1994), and McClellan et al. (1997), should form the basis of good clinical practice.

CHAPTER EIGHT

CASE STUDIES: ONE.

8.1. Introduction:

The two cases presented below and in Chapter Nine are based on retrospective case material, obtained from file notes. These were cases identified by staff from the Inpatient Unit at Red Cross Children's Hospital, from the past 5 years, where a diagnosis of Childhood-Onset Schizophrenia was made. I was not personally familiar with the cases, and am working within the constraints of the information available.

8.1.1. Introduction to case:

Case 1 will be called Peter. He was 11 years old when he was referred to the Inpatient Unit at the Red Cross Child and Family Unit (CFU), for diagnostic assessment and advice, regarding further management. He was admitted to the Inpatient Unit for a period of 5 months, going home weekends, and during the winter school holiday.

During his admission he was allocated a Professional Nurse Therapist, attended the CFU school, and was assessed by the Remedial Teacher. He was seen regularly by the Consultant Child Psychiatrist and observed over 24 hours by the Nursing Staff.

8.2. Presenting history:

At the time of referral, Peter, a white Afrikaans speaking boy, was an inpatient at another Unit, following a period of depression. His condition did not improve after two months treatment with Imiprimine 25mg bd and Lithium Carbonate 250mg bd. The precipitant seemed to be his transfer to a school for children with Mild to Moderate Mental Handicap. Another precipitating factor was that his younger sister had started school, and was beginning to read, and he could not read or write at an age appropriate level.

According to Peter`s parents, he had been hearing voices for years telling him to do things, including killing his sister. In addition to this, he had also had episodes over previous years, when he talked and laughed to himself.

Two years ago, he locked himself into his room for three days and was talking and laughing with people who were not there. Furthermore, he had regularly became frightened of non-existent things, and talked very violently at home, and acted out when he was afraid.

He had been at his best when on Chlorpromazine, but this was stopped due to a photosensitivity reaction, resulting in him developing pigmented patches.

8.3. Past psychiatric history:

He was seen at the age of four years and diagnosed as having Attention Deficit Disorder and Developmental Speech Delay. The Speech Therapist diagnosed additional phonological problems. His hearing was assessed as normal. An electroencephalogram was reported as normal. Peter's mother was referred to the Clinical Psychologist for parental guidance.

Two years later, aged six, he was again referred to the above Unit with a history of hyperactive behaviour, talkativeness, distractibility, short attention span, sleep difficulties and poor progress in Sub A. He also complained of weakness in his legs, fatigue, and poor appetite.

He was then admitted to the Inpatient Unit for three weeks and a diagnosis of Bipolar Affective Disorder was made. He responded well to Chlorpromazine syrup (25 mg twice daily) and Lithium Carbonate (125mg three times daily). Special investigations then showed normal blood tests. The EEG showed mild (non-specific) abnormalities.

Two years later, aged 8, he presented with a depressed mood, poor appetite, and insomnia for two months. At that time, he spoke continually of dinosaurs and space ships. He also apparently reported that other people were 'controlling' him.

He was again admitted to the same Unit, where a diagnosis of Bipolar Disorder- depressed phase, was made. He was treated with Lithium Carbonate 125mg three times daily and Imipramine 25mg twice daily. After one week the depressive symptoms resolved, and he then became Hypo-Manic. He was discharged to a specialist school, primarily for Autistic children. He was well until his most recent admission, 3 years later.

8.4. Past Medical History

He was hospitalized for viral meningitis at 18 months. As a toddler he suffered repeated ear infections and had grommets inserted.

8.5. Family history :

Peter's mother, Anna, was 27 years old. She was in her final year at high school when she became pregnant with Peter. She subsequently left school and married Peter`s father, John. She worked as an Assistant Nurse for four years after Peter's birth. She had been a housewife for the past seven years. She was very attached to Peter, but had difficulties in dealing consistently with him.

Peter`s father, John, was 33 years old. He completed high school and then had a career in the army. After leaving the army, he worked as a security guard. He had a good relationship with Peter.

There were current stresses in the family, due to financial difficulties.

There was one younger sister aged five. Peter had displayed much aggression towards her.

8.6. Family history of psychiatric illness:

There was a family history of Depression. Peter`s mother had been treated for Depression. An uncle had also committed suicide, but it was not clear what the psychiatric diagnosis was.

8.7. Personal history:

Anna was depressed and anxious during the pregnancy. During this period the couple lived with the paternal grandmother. There were frequent arguments.

She developed pre-eclampsia in the last trimester and an assisted delivery was performed. Anna experienced the delivery as traumatic. Post delivery Peter was not well and remained in hospital for ten days. The details of the postpartum period could not be recalled.

He was reported as being a difficult baby who slept poorly, was colicky, and refused the breast. He was diagnosed as having milk allergy and was placed on soya milk. Despite these difficulties, the bonding was reported to be good.

Peter did not crawl but slithered along the floor. He started walking at nine months and was saying words at one year. He started using sentences at three years. He was dry by day at thirty months. He had occasional nocturnal enuresis until four years of age.

At seven months he was placed in a creche because his mother started work. When he was three years old he was called a 'little terrorist,' because he was 'on the go all the time,' having temper tantrums and destroying things, and 'acting like a mad thing'. (Peter had been exposed to the use of live ammunition and the killing of animals since he was 2 years old, apparently as part of his 'character training').

He started Sub A in a mainstream school at the age of six. After three months he was not making progress, and was not at school again, until he was eight years old. The reason for this was not clear. He started at the special school with small classes, at the age of eight .

He spent two years at this school, but was then transferred to a school for mentally handicapped children, because he was not making academic progress and was unable to make use of the teaching.

After the transfer, he became increasingly hostile towards the other children at his new school. He also became angry with his sister who, although six years younger, was able to accomplish academic tasks that he was struggling with.

8.8. Special Investigations:

8.8.1. Psychometric:-Report compiled November 1994.

Due to his scholastic difficulties, Peter was referred for a psychometric assessment, at his previous school. The summarized report is presented below.

(a) Cognitive/ Intellectual:

I.Q. (S-SAIS) Verbal: 101 pts.

Non-Verbal: 118 pts.

Full Scale I.Q.: 109 pts.

This placed him within the upper limits of the average range of intelligence. His scholastic problems do not therefore seem to stem from global cognitive difficulties.

However, the report stated that there was a considerable difference between the verbal and non verbal scores, with lower verbal scores. This difference was caused by the very low scores on Arithmetic (4). A test of memory and attention also revealed difficulties. Digit Span was low (6 as a standardized score, with 10 being the norm), while Coding was only 2.

Coding is the test most sensitive to organic problems, as well as attentional difficulties. Digit Span is also sensitive to concentration problems - the fact that Peter did reasonably well on Story Memory (9) indicates that general memory functioning is not the central concern, but attention may well be.

The low score for arithmetic indicated an inability to do basic mathematics, to reason, and to productively concentrate on number problems. This limited concentration span influences short term memory, and this is replayed in the scales concerning digit span (6).

Informal evaluation of his reading and spelling ability showed a complete inability with regard to displaying this skill.

The report concluded that although he scored within the average range of intellectual functioning, this intelligence was not functional. In addition to this, he appeared to exhibit attention difficulties.

8.8.2. Speech Therapy Report- November 1994

Language: Peter's language was assessed as being functional, with his comprehension and expression being age appropriate.

With the Peabody Picture Vocabulary Test, and the Test of Problem Solving, he scored in the average range.

The Pendulum Test was used to assess auditory perception. He had difficulty in all areas, with severe delay in auditory analysis and synthesis, which results in severe difficulties in reading and spelling.

The recommendation was that his good ability in oral vocabulary and problem solving, be stimulated through activities presented in the oral, rather than written form.

8.8.3. Occupational Therapy (O.T). Report- November 1994

The tests administered were 1: Developmental Test of Visual Motor Integration

2: Test of Visual Motor Skills

With both tests he was functioning 4 years below the norm for his age.

8.9. Summary of his 5 month admission:

8.9.1. Behaviour on the Unit:

Peter was extremely anxious and exhibited separation difficulties. He showed marked obsessional features initially, spending a copious amount of time sorting and ordering utensils. He also displayed excessive guilt, believing he was responsible for all the difficulties at home, and worrying about the future.

Peter demonstrated tightly controlled aggression on the Unit, with clenched teeth, balled fists, and violent and hostile drawings and comments. He exhibited extreme racist and sexist attitudes, picking fights with the two Xhosa speaking boys on the Unit, stating that they 'should be gassed'. He acted out physical aggression towards inanimate objects.

Peter seemed to actively avoid activities and challenges. He preferred solitary play, building objects with which to 'protect' himself, such as guns, bombs, and tanks. At times he talked and laughed to himself.

He also complained of 'rushing thoughts,' and believed the staff could read his mind. He slept poorly at night, complaining of frequent nightmares.

Midway through his stay in the Unit, a diagnosis of Schizophrenia was made, and the decision was made to commence medication. This was discussed with his parents, and with their consent, he was started on Zuclopenthixol Decanoate depot 50 mg intra-muscularly every month.

After the medication started, there was a gradual improvement in behaviour, so that he no longer complained about hearing voices - as he had prior to admission - or having his mind 'read'. His obsessional behaviour had disappeared and he was less anxious and fearful about the future.

Peter showed improved self esteem, as manifest in a greater willingness to confront activities and tasks. He was also interacting more with the other children, although his aggressive outbursts had increased, and he was involved in more fights with the other children.

His sleeping difficulties persisted, especially initial insomnia, but he had stopped laughing and talking to himself. However, he needed supervision with his self care (e.g. washing and dressing).

8.10. Further special investigations:

8.10.1. Scholastic:

Peter was verbally fluent in both English and Afrikaans, but particularly his home language, Afrikaans.

He was right hand/left foot dominant, but displayed generally poor gross motor skills. (He was un-coordinated and rigid). His fine motor skills were also poor, showing awkward dexterous manipulation, and a continual tremor. His writing was thus slow and laborious.

He had difficulty forming and spacing letters, and needed to draw lines to write on. He also had problems with 'marrying sounds' (phonological processing), which made reading exceptionally difficult (e.g. op is read as o-pe).

Furthermore, Peter struggled with written mathematics, relying heavily on concrete methods of support, and being confused by numbers greater than 10. His major identified impairments were in the following areas:

Visual - motor coordination.

Spatial relations.

Sequencing.

Short and long term memory.

Auditory analysis, synthesis, and discrimination.

In tests of reading, spelling and phonics, he scored 0.

He impressed as a generally intelligent boy who was immensely distressed by his inability to overcome his academic difficulties. His educational prognosis is poor, despite his very good verbal skills and desire to learn. Application was thus made for admission to a Special School for Autistic Children.

8.11. Final Discharge Diagnosis and Management Plans:

Axis I : Childhood Schizophrenia

: V-code Parent - child Problem.

Axis II: -

Axis III: Severe Learning Handicaps (?Related to meningitis at 11 months old).

Axis IV: Chronic and Severe

Axis V: Extremely Poor

1) Discharge medication was Zuclopenthixol Decanoate 50mg.I.M./month. A Community Sister was allocated to do home visits to ensure compliance.
2) Special School placement was recommended.
3) Support for mother was referred through her Church Minister, as she was not open to suggestions made by a black Social Worker.

8.12. Discussion:

Given the presenting symptoms and Peter's initial behaviour on the Unit, it is difficult to see how the diagnosis of Childhood-Onset Schizophrenia was reached. There is no clear-cut evidence of :

A: (1) delusions.

(2) hallucinations.

(3) disorganized speech(e.g. frequent derailment or incoherence).

(4) grossly disorganized or catatonic behaviour.

(5) negative symptoms, i.e., affective flattening, alogia, or avolition.

According to the DSM-IV (American Psychiatric Association, 1994), two of the above need to be present, each for a significant portion of time, during a 1 month period.

It was possible that he may have been observed to be talking and laughing to himself while playing, as he was initially isolated in his play. Children in solitary fantasy play may be more prone to 'talking to themselves' than children engaged with others (Talay-Ongan, 1998). This behaviour was noted to decrease, when his play involved more interaction with his peers, later on during his stay in the Unit.

Although it was difficult to analyze a case 'post-hoc' - and with limited documented information - it appears that at no stage did Peter himself clearly acknowledge hearing voices, which were separate from his own thoughts. (Given the parental pathology noted in Sections 8.6 and 8.7, it was hard to know how reliable their information was on Peter's symptomatology).

It was noted that he believed the staff could read his mind. However, young children frequently entertain this fantasy of powerful and significant others. (Even some adults have similar fears about psychiatrically trained professionals).

It was hard to assess how intensely he believed this, as there was no clear elucidation of this as a potential delusion - which could perhaps have been an uncertainly held fantasy. Even if of delusional proportions, it did not appear to be *pervasive*.

Unfortunately, there were no clear and ongoing mental status examinations documented. This appears problematic, given the seriousness of the diagnosis. Furthermore, given initial ambiguity about the diagnosis (which was changed mid-way through Peter's stay)[9], it seems that more structured assessment methods may have been more helpful. An example of a variety of these tasks have been described in Section 2.4: for example, the Story Game or Kiddie Formal Thought Disorder Scale (Caplan et al. 1989), or Andreasen and Grove's (1986) 'Thought, Language and Communication' (TLC) Scale.

Although there appears to have been some positive response to Zuclopenthixol Decanoate, this does not necessarily validate the diagnosis. Improvement could also possibly have arisen from the containment and structure provided by a long term milieu therapy stay, away from parental dysfunction and scholastic stress.

Given his history and reported symptomatology, what other potential differential diagnoses could possibly have been considered? It seems likely that Peter may well fall under the (possibly heterogeneous) label of 'Multi-Dimensionally Impaired' (MDI) (see Section 5.2).

Consider the exposition of typical MDI development noted by McKenna et al. (1994) and Gordon et al. (1994): 'They exhibit early developmental difficulties (by 7 years), usually noticeably earlier than most childhood-onset Schizophrenia cases, as well as vague psychotic symptoms that do not meet DSM-III-R criteria. They also reported hallucinatory experiences, that on further questioning were found not to be true hallucinations, or were not pervasive'.

[9] Another Child Psychiatrist who followed Peter up after discharge, also expressed reservations about his diagnosis as Childhood-Onset Schizophrenia.

In addition to the above, they had moderate to severe neuro-psychological deficits, e.g. Receptive Language Disorder, visual spatial problems, and memory impairment. The co-morbid diagnosis in 85% was Attention Deficit Hyperactivity Disorder (ADHD).

Peter has had early developmental difficulties, as manifest in the diagnosis of ADHD, when he was 4 years old. He has also exhibited severe scholastic problems, which may (at least in part) stem from neuro-psychological deficits emanating out of an episode of meningitis, at the age of 18 months.

Peter's scholastic difficulties appear to be specific, as his intellectual functioning is overall within the average range. They are focused around developmental speech delay, auditory synthesis and analysis delays - with phonological processing problems ('Receptive Language Disorder'), as well as visual-spatial problems (see O.T. report). Furthermore, he demonstrated marked attentional difficulties and memory impairment. All of these features have been specifically linked to 'MDI'.

Regarding vague or lack of pervasive psychotic symptoms in 'MDI' children, this appeared characteristic of Peter's reported symptomatology. 'MDI' children are also frequently said to have excessive age in-appropriate fantasy and affective instability, with nearly daily tantrums or mood swings. Despite being eager to make friends, they have poor social skills, but not the pervasive difficulties seen in Pervasive Developmental Disorder (Gordon et al. 1994; Kumra et al. 1997).

Peter also exhibited age in-appropriate fantasies (gassing other children, making bombs and tanks), and affective instability, with tantrums and mood swings. When he settled in the Unit, he became more eager to interact with the other children. However, due to his poor social skills, he ended up being almost constantly in conflict with his peers. This social interest and affective instability also distinguishes 'MDI' from Schizotypal Personality Disorder (Jacobsen & Rapoport, 1998).

It has been suggested that 'MDI' children may constitute a sub-group within Childhood-Onset Schizophrenia, with a greater degree of neuro-developmental impairment (McKenna et al. 1994). Kumra et al. (1997) have noted that this syndrome is generally fairly stable, and does not (as yet) progress on to Schizophrenia - implying it is not a pro-dromal form of Schizophrenia. However, a few diagnosed 'MDI' children did deteriorate, and due to their affective symptomatology as well, were subsequently diagnosed 'Schizo-affective Disorder'.

Given Peter's affective presentation, and earlier diagnosis of Bipolar Disorder, an alternative differential diagnosis to be considered, could thus possibly be Schizo-affective Disorder. However, given the development and variety of his difficulties, 'MDI' seems the most likely diagnosis. Although this is still waiting confirmation as a stable and valid diagnostic entity (Kumra et al. 1997), Peter appears to fulfill almost all of the criteria for a 'Multi-Dimensionally Impaired' child.

Although it is easy to offer a retrospective diagnosis with hindsight, this has been done to indicate the difficulties of accurate diagnosis in the complex (and still evolving) field of developmental psycho-pathology. There is a clear need for clinicians to stay abreast of the latest research developments.

The really important question is how a different diagnosis could potentially have impacted on management decisions. This remains to be discovered, as research into these children is still in its infancy.

Unfortunately, however, early longitudinal results suggest this is also a condition with poor long term prognosis (Kumra et al. 1997). This appears to be especially likely in this case, where parental compliance and change had not been achieved.

Gains which were achieved were via intensive, structured milieu therapy input. This is not feasible as a long term option - however, if some of these features can be replicated in the educational placement (allied with an intensive remedial programme), some small - yet possibly significant - gains may still be made.

CHAPTER NINE

CASE STUDIES: TWO.

9.1. Introduction:

Case 2 will be called Anna. She was 11 years old when she was referred to the Inpatient Unit at the Red Cross Hospital Child and Family Unit, for a diagnostic assessment, and advice regarding further management. She was an in-patient on the Unit for 4 weeks, after which she was followed up as an out-patient.

She was re-admitted for a brief period of stabilization a year later, after what looked like a psychotic relapse. She was seen regularly by the Consultant Child Psychiatrist, and observed over 24 hours by the Nursing Staff.

9.2. Presenting history:

At the time of referral, Anna, an English speaking girl from the Cape Flats, had presented with a deterioration in scholastic functioning, and masturbation. Her mental state had deteriorated over the course of about seven to eight months, after an apparent precipitating event of a burglary in the house, and a double murder in a block of flats nearby.

Prior to admittance, Anna had been talking to the walls, disturbing the family at night with complaints of 'feeling sick,' 'something is coming up,' and 'not being able to breathe' (she also suffers from asthma). Her continued fearfulness at night was not responsive to parental efforts to calm her. At school, the teachers reported being unable to deal with her, as she had become withdrawn and was unable to concentrate.

9.3. Past Psychiatric history:

She presented for the first time shortly after her eleventh birthday, having refused to go to the bathroom alone, and dropping marks at school. Her parents had also noted that she was rubbing her perineum. They attributed her change in behaviour to the precipitants noted above (8.2). She was diagnosed as suffering from an 'Anxiety State,' operating within a 'dysfunctional family'. She failed to attend follow-up appointments.

Anna was referred again by her General Practitioner (G.P). a few months later, her parents having complained of her continued fearfulness, irrelevant speech, and masturbation. She was interviewed as an out-patient, and said that she was constantly very frightened, saw 'faces' in the wall to whom she mouthed silent words, and shouted at times that she didn't want to die. She also mentioned a feeling that 'something' was coming up from her xiphisternum, and felt hemmed in at home, whereupon she would insist on being picked up and taken outside.

Her symptoms continued to deteriorate and, allied with a worsening school performance, she was admitted to the Unit several months later.

9.4. Past medical history:

Anna had developed asthma as a young child, and was seen every three months at Groote Schuur Hospital's Asthma Clinic.

9.5. Family history: (No geno-gram or occupational details noted in the file).

Anna was the youngest of three children, with an older brother and sister. She was an 'unplanned' pregnancy, with the mother eventually accepting it, but 'wanting a boy'.

Mother had to apparently give up work in order to look after Anna, and there were current financial difficulties in the family.

Anna's father was a withdrawn and passive man, but had become more involved with Anna, since she exhibited her symptoms. Mother achieved responses from family members by screaming and shouting at them, and was dominant in the family. The two elder children were reported to clash with her frequently. Family members appeared concerned about Anna's symptoms, but there was conflict as how best to deal with her.

She related best to the males in the family, having most conflict with her mother and elder sister.

The family appeared to be dysfunctional, with a high level of negative emotional charge - described as "high Expressed Emotion (E/E)" by the Consultant Child Psychiatrist.

9.6. Family history of psychiatric illness:

Anna's father was epileptic. Her one uncle was characterized as an 'odd, quiet, and withdrawn person'.

9.7. Personal history:

There was an 8 year gap between the last sibling and Anna. She was a large baby (9lbs)., born by Caesarian-Section. She was a healthy baby, being breast fed up until 18 months of age. Mother reportedly became 'bored' with looking after her at home, and so she was placed in a creche.

Her developmental milestones were normal and she attended creche until she was 5 years old. (It was during this period that she developed asthma).

Anna attended school from 6 years of age, and passed every standard. Her work was noted to deteriorate markedly after the precipitating events described in section 8.2. (above).

She was described as a 'serious' personality, being a quiet girl and a 'loner' at school, with few friends. She was described by her family as hiding away from the window, if her school friends walked by.

Despite being generally anxious and withdrawn, Anna could reportedly become voluble and 'shouts and screams' when she did not get her own way, and had been described by family members as a 'loud mouth'. Prior to admission, her level of irritability had increased, and she was fighting more frequently with her elder sister. Levels of conflict had also increased with peers and teachers at school - at home, when unable to get her own way, she reportedly shut herself up and threatened to kill herself.

9.8. Behaviour in the Unit:

Anna was quiet and withdrawn. She occasionally became thought-disordered and appeared to be hallucinating, but never revealed the content. She exhibited profound poverty of ideation, neglect of personal appearance and paranoia. However, her behaviour was at all times manageable. She could not relate to peers, just sat smiling in a facile way, with no spontaneous speech or activity.

9.9. Mental State Examination:

9.9.1. Behaviour:

Anna presented as a hesitant, softly spoken and neatly dressed young pubertal girl. She tended to sit at the edge of her chair and avoid eye contact, generally staring at the wall, or out of the window. She volunteered little information and responded only to direct questions.

When asked questions, she would often respond only after a considerable initial silence, sometimes stopping and starting again. She was agitated and restless during the interview.

9.9.2. Cognitive functions:

Apparently adequate for her age, as per school report. However, a fall off in scholastic performance was noted, subsequent to precipitating events mentioned in 8.2. Her attention span was also impaired, she frequently stared out of the window, and appeared to lose the thread of questions.

9.9.3. Mood state:

This was apparently difficult to assess, as she was forthcoming with so little. However, her predominant mood appeared to be anxious and irritable, with evidence of psycho-motor agitation.

9.9.4. Delusions:

Anna had a fixed unshakable belief about her family wanting to harm her - her family reported her as being 'paranoid'. She also believed that men may come into the home and her bedroom, in order to harm her. She denied a history of physical or sexual abuse.

9.9.5. Perceptual experiences:

Anna reported hearing men's voices coming from the 'faces in the wall' - but these were apparently indistinct. The 'faces' were of strange men.

9.9.6. Diagnosis:

The primary diagnosis of Paranoid Schizophrenia was made - with a note: 'Paranoid psychosis in pubertal child'. A tentative diagnosis of epilepsy on Axis III was made. The burglary, murder, and familial conflict was noted on Axis IV, with a significant deterioration in functioning on Axis V.

9.10. Special investigations:

9.10.1. Physical:

With regard to neurological disorder, temporal lobe epilepsy (T.L.E)., or Tuberose Sclerosis were considered. However, investigations via an E.E.G. and C.T. Scan were normal.

9.11. Follow-up:

The family were unable to accept the diagnosis of Schizophrenia, and sent Anna back to school early, against the recommendations of the Unit. She was followed up as an out-patient. Despite the normal E.E.G., Tegretol was prescribed as the main treatment, with a Phenothiazine (Meleril), to be added when she was psychotic.

The follow-up notes indicated that familial conflict continued, with the mother particularly feeling that Anna's behaviour was deliberately defiant and 'manipulative'. The father tended to handle her more gently, and marital conflict increased, around the issue of discipline. Her school work also continued to deteriorate.

Anna also complained of 'people watching me on their TV's when I bathe'. She was still seeing 'faces' in the wall, and 'hearing' sounds like people clapping in her ears. She reported feeling largely irritable and unable to sleep at night. She was still masturbating. She also mentioned feeling that people were following her around and that people at school laughed at her behind her back.

Parental compliance with the medication regime was poor - they stated that it was making her too drowsy during the day, and were giving her a nocturnal dose instead.

Her behaviour deteriorated further, and she had bouts of uncontrolled aggression, in which she would throw pieces of furniture around. She was admitted to Ward B2 at Red Cross Children's Hospital five months after her discharge from the In-Patient Unit, due to her 'unmanageable behaviour'. A period of in-patient stabilization was requested.

Subsequent follow-ups continued to note a deterioration in her functioning. She was assessed further as an out-patient. Assessments 3 years on from her first reported symptoms after the precipitating events of the burglary and nearby double murder, indicated the following:

9.12. Further special investigations:

9.12.1. Occupational therapy assessment:

Anna's abilities fluctuated, with her disrupted thought processes disturbing her progress. Her short term memory appeared impaired. There was illogical thinking, for example: 'I don't like these clothes, that's why I'm tired'. She laughed inappropriately at times, or else looked blank.

A placement at Vera School was recommended, to try and prevent further loss of functioning and for better control of medication.

9.12.2. Speech therapy assessment:

Again, her performance was noted to fluctuate. She appeared 'in a world of her own,' and was fatuous and giggled to herself. She generally had a slow and inappropriate response to tasks, often answering irrelevantly.

The Peabody Picture Vocabulary Test (receptive vocabulary) was at a 3 year 8 month level. Considering she was 14 at the time of the test, this would seem to indicate a significant deterioration in functioning.

9.12.3. Psychological assessment:

Anna talked to herself during assessment and drew 'God, the witch'. She reported that her tongue was 'white and yellow and it stinks'.

She was impulsive and shifted from one subject to another. She exhibited difficulties completing a task. Her responses were generally 'brief, concrete and irrelevant'. She said the 'voices' made her aggressive.

She was unable to cope with scholastic demands. An intellectual assessment revealed:

Verbal I.Q.: 63

Performance I.Q.: 72

Full-Scale I.Q.: 63

This placed her within the Mild Range of Mental Retardation (i.e. I.Q. between 50-70 points). Bearing in mind her appropriate scholastic performance up until her initial symptoms, this appears to indicate a fall-off in intellectual functioning.

9.13. Management Plans:

Anna was treated with medication and followed-up as an out-patient. There was an attempt to engage the family in family therapy. In addition, she was referred to a special school for children needing small classes, and specialized teaching staff. This was a school for psychiatrically disturbed children, where the staff were specially trained to provide a psycho-educational approach.

9.14. Discussion:

Anna's clinical presentation had features described in the literature on children with Schizophrenia. There was the pro-dromal period, during which she presented with symptoms of anxiety, following the burglary and murders near by. This behaviour deteriorated to the point where she was not coping academically - she was withdrawn and unable to concentrate.

It was very difficult to separate the pro-dromal period from the onset of the illness. This difficulty had been highlighted by Kolvin et al. (1971a)., amongst others. The onset of illness had been insidious and evolved over a period of 6 to 8 months. This was in keeping with the reports on children with Schizophrenia younger than 14 years, where the onset was predominantly insidious (Alaghband et al. 1995; Hollis, 1995; Asarnow, 1994; Russell, 1994; Werry, 1992; Kolvin et al. 1971a).

Anna's pre-morbid personality was described as serious, quiet, and a loner at school, characteristics described in their samples of children with Schizophrenia (Remschmidt et al. 1994; Werry et al. 1991; and Kolvin et al. 1971b).

There was no evidence from the developmental history that there were any developmental delays.

During the period of admission to the Unit, she had a combination of positive and negative symptoms: delusions, thought disorder and hallucinations present for at least 1 month. The negative symptoms were the poverty of speech and thought and a significant decrease in the initiation of goal-directed behaviour.

There was a clear history of deterioration in social and occupational functioning - she was masturbating constantly, and her academic performance had deteriorated over a period of 6 to 8 months.

Considering the above symptoms, there was a picture of an 11 year girl who met the adult diagnostic criteria (DSM-IV and ICD-10) criteria for Schizophrenia.

The other differential diagnoses that were considered included Tuberosclerosis and TLE, both conditions that could present with a similar clinical picture. The special investigations excluded these possibilities. In addition, the longitudinal deteriorating course indicated that her illness was similar to that of other children with Schizophrenia (Rutter, 1995).

It was unfortunate that there was no baseline assessment of her intellectual functioning. However, given the history that she was coping at school until she became ill, it is clear that there had been a significant deterioration in functioning over 3 years, with the intellectual assessment placing her in the Mild Range of Mental Retardation. Similarly, the result of the Peabody Picture Vocabulary, showed her to be functioning at a 3 year 8 month level, a large and significant delay.

Jacobsen and Rapoport (1998), reported on a significant deterioration in the intellectual functioning of their sample, over 2 to 4 years. They suggested that "this pattern of intellectual decline, if it continues, together with the insidious onset of this disorder, suggests that there may be an underlying pathologic process that continuously erodes brain function in childhood-onset Schizophrenia."

The treatment in this case was Thioradazine and Carbamazepine. There are no controlled trials indicating that this medication is beneficial. At the time that Anne was being treated, there were no guidelines for the treatment of Childhood-Onset Schizophrenia. A report by Green et al. (1992) suggested that Thioridazine, Haloperidol, Chloropromazine and Trifluoperazine produced only a little therapeutic response, with no child achieving symptom remission.

The current evidence suggests that Clozapine may have been the next choice, as Anna had been unresponsive to a typical neuroleptic (Mozes et al.1994; Towbin et al.1994).
As discussed under section 7.3, in a double-blind trial in children with Schizophrenia, Clozapine was superior to Haloperidol on all measures of psychosis.

The side-effects of neutropaenia and seizures resulted in one third of the group discontinuing the medication (Kumra et al. 1996).

The family conflict at Anna`s home showed no improvement over time. The family made no attempt to cooperate with clinicians and returned her to school earlier than recommended by the Consultant Child Psychiatrist. The family also complied poorly with the medication regime. It was mentioned that the family had great difficulty accepting the diagnosis of Childhood-Onset Schizophrenia. The family was considered to be high EE. This referred to the critical and over involved attitudes by key relatives.

The adult literature on Schizophrenia suggest that family intervention studies, in conjunction with medication therapy, had significantly decreased the relapse rates during the first year of treatment. This family had not responded to attempts to engage them and this was reflected in the medication non-compliance. Their cooperation may have resulted in a better support system for Anna at home. It cannot be assumed that the family caused the Schizophrenic illness, as the discussion on aetiology, indicated the predominant biological component. However, the high EE most likely contributed to her relapse (Nugter, Dingemans, Van Der Does, Linszen, and Gersons,1997).

The long-term prognosis for this girl was unfortunately poor. The poor prognostic factors were: early onset (she presented with an onset of psychotic symptoms by the age of 11 years), pre-morbid personality characterized by shyness and withdrawal, a long pro-dromal period (6 to 8 months), combined with a poor response to medication and marked decline in functioning over a period of three years (Eggers and Bunk, 1997; Werry et al. 1991, 1994).

This poor prognosis has enormous implications for the family and the psychiatric resources, "requiring a continuum of services and treatment providers. In addition to psycho-pharmacology management and psychotherapy, many of these youth will need extensive case management and community support services" (McClellan et al. 1997). Where the community support services are not well developed, the burden of care falls upon the family, as is often the case in South Africa.

CHAPTER TEN

CONCLUSION

Much progress has been made with regard to the classification of Schizophrenia in childhood. However, it is still a relatively young field, and much still remains to be done. Regarding the research questions raised in the Introduction of Chapter One, it is now possible to make reasonably informed comments on these. To facilitate this process, it appears pertinent to specify these questions again.

1) Is Schizophrenia with childhood onset a discretely homogenous entity or is the condition on a continuum with adult Schizophrenia?

2) Are the current classification systems diagnostically valid in children with Schizophrenia?

3) Do phenomenological descriptions of the condition assist the clinician diagnostically, especially with the financial constraints limiting the extent of special investigations in the South African context?

4) What is known about the etiology of Schizophrenia in childhood - the evidence will be critically evaluated.

5) Do current treatment models have any relevance to clinical practice in South Africa, especially with regard to the need for cost-effective solutions?

6) Two cases obtained from the in-patient Unit of the Red Cross Hospital's Child and Family Unit will also be examined, in the light of the literature.

Regarding questions one and two, there appears to be a general consensus that the phenomenology of Schizophrenia with Childhood-Onset is similar to Schizophrenia in adults, and can be reliably diagnosed using the same criteria - with developmental modification.

The developmental aspect perhaps needs to be emphasized more, in any prospective revision of the diagnostic criteria. Variations in presentation may extend beyond degree of delusional organization (Hafner et al. 1993) - certainly language and developmental level may mask or obscure classical presentations (Cantwell et al. 1979).

However, it seems that Early-Onset Schizophrenia (especially with insidious onset), may be a particularly pernicious form of the disorder, with a relatively worse prognosis than in adult Schizophrenia (Amminger et al. 1997). Although it is generally accepted that Schizophrenia with Childhood-Onset is homogenous and represents the extreme end of the spectrum of Schizophrenia, only continuing longitudinal data will confirm or refute this.

A greater research emphasis on varying developmental manifestations of the disorder may also help to clarify whether important sub-types exist. Now that there are reliable, valid instruments available, hopefully further research will help in determining the potential existence of sub-types and the significance of positive and negative symptoms in children with Schizophrenia - especially with regard to intervention and long term outcome.

Thus, for example, much interest has been generated by the description of the category, Multidimensionally Impaired (M.D.I).. Whether this constitutes a phenotypic variation of Childhood-Onset Schizophrenia (Jacobsen and Rapoport, 1998), or a clinically separate syndrome, remains to be seen.

This is not an idle academic question - it could have important prognostic and treatment implications. Ongoing research will help to elucidate the relationship of M.D.I. to Schizophrenia.

With respect to question three, phenomenological descriptions of Schizophrenia do appear to assist clinical diagnosis, but there is a need for ongoing assessment and mental state evaluations. The wide range of developmental disorders means that the clinician needs to constantly keep a variety of differential diagnoses in mind, and not foreclose on a diagnose too quickly.

Regarding the etiology of Schizophrenia (question four), the emphasis in research has shifted from environmental to biological factors. Although there is a surfeit of evidence detailing genetic and neuro-developmental contributions to the pathogenesis of the disease, the actual interconnecting sequence of biological events is still unknown (Jacobsen & Rapoport, 1998).

It appears that environmental factors (e.g. a high 'EE' family) may help to shape the manifestation of the illness, but the removal of psycho-social factors as causative phenomena, may also help to reduce some of the 'blaming' - that in some earlier cases earmarked family interventions with schizophrenics (Werry, 1990). Furthermore, differential prognostic indicators for cases of Schizophrenia in 'developing' versus 'developed' countries may provide important clues for treatment. Certainly, if 'cultural' factors that are helpful to the curtailment of Childhood-Onset Schizophrenia could be identified, these may make a positive contribution to the development of a culturally relevant, holistic and cost-effective treatment package for South Africa (question five).

There is a need to empirically evaluate the response to treatment, which includes medication and psychological intervention. The new medications, Clozapine, Risperidone and Olanzepine have brought new hope in the treatment of adults with treatment resistant Schizophrenia.

However, although there have been a few promising case reports, these drugs need to further evaluated in children.

Finally, the case analyses indicated the importance of ongoing symptom monitoring and mental state evaluations for the accurate diagnosis of Childhood-Onset Schizophrenia. Although it is a rare disorder, it has serious prognostic implications, and accurate diagnosis and relevant treatment are thus critical.

The harnessing of familial and wider socio-cultural resources seems to be crucial in helping to achieve positive gains. Where familial cooperation sabotages intervention, the use of other resources (e.g. educational placement) may be indicated, to circumvent this. Both cases obviously required a great deal of psychiatric input. It is hoped that this literature and case review may contribute to the positive streamlining of resources, with the ultimate aim of fostering our collective goal - to alleviate suffering. Although Childhood-Onset Schizophrenia is a rare disorder, it does appear to exist - and we await further exciting developments in the attempt to accurately describe, classify, and treat this illness.

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