THE EFFECTS OF CHILDHOOD IMMUNIZATIONS ON THE ONSET OF AUTISM SPECTRUM DISORDERS AND RISK FACTORS THAT PREDICT CURRENT LEVELS OF AUTISTIC SYMPTOMOLOGY AND ADAPTIVE FUNCTIONING

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CHAPTER I

INTRODUCTION

Autism is a devastating neurological disorder that was first described approximately 60 years ago by Leo Kanner. At approximately the same time a German scientist, Hans Asperger, described a milder form of the disorder that became known as Asperger's Syndrome. Our understanding of these two disorders have evolved over the years and are today listed in the *Diagnostic and Statistical Manual of Mental Disorders* DSM-IV-TR (fourth edition, text revision) as two of the five pervasive developmental disorders (PDD), more often referred to today as autism spectrum disorders (ASD). Pervasive developmental disorders impact a wide range of adaptive attributes. All these disorders are characterized by varying degrees of impairment in communication skills, social interactions, and restricted, repetitive and stereotyped patterns of behavior. The pervasive developmental disorders, or autism spectrum disorders, range from the more severe form, called autistic disorder, to a milder (and sometimes more functionally adaptive) form, Asperger's syndrome. Autism and Asperger's syndrome seem to represent extreme points on a scale of severity within the autistic spectrum. Those with Asperger's are perceived to be similar to, but more capable than individuals with classical autism. In individuals with Asperger's Syndrome, deficits in social interaction and unusual responses to the environment, similar to those in autism, are observed. Unlike autism, however, cognitive and language development are more likely to fall within the

average range in the first years of life, and verbal skills are usually an area of relative strength. Idiosyncratic interests are also common and may be displayed as unusual and/or limited interest (e.g., memorizing bus/train schedules, preoccupation with facts related to a specific subject or class of objects). If an individual exhibits symptoms of either of these disorders, but does not meet the specified criteria for either, they are typically diagnosed with pervasive developmental disorder not otherwise specified (PDD-NOS). Additional severe disorders that are included within the autism spectrum disorders but will not be discussed in this paper are Rett's syndrome and childhood disintegrative disorder.

As noted above, autism and Asperger's appear to be extreme points on a continuum of severity. "The findings from research and clinical work are best explained on the hypothesis of a continuum of impairments of the development of social interaction, communication and imagination and consequent rigid, repetitive behavior" (Wing, 1991, p. 111). Kanner (1973) stated that it was not uncommon for any illness to present in different degrees of severity and that it was possible this variation existed within autism. The continuum for these disorders ranges from individuals with the most profound mental and physical impairments, who have significant social and language impairments, to the most capable and highly intelligent individual with a subtle form of social impairment. Perhaps Wing (1991) explained it best:

> It is necessary to emphasise (sic) that this triad of social impairments, thought of primary importance, is not the only variable involved in the clinical pictures. Language, non-verbal communication, reading, writing, calculation, visuo-spatial skills, gross and fine motor co-ordination and all other aspects of psychological

> and physical function may be intact or may be delayed or abnormal to any degree of severity in socially impaired people. Any combination of skills and disabilities may be found and any level of overall intelligence. The overt clinical picture depends upon the pattern seen in each individual. (p. 111)

Research has established that ASD has a genetic base, however, exposure to particular stimuli during pre and post natal periods of development have also been suspected in attributing to the cause and differences in severity among individuals. While the symptoms associated with ASD often occur with varied intensity it is not completely understood what variables are related to these variations among individuals. Rimland (1964) noted, it was of interest that in several cases of identical twins stricken with autism, the degree of affliction was not identical, suggesting that while genetic factors may predispose toward autism, post-conceptional factors could also be operative. Research is somewhat inconsistent due to the varied methodologies in defining and assessing severity as well as varied classification criteria used over the decades (Glasson, Bower, Petterson et al., 2004). Severity has not been well defined within the literature as definitions of severity varied widely among researchers. Defining severity, as it pertains to ASD, can include assessment of adaptive behavioral functioning, standard scores from cognitive and/or diagnostic rating scales, or by the number of symptoms exhibited. For the purpose of this study, severity was defined by standard scores on adaptive functioning and specific diagnostic rating scales.

Most children with ASD have some degree of impairment in adaptive functioning (Liss et al., 2001). Information related to adaptive functioning and symptomology along with other prognostic data can be helpful in determining the severity of the disorder. But

minimal research has been conducted on which variables correlate specifically with adaptive functioning and diagnostic criteria in predicting the severity of ASD.

Because all the PDD disorders are characterized by varying degrees of the same symptomology there is confusion and continuous debate as to whether Asperger's is a separate disorder than autism (Cohen & Volkmar, 1997; Woodbury-Smith, Klin, & Volkmar, 2005; Wing, 2005). Review of the literature indicated that most researchers view the disorders as synonymous and therefore discuss them collectively under terms such as autism, autistic disorders, autism spectrum disorders, and/or pervasive developmental disorders. Asperger's syndrome wasn't truly recognized in the United States until 1991 when Hans Asperger's original paper was translated into English (Wing, 2005). Prior to that its only introduction was noted by a large scale review of literature and case studies published by Wing in 1981. Additional recognition for Asperger disorder followed its inclusion in the *International Classification of Diseases, Tenth Edition* (World Health Organization, 1993) and *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (American Psychiatric Association, 1994). And although the condition has received increased attention during the last two decades, data are still sparse in comparison to autism (Wing, 2005). A lack of definitive data limits information regarding the prevalence of Asperger's (APA, 2000), however it appears to be lower than autism (Fombonne, 2001). Furthermore, due to the lack of recognition within the United States until the 1980's, because the two have not been definitively distinguished as separate disorders, and because the prevalence of Asperger's is estimated to be lower (Fombonne, 2001), the two conditions are often accounted for under the term autism or autism spectrum disorders. Because of these circumstances, those who

pioneered research on Asperger's were unlikely to obtain enough participants for adequate analysis of these individuals independently. Therefore this paper more frequently uses the term autism as that is how the spectrum was commonly portrayed throughout the literature. However, when applicable, separation of these disorders was noted.

Autism spectrum disorder is often mistakenly referred to as a rare disorder, but advances in understanding of this disorder have shown that it is more common than previously believed. The diagnosis of autistic disorders may have increased by 273% between 1987 and 1988 and by 97% between 1998 and 2002. (California Department of Developmental Services, 2003 as cited in Purssell, 2004). The incidence of autistic disorders in most studies conducted 15 to 20 years ago estimated the frequency of autism to be 4-5 per 10,000 (Bohman, Bohman, & Bjork, 1983; Gillberg, 1984, 1988; McCarthy, Fitzgerald, & Smith, 1984; Steinhausen, Gobel, & Breinlinger, 1984; Tanioue, Oda, Asano et al., 1988; Trevarthen, Aitken, Papoudi et al., 1996; Volkmar, Klin, & Cohen, 1997) while recent sources indicate a higher incidence and estimate the frequency of ASD to be from 10 to 60 per 10,000 (Baird, Charman, Baron-Cohen et al., 2000; Bertrand, Mars, Boyle et al., 2001; Chakarabarti & Fombonne, 2001; Horton, 2004; Medical Research Council, 2001 as cited in Purssell, 2004; Yeargin-Allsopp, 2003). The prevalence for Asperger's syndrome has been estimated to range from .3 to 48.4 per 10,000 (Baird et al., 2000; Chakarabarti & Fombonne, 2003; Kadesjo, Gollberg, & Hagberg, 1999; Sponheim & Skjeidal, 1998; Taylor, Miller, Farrington et al., 1999). This enormous variation likely reflects the differences in methodologies across the research. However, a review of literature by Fombonne (2001) indicated the rate of Asperger

disorder was consistently lower than that of autistic disorder and that the number of children with autism was on average five times higher, suggesting the prevalence of Asperger disorder to be approximately 2 per 10,000. Despite the difference in prevalence, both disorders are found to occur more often in males than females (APA, 2000).

There is no single etiology for autism spectrum disorders, but there are several theories which have generated research over the past 60 years. There is evidence for a neurological and genetic basis of autism. There is also evidence that a genetic link to ASD may be a result of a weakened immune system. Although there is likely a significant genetic component, genetics do not appear to account for all cases. This is illustrated by the increasing number of children being diagnosed each year. As Horton (2004) noted, this raises the possibility that there might be psychological and organic factors contributing to autism's cause and course. Additionally, there is a growing concern that viruses associated with thimerosal-containing vaccinations/immunizations, particularly the Measles Mumps Rubella (MMR) vaccine, have a role in causing autistic disorders. Furthermore an increase in autistic disorders was noted after the introduction of the multi-component MMR vaccine. The combined MMR vaccine was licensed for use in the United States (US) in 1971 (Kennedy, Byers, & Marchalonis, 2004) and within the United Kingdom (UK) in 1988 (Shattock & Savery, 1997). As noted by Geier and Geier (2003), the Vaccine Adverse Events Reporting System (VEARS) database indicated an increase in the prevalence of autism and other neurodevelopmental disorders after the introduction of thimerosal-containing vaccines. Shattock and Savery (1997) also noted an increase in the number of concerns reported following the introduction of the multi-component MMR vaccine.

Although rare, side effects are reported to occur with some vaccines. Examples noted by Hsu (1999) included a concern over the rotavirus causing a rare and dangerous bowel disorder, seizures as a result of a new strain of the Pertussis vaccine and the chicken pox vaccine, as well as paralization from polio vaccines. In fact, in 1986 the Vaccine Adverse Effect Reporting System (VAERS) was established for parents and/or doctors to report vaccine related injuries and side effects. It is further noted by Hsu (1999) that the VAERS receives approximately 1000 reports per month from parents and doctors. Review of information published online by VAERS indicates that during the years 2000 and 2005, between thirteen thousand and sixteen thousand reports were received per year (http://vaers.hhs.gov/info.htm). Therefore the notion that a vaccine could play a role in the cause of autistic disorders need not be readily dismissed without proper investigation.

One of the questions raised in early literature from the 1960's about autism was the possibility of an infectious etiology to the syndrome (Chess, 1971, 1977; Chess, Korn & Fernandez, 1971; Crook, 1983; Desmond, Wilson, & Melnick et al., 1967; Dykens & Volkmar, 1997; Freedman, Fox-Kolenda, & Brown, 1970; Gillberg, 1985, 1986; Knobloch & Passamanick 1975; 1970; Rutter, 1977). Although this notion has advanced, concerns remain that a child's weakened immune systems and susceptibility to psychological illness may contribute to the disorder. These early studies portrayed concerns regarding pre- and post-natal infectious diseases and the impact on children's immune systems as a result of these infections. Studies were conducted that investigated whether children who experienced pre- or post- natal infections and/or a suppressed immune system developed autistic disorders (Chess, 1971, 1977; Chess, Korn, &

Fernandez, 1971; Coleman & Gillberg, 1985; Dykens & Volkmar, 1997; Knobloch & Passamanick, 1975; Kennedy et al, 2004; Krause, He, Gershwin et al, 2002; Ritvo & Ritvo, 1982; Stubbs & Magenis, 1980). It has been noted that a small but significant proportion of children develop autism as a result of pre-or post-natal infections; for example with rubella, cytomegalovirus, herpes, and others (Gillberg & Coleman, 1992). Although the occurrence was rare, Rutter, Bailey, Simonoff et al., (1997) noted cases of autism associated with postnatal encephalitis, while both Delong et al. (1981) and Gillberg (1986) reported on a case of autism associated with herpes encephalitis. Knobloch and Passamanick (1975) reported on cases associated with meningitis, varicella, and syphilis. Although only based on anecdotal evidence, it was suggested by Crook (1983) and Campbell (1983) that autism was associated with a condition known as candida albicans; a sign of impaired immune functioning resulting from the overgrowth of yeast in the body. Later studies also assessed risk factors related to utero exposure with the use of birth-defect causing substances such as ethanol, valproic acid and prescriptive drugs (Rodier, 2000). Although the evidence somehow escaped the attention of earlier researchers, evidence linking the use of thalidomide, a morning-sickness drug used in the 1960's, with some cases of autism was discovered by Stromland, Nordin, Miller et al., (1994).

Dykens and Volkmar (1997) noted that "interest in the immune system and autism arises from the various case reports in which infections (and possibly altered immune response) are associated with the development of autism or autistic features" (p. 398). Significant research regarding pre- and post-natal infection and autism was particularly sparked by the Rubella epidemic that occurred in 1964 (Chess 1971, 1977; Chess et al.

1971; Coleman & Gillberg, 1985). It was estimated that approximately 20,000 children born within the United States alone were negatively affected by the rubella epidemic (Coleman & Gillberg, 1985). Studies found that mothers who contracted measles during pregnancy were more likely to have a child who developed autism (Chess 1971, 1977; Chess et al., 1971). In a study conducted by Chess (1971) it was found that out of 243 children studied (with congenital rubella) they identified 10 as having autism and eight more who had a "partial syndrome of autism" (p. 35). However, the significance of this finding was modified by follow-up data, collected by Chess et al. (1977), indicating that these identified children, as they grew older, ceased to exhibit autistic symptoms.

Even in the early literature, a small amount of evidence suggested that infectious agents in the post-natal period may have been a factor in the development of autistic syndromes. Although the suggestion that autistic disorders could be caused by vaccination has been in circulation for many years, the interest appears to have once again moved to the forefront of research; however, the studies thathave been conducted have yielded inconsistent findings (Bernard, Enayati, Redwood et al., 2001; Bernard, Enayati, Roger et al., 2002; Coleman & Gillberg, 1985; Kennedy et al., 2004; Krause et al., 2002; Shattock & Savery, 1997).

There appears to be little middle ground on this issue, researchers and/or clinicians seem to adhere to either a fanatical anti-vaccine position or dismiss any possibility that a problem could exist at all in relation to vaccines causing ASD. Wakefield has been a primary investigator in researching the link between autistic disorders and vaccination; and at times appears to be alone in his support for evidence of a link between vaccines and ASD. Singh (2000) is also convinced of a possible link

between vaccines, particularly the MMR vaccine and autistic disorders. During a committee government reform meeting in April of 2000, Singh related additional evidence in support of a link between the MMR vaccine and autism. Singh (2000) spoke of research related to autoimmunity and its explanation for a link between vaccines and autism and other autoimmune diseases. Bernard et al. (2001) has even equated the onset of autism with symptoms readily seen in cases of mercury poisoning, indicating autism to be a novel form of mercury poisoning. Research conducted by Geier and Geier (2003, 2004, 2005) also suggest an association between the onset of autism and other neurodevelopmental disorders following immunization, particularly with the use of vaccines containing the preservative thimerosal. In addition, Krause et al. (2002) reported that "because immune system abnormalities similar to those induced by mercury in experimental animals have also been observed in autistic children, a link between vaccination with thimerosał containing vaccines and autism has been suggested" (p. 341). It was even suggested as early as 1967 by O'Gorman that autism was possibly the consequence of an individual's inability to metabolize lead.

There is an increasing amount of research presently being conducted into the possible link between autistic syndromes and vaccinations. This increase in current research has resulted from the elevated incidence of parents claiming that their child's autism was the result of, or compounded by, vaccination. These parents often describe distressing accounts of extremely rapid regression, from perfectly average developing children to children who begin to exhibit severe behavioral and physiological problems. Clinicians, researchers, and parents alike would agree that by the very definition of autism, a period of regression often accompanies the onset of autism, but the timing of

vaccinations with autism, by some is simply interpreted as mere coincidence. Lingam et al. (2003) reported that parents, who had observed regression of skills in their autistic child rather than delayed development, were more likely to speculate about the MMR vaccine and other possible causes of ASD.

There is little doubt that these parents are convinced that their children changed dramatically and quickly after an immunization program had been implemented. To completely ignore such reported cases, without investigating circumstances, is irresponsible, promotes fears and concern among the general public, and does nothing to combat these fears. Suspicions about the role of vaccines in the cause of ASD exist and data would suggest that these suspicions should be considered for investigation.

If those who proclaim the existence of a link between ASD and certain vaccinations are correct, then the consequences could be quite serious for many people. On the other hand, if they are incorrect then the message is that vaccines are safe and effective. Yet public confidence has been unnecessarily harmed and the control of potentially lethal diseases is at risk of being jeopardized by the attitude of uncertainty about vaccination.

The very nature of a vaccine is intended to help ones body establish immunity to a specified disease by creating antibodies. So how is it that a vaccine can cause an illness that is unrelated to the actual disease for which it is created? Those who protest the safety of vaccinations claim that the danger is related to a particular ingredient that is contained within these vaccines. The ingredient thimerosal, used as a preservative since the 1930's is present in some vaccines and considered harmful by some individuals (Bernard et al., 2001; Geier & Geier, 2003, 2004, 2005; Shattock & Savery, 1997). The concern over

thimerosal is the fact that it contains 49% mercury. Exposure to mercury can have potentially significant health effects. Although the level of mercury within any individual vaccine is not harmful, the additive amount of mercury that is contained in the usual dosage of vaccines given during one visit could allow an excessive amount of mercury, which exceeds government-recommended levels, to be ingested (Bernard et al., 2001, 2002; Freed, Andreae, Cowan et al., 2002; Geier & Geier, 2003, 2004, 2005; Parker, Schwartz, Todd et al., 2004). As noted by Freed et al. (2002) the exposure during the first six months of a child's life, assuming they received all recommended vaccine doses was as much as 187.5μg of mercury. Research conducted by Geier and Geier (2005), Parker et al. (2004), and Redwood, Bernard, and Brown (2001) further noted that the levels of mercury children are exposed to not only exceed the Federal Safety Guidelines but that it also exceeds the United States Environmental Protection Agency's permissible hair mercury limit. Researchers have shown that exposure to low doses of methyl mercury during the prenatal period as well as critical stages of postnatal development was associated with minor neurodevelopmental abnormalities(Cox, Clarkson, Marsh et al., 1989; Marsh, Clarkson, Myers et al.,1987; Redwood et al., 2001). It is clear that children are given an aggressive dosage of vaccines throughout their first year of life. While some proclaim that the amount of mercury that a child is exposed to within the first year of life through these vaccinations exceeds a safe level; government agencies insist that these levels are safe over the extended period of time in which these immunizations are administered.

The reaction of new parents to the schedules of vaccinations received during the first year of a child's life is likely one of shock. Vaccination schedules for infants do

differ in various parts of the world; however, Shattock and Savery (1997) indicated that "schedules used in the United States of America are amongst the most aggressive" (¶8). A comparison of immunization schedules in the United States and the United Kingdom are shown in Table 1. For the most part immunization schedules are fairly consistent, with the exception of influenza added to the immunization dosage during the first year. The age of 12 to 15 months is a time in which much difference is noted; children in the U.S. appear to be given more immunizations during this time period than children in the U.K.

Table 1 *Comparison of Immunization Schedules*

Age Received	United States	United Kingdom
2 months	Diphtheria Tetanus Pertussis Hepatitis B Polio Influenza	Diphtheria Tetanus Whooping Cough (pertussis) Hepatitis B Polio
3 months		Diphtheria Tetanus Whooping Cough Hepatitis B Polio
4 months	Diphtheria Tetanus Pertussis Hepatitis B Polio Influenza	Diphtheria Tetanus Whooping Cough Hepatitis B Polio
6 months	Diphtheria Tetanus Pertussis Influenza	
12 to 15 months	MMR Hepatitis B Vericella Polio Diphtheria Tetanus Pertussis	MMR
4-6 years	Diphtheria Tetanus Pertussis Polio MMR	Diphtheria Tetanus Whooping Cough Polio MMR

Those who adhere to the vaccine-autism link further indicate that a child with a weakened immune system is at greater risk for developing autism than the average child, and that they are more susceptible to the harsh side effects that can occur with the administration of these vaccinations. The effects of such an intense battery of vaccinations in such a short period of time could be serious.

> Thus in the first year of life, the immune system of an infant, as well as the infant itself, is challenged by injections, directly into its body, of at least 10 diseases. Many of these are derived from attenuated strains of living bacteria or viruses. An infant with an underdeveloped immune system or one which is already challenged or compromised for any reason must be vulnerable when such a battery of vaccinations are used in such a short period of time (Shattock & Savery, 1997, ¶8).

Vaccinations have also been speculated to be linked to the cause of ASD after a dramatic increase in the number of children identified was seen in relation to the introduction of the multi-component MMR vaccine (Bernard, 2000; Shattock & Savery, 1997; Taylor et al., 1999). The number of different vaccines contained within a single injection is referred to as the valency. MMR is therefore a tri-valent vaccine because it contains measles, mumps, and rubella vaccines. There has been controversy about the immune systems ability to handle a polyvalent vaccine, in that it may in some way overload the immune system.

> There is little evidence, even anecdotal evidence, that the older, single component vaccines, could result in such problems as autism. Reports of such problems

> appear after the introduction of the multi-component MMR vaccine. If these reports are correct it would seem that it is the combination which is responsible for these problems. Given the fact that the Measles virus is known to be immunosuppressant, its inclusion in combination with other disease causing organisms is, in any case, inherently problematic (Shattock & Savery, 1997, ¶15).

As a result of the controversy, the Food and Drug Administration (FDA) reviewed thimerosal-containing products. In 1999, the FDA discovered that "children could be exposed to an amount of mercury from vaccines that exceeded 1 of 3 existing federal safety thresholds" (Freed et al., 2002, p. 1153). In response to the findings related to safety guidelines being exceeded, the FDA requested that the vaccine manufacturers eliminate thimerosal wherever it was deemed possible. Although excessive amounts of thimerosal as a preservative are no longer present in most recommended vaccines in the United States, for children younger than 7 (Parker et al., 2004), thimerosal-containing vaccines continue to be used throughout the world. Although various government and health organizations continue to refute any causal relationship, Geier and Geier (2005) noted that vaccine manufacturers continue to advocate for the use of thimerosal in pediatric vaccines.

Speculation about a link between vaccinations and ASD has not been intended to scare parents and/or discourage immunization practice. If there is a link then research could benefit many children who are highly susceptible to elevated doses of mercury that exist in some vaccines.

Given that autism and Asperger's are pervasive disorders that appear to have increased in prevalence, continued research into causes and treatment for these

devastating disorders is needed. This study contributed to the growing body of literature about possible causes associated with the onset of autism spectrum disorders and risk factors that impact the current level of autistic symptomology and adaptive functioning. Specifically, this study investigated the use of multi-valent and thimerosal-containing childhood vaccinations (particularly MMR) and the child's state of health at the time of immunization and their possible link to the onset of ASD. It is hypothesized that a weakened immune system/poor health may compromise a child's susceptibility to adverse reactions of vaccinations. Additionally, factors related to pre- and post natal experiences, were examined to determine their contribution to the current level of autistic symptomology and adaptive functioning associated with an individual's diagnosis. It is not believed that any particular factor alone is associated with increased severity of ASD. It was investigated whether parent risk characteristics (a family history positive for psychological and learning disorders, length of gestational period, and maternal illness during pregnancy) as well as the presence of child risk characteristics (e.g., physical sensitivity, impaired social interaction, developmental regression and stereotypical/unusual behaviors) to a marked degree during the first five years of a child's life predict an individuals' current level of autistic symptomology and adaptive functioning.

CHAPTER II

REVIEW OF LITERATURE

Autism and its related syndromes have attracted the interest and concern of clinicians and researchers, from the time it was first described in scientific terms approximately 60 years ago by Leo Kanner. Autism, Asperger's, and PDD are severe and life long disorders that affect socialization, language, communication, cognitive functioning, and behavior. These disorders have been studied in the areas of developmental psychology, neurobiology, therapeutic treatment, and education. The literature is filled with examples of theories that have examined the impairments and symptomology associated with autism spectrum disorders. The literature for Asperger's specifically, however, is lacking in comparison because it was not readily recognized in the United States until the 1990's, when Asperger's original paper (published in 1944) was translated to English. Despite the abundance or lack of literature for each disorder, the etiology of autism spectrum disorders continues to be unknown.

Foundational research for autism and Asperger's syndromes

Kanner (1943) published an article concerning eleven children whom he had encountered through his clinical practice and whom were believed to exhibit characteristics of infantile autism. As Volkmar and Lord (1999) stated:

> Kanner noted that his patients exhibited a disorder characterized by a profound lack of social engagement from, or shortly after, their birth....his cases also

exhibited a range of communication problems and unusual responses to the inanimate environment as well (p. 2).

Kanner noted that these children exhibited a number of common characteristics. Through his individual and collaborative work with Eisenberg in 1956 five diagnostic criteria were established. The following criteria were noted from Eisenberg & Kanner (1956, pp. 556-557), Kanner (1943, pp.) and Wing (1981, pp. 93-94):

1. A profoundly impaired ability to exhibit affective contact with other people. "The children's inability to relate themselves in the ordinary way to people and to situations from the beginning of life."
2. A failure to use language for interpersonal communication. Noted by Wing as kind of "mutism".
3. An anxiously obsessive need for the perpetuation of sameness. With interference of the pattern/routine to result in episodes of anger or extreme anxiety.
4. "A fascination for objects, which are handled with skill in fine motor movements."
5. The presence of "good cognitive potential" with distinguishably strong skills in memory and use of language.

In 1944, Hans Asperger had published an account of children with several similarities to Kanner's autism but who had greater abilities, including language and cognitive skills that appeared in the average or above average range. Although Asperger was not aware of Kanner's work on autism, he also used the word autism to describe the social deficits he observed in a group of boys. Asperger did not specifically define diagnostic criteria, instead he described several commonalities of the children he saw. As noted by Wing (1998) and Gillberg (1985) he emphasized the following features:

1. The children were socially odd, naïve, inappropriate, and emotionally detached from others.
2. They had a marked degree of egocentricity and were particularly sensitive to any perceived criticism. They were unmindful to others feelings.
3. They had good grammar skills and extensive vocabularies. There speech was described as pedantic and literal and they were noted to have difficulty with reciprocal conversation.
4. They had poor nonverbal communication skills and their voice lacked intonation when speaking.
5. They had restricted interest in facts related to specific subject matter or for collections.
6. Despite their average to above average cognitive abilities they appeared to have difficulty learning in conventional ways.
7. They displayed poor motor coordination and organization.
8. They appeared to lack common sense.

There are continuing debates concerning the relationship between Asperger and Kanner syndromes yet it is undisputable that they have in common impairments of social interaction, communication, and restricted, repetitive patterns of activities (Wing, 1981; 1991). Similarities between Kanner's and Asperger's syndrome were described by Wing (1998, p. 96) and are summarized in the following points:

1. Both Kanner and Asperger emphasized the marked prevalence of boys over girls.
2. Both syndromes are characterized by a child's tendency to be egocentric, socially isolate themselves, and to have little interest in feelings and ideas of others.
3. Both noted problems regarding the way language was used, as well as the lack of use to engage in and/or maintain reciprocal conversations. Impaired non-verbal skills were also noted by both.

4. Both described a lack of imaginative play.
5. A need for repetitive patterns/routines and sameness within the environment was noted by both.
6. Both described abnormal responses to "sensory stimuli, including hypersensitivity to noise, love of strong-tasting foods and fascination and skill with spinning objects."
7. Both noted concerns for dexterity of motor skills. While Kanner noted it in some of his patients, Asperger described it as a more consistent characteristic.
8. Both noted behavior problems such as "apparent negativism, aggressiveness to people, destructiveness to objects and general restlessness."
9. Each noted specific strengths for memory skills and numbers.

Despite the obvious similarities, Van Krevelen promoted that the two syndromes were distinctly different and noted these differences in 1971 in the first issue of *Journal of Autism and Childhood Schizophrenia.* Van Krevelen (1971) contrasted Kanner and Asperger syndromes concluding that they were different but acknowledging that they could occur in members of the same family. As Wing (1998) noted:

> Van Krevelen listed a number of reasons for regarding the syndromes as different; for example, a child with early infantile autism walks early and talks late, if at all, whereas the converse is true for Asperger syndrome; in autism, speech, if present, is not used to communicate, whereas the child with Asperger syndrome tries to communicate but in a one-sided way….and that early infantile autism is a psychotic process, whereas Asperger syndrome is a personality trait. Further suggesting that an autistic child had the genes for Asperger syndrome but became autistic because of some perinatal organic brain damage (p. 16).

Additionally, differences in the onset of some symptoms were notably different with the children described by Asperger developing language/speech prior to age 3 and commonly portraying extensive and impressive vocabularies (Wing, 1998).

Kanner's early theoretical views regarding the etiology of autism were often the subject of debate in years to follow. Ambivalence of theories and viewpoints concerning the etiology of autism plagued not only Kanner but others as well. Kanner first suggested that the symptoms exhibited of autism stemmed from an "innate inability for interpersonal contact, implying that a disturbance in the growth of the brain is responsible" (Trevarthen et al., 1996, p. 48). Kanner eventually placed greater importance on the emotional coldness and obsessive qualities of parents and concluded "that although the children had some inborn defect, nevertheless in part the disorder was due to lack of affection from the parents - that autism was partly a psychogenic disorder due to "emotional refrigeration" (Rutter, 1968, p. 1). Trevarthen et al. (1996) noted that Kanner first presented autism as a disorder of affective contact. Kanner postulated that the emotional characteristics of the mother, with a possible link to high intelligence and upper social class of the parents, could be a cause. Kanner would later ascribe to opinions that appeared to relieve parents of guilt in relation to the impairments their children exhibited and instead promoted theories that were encompassing of the interplay between nature and nurture.

Early research on Asperger's syndrome was predominately confined to non-English speaking countries until 1981 when Wing published an extensive review of literature and case studies and then again in 1991 when Frith published a translation of Asperger's original paper from 1944. By the time Asperger's syndrome was recognized

in the United States, researchers had established that biological and genetic factors were highly associated with the development of autism (Rutter, 1977). And even though the two disorders shared similarities the etiological basis of Asperger syndrome was still speculative (Gillberg, 1985).

Terminology

Kanner (1943) paved the way for additional theoretical viewpoints to be considered that could help explain and define this phenomenon. Disagreement among researchers has long been evident when naming these disorders, defining the symptoms associated with autism spectrum disorders, and determining their etiology. Many different diagnostic labels have been used to characterize the large group of young children, such as; psuedoretardation, atypical development, symbiotic psychosis, childhood schizophrenia, infantile psychosis and autistic psychopathy (Ornitz & Ritvo, 1968; Rutter, 1968; Volkmar & Lord, 1998; Wing, 1989). The major criteria for the diagnosis of early infantile autism, established by Kanner in the 1940's, were the "inability to relate to people in the expected manner, failure to use language for communication, an apparent desire to be alone and to preserve sameness in the environment, and preoccupation with certain objects" (Ornitz & Ritvo, 1968). Asperger did not specify diagnostic criteria but simply reported on the characteristics and symptomology that was exhibited by his subjects. These characteristics were noted above.

The term psuedoretardation referred to the fact that many of these children appeared retarded while also indicating some intellectual potential, which distinguished them from the general population of retarded individuals. The term atypical development

was used to refer to children who exhibited "uneven ego development" (Ornitz & Ritvo, 1968). Symbiotic psychosis was used by Mahler (1952) to describe children who appeared to exhibit behavior opposite of those with autism. The term childhood schizophrenia was often used as either an interchangeable term for early infantile autism or to describe a separate disorder/syndrome. As Volkmar and Lord (1998) noted:

> The controversy surrounding the nature of autism and the dearth of careful research studies impeded progress for many years. Starting in the 1970's, however, there was a growing appreciation that autism was indeed a distinctive condition, not simply the earliest manifestation of childhood schizophrenia (p. 8).

Reiser (1963) recommended the term infantile psychosis to describe the time in which the pathological process develops during the first fives years of life. He suggested the term was all inclusive and therefore should replace all other terminology proposed. Reiser (1963) indicated:

> The designation "psychotic" is merited by virtue of impairment in perception, Failure to test reality, social isolation and withdrawal, impaired control of instinctual energies, and disturbances of feeling, thinking, and behavior (p.78).

Although Asperger's syndrome would eventually be named after him, Asperger initially used the term autistic psychopathy to describe the abnormal personality traits he was noticing in his subjects (Wing, 1989). Even though Asperger was not well known or mentioned by many of the early researchers (e.g., Adams, 1973; Robinson & Vitale, 1954) the descriptions of individuals within their studies indicated they likely exhibited Asperger's syndrome. A number of researchers prior to and following Kanner and Asperger pushed for these children with known impairments of social interaction,

communication, and stereotyped behavior to be grouped together as one single condition, namely, childhood psychosis, which at the time was regarded as a variant of schizophrenia (Bender, 1947; Rank, 1949; Szurek, 1956).

Theoretical Viewpoints and Etiologies

As the terminology used to describe autism evolved, so did a number of theories presented by researchers during the 1950's and 1960's. As research on autism was beginning in the 1960's there was little consensus of facts. As noted by DeMyer (1975), most researchers of this time did agree that the children they were seeing exhibited significant social withdrawal and impaired communication skills while also observing that they were of high socioeconomic status, had few or no siblings, and were more commonly male. Despite the variation of opinions regarding many aspects of the disorder, most researchers theories could be categorized into one of three major views: "(i) defective parental nurture, (ii) defective biological system in the child ("nature") or (iii) defective "nature-nurture" interaction" (DeMyer, 1975, p. 433).

Psychogenic etiologies/nurturebased theories

As a result of Kanner's early theoretical statements, several interpretations of deficient parental nurture were proposed during the 1950's, 1960's, and even into the 1970's. These theories assumed that the infant was born normal and that the development of symptoms was attributable to poor nurturing. Two versions that dominated the early research indicated that parents of autistic children had higher amounts of psychopathology than other parents and/or that they possessed personality types or traits that were considered extremely negative. These various theories have postulated that the parents of autistic children were deficient either in touching, in feeding practices, in

speech practices and/or in eye-to-eye contact with the child, or were thought to project dehumanizing fantasies onto their infant….They were viewed as extreme personality types; either very depressed, or cold, or full of rage, or without a sense of self, or actually psychopathic (Anthony, 1958; Eisenberg & Kanner, 1956; Ekstein, Seymour, & Friedman, 1974; Fraknio & Ruttenberg, 1971; King, 1975; Masse, 1978; Szurek, 1973; Williams & Harper, 1973; Victor, 1983). Eisenberg and Kanner (1956) even suggested that the children themselves show a "full emergence of the latent structure" while the parents themselves represent a milder manifestation (p. 561). Researchers of this time elaborated on this argument when suggesting that ASD was mainly due to psychogenic factors (Bettelheim, 1967; Despert, 1951; Goldfarb, 1961; Meyers and Goldfarb, 1961; Kaufman, Rosenblum, Heim et al., 1957). Ferster (1961) indicated that autism was due to faulty learning and that the autistic child had not been conditioned properly by his or her parents. Additional researchers, who attributed autism to the presence of extreme levels of psychopathology in the parents, further offered a plausible explanation indicating that the infant could simply be mimicking the extreme personality traits of the parent(s) (Eisenberg & Kanner, 1956) or, as Szurek (1956) stated, the psychotic child was a "magnified mirror opposite" of the unhealthy parent personalities (p. 533).

Many other authors and researchers who were influenced by emotional trauma in infancy as a cause for psychiatric disorders were additionally eager to proclaim their theories on the subject. Bettelheim (1967), who was deeply impressed by the serious mental illness of children who had experienced extreme neglect or maltreatment, concluded that an unsympathetic and neglectful mother could be responsible for the 'empty fortress' state of mind of a child with autism. Indicating that the child resorts to

autism as a response to their seemingly hopeless environment. Bettelheim explained the severity of the child's response as dependent upon the critical period in which the neglect occurred and suggested that the lack of language and emotionality was due to an inattentive audience within his or her environment. Bettelheim also noted that the reason siblings were not affected was because the parent's rejection was specific to the autistic child during one or more critical periods of development. Additional researchers such as Anthony (1958) and Eisenberg and Kanner (1956) added to this theory indicating that not only could deficient parental nurture be a cause for autism but that it could support its continued development. Through all of the variations of the deficient parental nurture theories, the belief that parents inadequately provided stimulation to their autistic infants was consistently emphasized (Anthony, 1958; Bettelheim, 1967; Despert, 1951; Eisenberg & Kanner, 1956; Ferster, 1961; Meyers & Goldfarb, 1961; Kaufman et al., 1957; Szurek, 1956). Ferster (1961) took a behavioral approach and proposed reinforcement and consequences in the context of the parent-child relationship caused the autistic disorder. Ferster (1961) even suggested that the autism could be weakened or eliminated if the parent employed systematic techniques. Reiser (1963) and Szurek (1956) postulated that autism resulted when the parent experienced an episode of great emotional distress during the critical period of infancy which subsequently compromised the parent-child relationship.

Clinicians responded to the notion of deficient parental nurture as a cause for autism with psychotherapy as the choice of treatment. It was hypothesized that psychotherapy would be able to address the emotional needs of both the parents and child. Kanner (1952) wrote that the condition usually could not be remedied because the

parents sabotaged treatment....Therefore, unless the mothers could be helped by psychotherapy, the only hope for most of these autistic children was to remove them from the home and subsequently place them with foster mothers. Therapy was also believed to be beneficial to the intellectual abilities that were hidden within the autistic child. Hence the "nurture" theorist believed that normal biological intelligence was locked within the autistic child....If the right treatment could be found, the child would accelerate in progress and eventually become normal or even supernormal in intelligence (DeMyer, 1975).

However, as controlled studies were completed throughout the 1970's, it became evident that the parents of autistic individuals did not exhibit a greater amount of psychopathology (Cox et al., 1975), extreme or unusual personality traits (McAdoo & DeMeyer, 1978) nor were any particular patterns of poor infant/child care noted (Cantwell, Rutter, & Baker, 1978). Additional studies evidenced that autistic children were not solely the product of families from any particular socioeconomic class or race (Schopler, Andrews, & Strupp, 1980; Wing 1980).

Biological etiologies/nature-based theories

In contrast to the nurture theories evident during the 1950's and 1960's was the opposing biological theories of the cause for ASD. This perspective inferred the cause resided in some biological abnormality within the individual, with emphasis on deficiencies of the central nervous system and brain. Rimland was one of the first researchers to suggest that parents themselves may not be at fault and that there may be some other etiological explanation for autism. Rimland opposed Eisenberg and Kanner's (1956) efforts to diminish the importance of the "heredity versus environmental" question

in autism along with their efforts to attribute the genesis of ASD to family dynamics. In contrast, Rimland (1964) and others (e.g, Anthony, 1958; Bender, 1959; Goldfarb, 1961; Rutter, 1965; Schopler et al., 1980, and Wing, 1976) suggested the involvement of organic factors. Rimland (1964) suggested the involvement of a biological deficiency associated with the reticular activating system. While Rimland (1964) suggested the autism was caused by the under-activity of the reticular system, Hutt, Hutt, Lee et al. (1965) suggested autism was due to over-arousal. DeMyer (1975) noted that in the pure "nature" theory, the parents were viewed as contributing little more to the child's illness than symptom variations....The illness was considered basically the expression of a biological abnormality. While nature theorist did agree that the cause of autistic disorders was due to some biological abnormality within the child, most investigators disagreed about the kind of biological dysfunction that might be attributing to the presence of autism in the individual (Anthony, 1958; Bender, 1959; Fish, 1960; Goldfarb, 1961; Knobloch & Passamanick, 1975; Rimland, 1964; Rutter, 1965; Schain & Yannet, 1960; Schopler et al., 1980, Wing, 1976).

Rimland's proclamations in 1964 brought about a surge of research. In order to diffuse the deficient parental nurture theories and gain evidence to focus on issues related to biological factors, investigators began studying parents of autistic children and comparing them to other control groups. Researchers found little if any differences between the two groups when examining various factors related to the interactions of parents and children (Byassee & Murrell, 1975; Cantwell et al., 1978; Cantwell & Baker, 1978; Cox et al., 1975; Frank et al., 1976; Goldfarb, Spitzer, & Endicott, 1976; and McAdoo & DeMyer, 1978). The literature on parents of autistic children produced during

the late 1960's and 1970's was reviewed by McAdoo and DeMyer (1978). They concluded that, as a group, parents of autistic children: a) displayed no more signs of mental or emotional illness than parents whose children have "organic" disorders, with or without psychosis; b) do not have extreme personality traits such as coldness, obsessive ness, social anxiety or rage; and c) do not possess specific deficits in infant and child care. With a remarkable amount of evidence against deficient parental nurture as a cause for autism, researchers could now focus their attention on biological causes.

Several theories were introduced by researchers during the 1950's and 1960's that claimed autism was predominately due to an organic brain disease or possible biological or physiological factors (Rutter, 1968). Rimland (1964) and Hutt et al. (1965) suggested the involvement of the reticular activating system, Schain and Yannet (1960) suggested the limbic system as a site of cerebral abnormality relating to the disorder, while Fish (1960) suggested the timing mechanism related to somatic development. Still others claimed that autism was due to organic brain disease related to conditions such as encephalopathy (Bender, 1947) or damage that had occurred during pregnancy or the delivery process (Bender, 1947; Knobloch & Passamanick, 1975). Bender suggested a disturbance in the rate of development and "emphasized a maturational lag at the embryonic level as being characteristic of and fundamental to the development of the entire syndrome" (Ornitz & Ritvo, 1968, pp. 87-88). Anthony (1958), Goldfarb (1961), Schopler et al. (1980), Rutter (1965), and Wing (1976) suggested that the autistic child's inability to respond normally to stimuli indicated a defect in perception. A more recent study conducted by Steffenburg (1991) concluded that 85% to 90% of ASD subjects evidenced some indication of underlying brain dysfunction.

Disturbances related to perception were suggested by several researchers. According to this view language was noted as the primary abnormality and that the abnormal development of language was similar to impairments involving deficits in comprehension or "cognitive auditory inperception" (Rutter, 1965). Researchers noted the similarities to include the autistic child's lack of response to sounds as indicated by the lack of a startle response (Anthony, 1958; Rutter 1966), suspected deafness (Kanner, 1943) and a frequent inability to be distracted (Rutter, 1966). It was further postulated by Ornitz and Ritvo (1968) that:

> Autistic children do not have the ability to maintain constancy of perception due to an underlying failure of homeostatic regulation within the central nervous system so that environmental stimuli are either not adequately modulated or are unevenly amplified….resulting in a random underloading or overloading of the central nervous system (p. 88).

As early as 1949, Bergman and Escalona observed abnormal sensory responses and suggested a low tolerance for external stimulation as being an important role in autism. Others studied perceptual difficulties from the notion of receptor preferences. Inferring that autistic children exhibited a notable preference for tactile sensation versus visual or auditory (Goldfarb, 1956) claiming this as evidence that early sensory deficits were linked to inadequate reticular arousal mechanisms (Schopler, 1965).

The research regarding the etiology of Asperger's syndrome specifically was scarce and was often perceived as evidencing similar etiology as classic autism. Asperger himself considered it to be genetically transmitted (Gillberg, 1985; Wing, 1981). Mnukhin and Isaev (1975) suggested organic brain dysfunction as the basis of the

disorder. Wing (1981) described cases where pre-, peri- or post natal conditions may have been associated with brain damage as well as a case which suggested an argument for genetic predisposition (Burgoine & Wing, 1983). Research related to perceptual and sensory deficits brought about theories suggesting the interaction between biological and environmental factors and their impact on the etiology of ASD.

Etiologies related to the interaction of psychogenic and biological factors

In addition to the nature and nurture theories proposed during the 1950's and 1960's, a variety of combined nature-nurture theories were also postulated (Anthony, 1958; Mahler, 1952; Mahler & Gosliner, 1955; Rank, 1955, Rimland, 1964; Sarvis & Garcia, 1961). There were two main views of the nature-nurture interaction theory. In one version all autistic infants were seen as biologically deficient and the parents viewed as failing to give proper emotional support….In another version, some infants were viewed as organically damaged and others as biologically normal, with the parents of nonorganic infant described as failing to a greater degree than parents of organic infants (Coleman and Gillberg, 1985, p. 5; DeMyer, 1975, p. 434). Studies that have investigated the prevalence of autism among identical twins have provided clear evidence of a strong hereditary component combined with environmental factors. As Rimland (1964) noted, it is of interest that in several cases of identical twins stricken with autism, the degree of affliction, while invariably severe, is not quite identical….This suggests that while genetic factors may predispose toward autism, post-conceptional factors could be operative.

Anthony (1958) expanded on his theory regarding the lack of responsiveness in the child by further indicating that autistic disorders were caused by a combination of

unresponsiveness in the child and unresponsiveness of the mother. Mahler (1952) suggested that autistic syndromes, which were called symbiotic psychosis, stemmed from a combined defective ego and a pathogenic mother-child relationship. The mother was emphasized as an etiological agent by not allowing the child to differentiate himself (Mahler 1952; Mahler & Gosliner, 1955). Her theory of separation-individuation detailed the child's struggle or failure to psychologically separate himself from his mother. Both Mahler (1952) and Anthony (1958) proposed that a "normal autistic stage" existed from the time of birth until the age of two month in which the infant was unable to see themselves independently of their mother. They further suggested that the pathology emerged if the child remained or returned to this stage. In contrast, Rank (1955) suggested a variety of dysfunctions that affected a child's social interactions and their impact on the ability to modulate anxiety. Sarvis and Garcia (1961) and Williams and Harper (1973) associated ASD with multiple organic and environmental etiologies such as faulty family psychodynamics, traumatic circumstances within the environment, significant physical illness, cerebral defects, and other neuropathology affecting perception.

The need for classification to support empirical research

With the work of Kolvin and Rutter (1998) establishing autism as a separate disorder from schizophrenia the need for a standard classification was evident, as the different definitions and characteristics used to describe autism at times appeared to impede research. Among the early attempts to create a more precise definition, Rutter (1978) was the most influential. His definition not only included basic concepts of Kanner's early descriptions but he also recognized the need for additional research.

Rutter (1978) suggested four essential features for the diagnosis: (1) an onset prior to 30 months of age, (2) impaired social development (not associated with any type of mental retardation), (3) impaired development in communication which was not related to any form of cognitive delay, and (4) the presence of unusual behaviors. These concepts appeared to shape the first official categorical definition of autism.

With the 1980 publication of the Diagnostic and Statistical Manual –Third Edition (DSM-III) autism was awarded diagnostic status for the first time. The information included within the DSM-III reflected heavily the research that had accumulated over the previous decade. The condition was included under a new category of disorders, the Pervasive Developmental Disorders (PDD), and was referred to as Infantile Autism. As Volkmar et al. (1997) noted; the newly termed category, PDD was "meant to convey that individuals with these conditions suffered from impairment in the development and unfolding of multiple areas of functioning" and was also intended to "avoid a theoretical presupposition about etiology" (p. 15). Childhood Pervasive Developmental Disorder, Atypical PDD, and Residual Infantile Autism were also included. Atypical PDD was used for individuals who appropriately fit into this category but did not meet enough criteria for a diagnosis of Infantile Autism (APA, 1980). Residual Infantile Autism was used to refer to individuals who had previously met criteria for autism but no longer did so (APA, 1980). However, the inclusion of the term residual autism created false hope as it implied that these children somehow outgrew the condition (Rumsey, Rapoport, & Sceery, 1985; Volkmar, Klin, & Cohen, 1997). The definition presented in the DSM-III indicated that pervasive symptoms presented during early childhood, yet it did not adequately depict that the condition remains with the individual into adulthood (Volkmar

& Lord, 1989). Due to these concerns and the need for a broader conception, changes were made to the definition with the publication of the *DSM-III-R* in 1987. Despite its shortcomings, the addition of the PDD category to the *DSM-III* and *DSM-III-R* allowed for international recognition and testing of the criteria; and more precise information for the publication of the *DSM-IV*.

In addition to the *DSM*, was the well recognized system of medical diagnosis known as the International Classification of Diseases (ICD). Coincidently, as the *DSM-III-R* was being revised so was the ninth edition of the *ICD*, which allowed for some consistency between the two systems (Cohen & Volkmar, 1997). However, the draft of the *ICD-10* proposed additional categories not included in the *DSM-III-R* such as; Asperger's Syndrome, Rett's Syndrome, Childhood Disintegrative Disorder, and Atypical Autism (Cohen & Volkmar, 1997). These differences likely influenced the revision and 1994 publication of the *DSM-IV*.

Diagnostic criteria for Autism Disorder for DSM-IV and ICD-10 are presented in Tables 2 and 3. For the diagnosis of autism, at least six criteria must be exhibited, including at least two criteria relating to social abnormalities (group 1) and one of each relating to impaired communication (group 2) and range of interests and activities (group 3). In addition, the onset must have occurred prior to age 3, as evidenced by a delay or abnormal functioning in social interaction, use of language in social communication, or symbolic/imaginative play. The disorder can not be better accounted for by a diagnosis of Rett's Disorder or Childhood Disintegrative Disorder.

Table 2

DSM-IV-TR Criteria for Autistic Disorder (299.00)

A. A total of at least six items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3):

(1) Qualitative impairment in social interaction as manifested by at least two of the following:
   (a) Marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction;
   (b) Failure to develop peer relationships appropriate to developmental level;
   (c) Markedly impaired expression of pleasure in other people's happiness;
   (d) Lack of social-emotional reciprocity.

(2) Qualitative impairments in communication as manifested by at least one of the following:
   (a) Delay in or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gestures or mime);
   (b) In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others;
   (c) Stereotyped and repetitive use of language or idiosyncratic language;
   (d) Lack of varied spontaneous make-believe play or social imitative play appropriate to developmental level.

(3) Restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following:
   (a) Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus;
   (b) Apparently compulsive adherence to specific nonfunctional routines or rituals;
   (c) Stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting, or complex whole-body movements);
   (d) Persistent preoccupation with parts of objects.

B. Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years: (1) social interaction, (2) language as used in social communication, or (3) symbolic or imaginative play.

C. Not better accounted for by Rett's Disorder or Childhood Disintegrative Disorder.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual 4th ed. text revision.* Washington DC: American Psychiatric Association., pp. 75.

Table 3
ICD-10 Criteria for Childhood Autism (F84.0)

A. Abnormal or impaired development is evident before the age of 3 years in at least one of the following areas:
   (1) receptive or expressive language as used in social communication
   (2) the development of selective social attachments or of reciprocal social interaction;
   (3) functional or symbolic play

B. A total of six symptoms from (1), (2), and (3) must be present, with at least two from (1) and at least one from each of (2) and (3):

   (1) Qualitative impairments in social interaction are manifest in at least two of the following areas:
      a. Failure adequately to use eye-to-eye, facial expressions, body postures, and gestures to regulate social interaction;
      b. Failure to develop (in a manner appropriate to mental age, and despite ample opportunities) peer relationships that involve a mutual sharing of interests, activities, and emotions;
      c. Lack of socialemotional reciprocity as shown by an impaired or deviant response to others people's emotions; or lack of modulation of behavior according to social context; or a weak integration of social, emotional, and communicative behaviors;
      d. Lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., a lack of showing, bringing, or pointing out to other people objects of interest to the individual)

   (2) Qualitative abnormalities communication as manifest in at least one of the following areas:
      a. Delay in, or total lack of, development of spoken language that is not accompanied by an attempt to compensate through the use of gestures or mime as an alternative mode of communication (often preceded by a lack of communicative babbling);
      b. Relative failure to initiate or sustain conversational interchange (at whatever level of language skill is present), in which there is reciprocal responsiveness to the communications of the other person;
      c. Stereotyped and repetitive use of language or idiosyncratic use of words or phrases;
      d. Lack of varied spontaneous make-believe play or (when young) social imitative play.

   (3) Restricted, repetitive, and stereotyped patterns of behavior, interests, and activities are manifested in at least one of the following:
      a. An encompassing preoccupation with one or more stereotyped and restricted patterns of interest that are abnormal in content or focus; or one or more interests that are abnormal in their intensity and circumscribed nature though not in their content or focus;
      b. Apparently compulsive adherence to specific nonfunctional routines or rituals;
      c. Stereotyped and repetitive motor mannerisms that involve either hand or finger flapping or twisting, or complex whole-body movements;
      d. Preoccupations with part-objects or nonfunctional elements of play materials (such as their odor, the feel of their surface, or the noise or vibration they generate).

C. The clinical picture is not attributable to the other varieties of pervasive developmental disorders; specific developmental disorder of receptive language(F80.2) with secondary socioemotional problems' reactive attachment disorder (F94.1) or disinhibited attachment disorder (F94.2); mental retardation (F70-F72) with some associated emotional or behavioural disorders; schizophrenia (F20.-) of unusually early onset; and Rett's Syndrome (F84.12).

World Heath Organization (1993). *International Classification of Diseases, 10th ed.* Diagnostic Criteria for Research. Geneva: World Health Organization, (pp.209).

Over the next decade the definition and characteristics associated with diagnosing autism would continue to evolve to its present status included in the recent edition of the *DSM-IV-TR* (2000) text revision. As noted by Cohen & Volkmar (1997), "from the start, DSM-IV was conceptualized as a more sweeping update of the nosology, based on detailed evaluation of current data….They considered issues involving clinical utility, reliability, and descriptive validity of categories and criteria (p. 18). While Autism Disorder and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) had been included in the *ICD-9* and the *DSM-III* /*DSM-III-R* it was not until the *ICD-10* and *DSM-IV* were published that Asperger's Syndrome was included. The lack of recognition in the United States and absence of an acceptable definition among clinicians and researchers contributed to confusion about the validity of this diagnostic concept (Cohen & Volkmar, 1997; Volkmar, 1998; Wing, 1981, 1991, 1998, 2005). Although Asperger's Syndrome had been included in the *ICD-10*, its validity as a separate disorder from autism had not yet been established and would continue to be questioned even after its inclusion in the *DSM-IV* (Cohen & Volkmar, 1997; Woodbury-Smith et al., 2005; Wing, 1981, 1991, 1998, 2005). It is further suggested by Woodbury et al. (2005) that this confusion was due to limitations inherent to the criteria. Even the most recent revision of the *DSM-IV*, the *DSM-IV-TR* which was published in 2000 indicated that definitive data related to the disorder is limited.

Diagnostic criteria for Asperger's Disorder for DSM-IV-TR are presented in Table 4. In the *ICD-10* (1993), *DSM-IV* and *DSM-IV-TR* the disorder differs from autism in that there is a lack of any clinically significant delay in language or cognitive development and self-help and adaptive behavior skills are within normal range of

development. In people with Asperger's Syndrome, deficits in social interaction and unusual responses to the environment, similar to those in autism, are observed. Unlike in autism, however, cognitive and communicative developments are within the normal or near-normal range in the first years of life, and verbal skills are usually an area of relative strength. Idiosyncratic interests are common and can be exhibited in unusual and/or highly limited interest (e.g., a specific animal such as dinosaurs, in bus/train schedules, various flavors of gum).The *ICD-10* and *DSM-IV-TR* also state that motor delays and motor clumsiness are typically exhibited but does not require they be present for diagnosis. As with autism, both the *ICD* and *DSM* definitions indicate that Asperger's Syndrome can not be attributed to other varieties of PDD or schizophrenia. For the diagnosis of Asperger's at least three criteria must be exhibited, including at least two criteria relating to social abnormalities (group 1) and one relating to impaired range of interests and activities (group 2). In addition, it must cause impairment in social or occupational functioning; there can be no clinically significant delay in language, cognitive development, or adaptive behavior and other PDD's and schizophrenia must be ruled out.

Table 4

DSM-IV-TR Criteria for Asperger's Disorder (299.80)

A. Qualitative impairment I social interaction, as manifested by at least two of the following:
   (1) Marked impairment in the use of multiple nonverbal behaviors such eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction.
   (2) Failure to develop peer relationships appropriate to developmental level.
   (3) A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by lack of showing, bringing, or pointing out objects of interest to other people).
   (4) Lack of social or emotional reciprocity.

B. Restricted repetitive and stereotyped patterns of behavior, interests, and activities as manifested by at lest one of the following:
   (1) Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus.
   (2) Apparently inflexible adherence to specific, nonfunctional routines or rituals.
   (3) Stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting, or complex whole-body movements).
   (4) Persistent preoccupation with parts of objects.

C. The disturbance causes clinically significant impairment in social, occupational, or other important areas of functioning.

D. There is no clinically significant general delay in language (e.g., single words used by age 2 years, communicative phrases used by age 3 years).

E. There is no clinically significant delay in cognitive development or in the development of age-appropriate self-help skills, adaptive behavior (other than in social interaction), and curiosity about the environment in childhood.

F. Criteria are not met for another specific Pervasive Developmental Disorder or Schizophrenia.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual 4th ed. text revision.* Washington DC: American Psychiatric Association., pp. 84.

With the publication of the *DSM-IV* the term atypical autism, which had been included in the *ICD*, was added under the subcategory of Pervasive Developmental Disorder Not Otherwise Specified. This subcategory was designed for diagnosis of individuals who exhibited severe pervasive impairments for some or all of the proposed symptomology but did not specifically meet the criteria for any particular Pervasive Developmental Disorder, Schizophrenia, Schizotypal Personality Disorder, or Avoidant Personality Disorder (APA, 1994).

Genetic etiologies

More than 20 years would pass after Kanner and Asperger's original descriptions before genetics was recognized as important to the etiology of ASD. With standard diagnostic criteria in place research appeared to regain its purpose. New causes for ASD would become the focus of research particularly with the technological advancements available to researchers. After twin studies during 1970's and 1980's concluded there may likely be a genetic component (Rimland,1964) etiological research began efforts to uncover genetic links. Of particular interest was determining chromosomal influence and the possibility of locating a specific gene(s) related to ASD (Petit, Herault, Martineau et al., 1996; Philippi, Roschmann, Tores et al., 2005; Skuse, 2000; 2005; Trottier, Srivastava, & Walker, 1999; Wassink, Piven, Vieland et al., 2005).

There are different genetic disorders in which those affected have higher rates of autism than would be expected (Folstein & Rosen-Sheidley, 2001). ASD has been associated with disorders such as Fragile X Syndrome, untreated phenylketonuria (PKU), neurofribromatosis, and tuberous sclerosis (Gillberg & Forsell, 1984; Gillberg & Rutter et al, 1997; Trottier et al., 1999). Although no disease gene has been definitely identified

with the etiology of ASD (Wassink et al., 2005) researchers appear to be getting closer. Studies also supported the involvement of the X chromosome as influential in ASD (Petit et al., 1996; Skuse, 2000). Regions of particular chromosomes (e.g., chromosomes 2, 4, 7, 10, 16, 18, 19, and 22) have been associated with ASD (Philippi et al., 2005; Trottier et al., 1999; Wassink et al., 2005). Of particular interest to researchers has been chromosome 15 as it appears to be a common site for abnormalities associated with autism (Folstein & Rosen-Sheidley, 2001; Rutter et al., 1997). Etiological relevance for this chromosome comes from the association of various regions with disorders such as dyslexia (Trottier et al., 1999), Prader-Willi (Martin, State, Koenig et al., 1998) and Angelman syndrome (Nurmi, Bradford, Chen et al., 2001).

Pre- peri- and postnatal factors and infectious etiology

One of the questions raised in early literature from the 1960's about autistic syndromes was the possibility of an infectious etiology to the syndrome (Chess, 1971, 1977, Chess et al., 1971; Crook, 1983; Desmond et al., 1967; Dykens & Volkmar, 1997; Freedman et al., 1970; Gillberg, 1985; Knobloch & Passamanick 1975; 1970; Rutter, 1977). Although research concerns today have advanced this notion, it indicates that a concern regarding children's weakened immune systems and susceptibility to psychological illness was recognized. These early studies portrayed concerns regarding pre- and post-natal infectious diseases and the impact on children's immune systems as a result of these infections. Studies were conducted that investigated whether children who experienced pre- or post- natal infections and/or a suppressed immune system developed autism (Chess, 1971, 1977; Chess et al., 1971; Coleman & Gillberg, 1985; Dykens & Volkmar, 1997; Knobloch & Passamick, 1975; Kennedy et al., 2004; Krause et al., 2002;

Ritvo & Ritvo, 1982; Stubbs & Magenis, 1980). It has been noted that a small but significant proportion of children develop an autistic disorder as a result of pre-or post-natal infections; for example with rubella, cytomegalovirus, herpes, and others (Gillberg & Coleman, 1992).

In 1979, Deykin and MacMahon conducted a retrospective epidemiological study of 163 autistic children and their unaffected siblings by using parent interviews and medical reports. They found a small number of cases in which infectious etiology could be established, indicating that the viruses studied were unlikely to have contributed to autism. However, in summary Deykin and MacMahon (1979) noted that for the children identified as partially autistic that there was a statistically significant difference between cases and sibling controls in their exposure to or illnesses of the mother with prenatal rubella as well as an increased frequency of maternal illnesses (rubella and mumps). For fully autistic patients they found that prenatal maternal influenza was four times as common and that during the postnatal period the exposure to mumps was greater (Deykin & MacMahon, 1979). Later studies also assessed risk factors related to utero exposure with the use of birth-defect causing substances such as ethanol, valproic acid and prescriptive drugs (Rodier, 2000). Although the evidence somehow escaped earlier researchers, evidence linking the use of thalidomide, an anti-nausea drug used with expectant mothers in the 1960's, with some cases of autism was discovered by Stromland et al. (1994). Their findings suggested that ASD may originate as early as the first few weeks of pregnancy, when the embryo's brain and nervous system are just beginning to develop (Stromland et al., 1994). Stromland et al. evaluated Swedish adults born between the late 1950's and early 1960's who exhibited malformations due to thalidomide

exposure (stunted arms and legs, misshaped or missing ears and thumbs, and neurological dsyfunctions of the eye and facial muscles). Because of advanced knowledge of embryonic development, stages of organ development related to pregnancy were useful in pinpointing exact times that malformations occurred for the subjects. Stromland et al. discovered that most thalidomide victims with autism had malformations in the external part of their ears but none associated with the arms or legs….indicating they had been injured during the early stages of gestation, possibly 20-24 days after conception.

Research regarding post-natal infection and autism was particularly sparked by the Rubella epidemic that occurred in 1964 (Chess 1971, 1977; Chess et al. 1971; Coleman & Gillberg, 1985). In a study conducted by Chess et al. (1971) it was found that out of 243 children studied they identified 18 as having "an autistic syndrome" and eight more who had a "partial syndrome of autism" (p. 35). However, the significance of this finding was modified by follow-up data, collected by Chess et al. (1977) indicating that these identified children, as they grew older, ceased to exhibit autistic symptoms. Additional researchers have also reported cases of children developing autism upon experiencing various post-natal infections (Crook, 1983; Desmond et al., 1967; Freedman et al., 1970; Gillberg, 1985; Knobloch & Passamanick 1975). Even in the early literature, a small amount of evidence suggested that infectious agents in the post-natal period may have been a factor in the development of autistic syndromes. The suggestion that autism could be caused by vaccination has been in circulation for many years; however, the amount of literature that exists is often inconsistent (Bernard et al., 2001; Bernard et al., 2002; Coleman & Gillberg, 1985; Kennedy et al., 2004; Krause et al., 2002; Shattock &

Savery, 1997). Additionally, there is a period of time in which the literature appears to be lacking the investigation of this topic.

Wakefield et al. (1998, 2000) has been a primary investigator in researching the link between ASD and the MMR multi-component vaccination. Hilts (2000) reported Wakefield became interested in investigating the possible link between MMR and autism in response to reports from parents whose experience of autism seemed to be different from the usual…parents reported an onset of autism rather suddenly, over a period of months, and often just after vaccination with the MMR multi-component vaccine. Research findings from a case study of 30 children, reported by Wakefield during 1998 conference proceedings of Pyschobiology of Autism, indicated that onset of behavioral symptoms was associated, by the parents or referring physician, with MMR vaccination in 11 of the 30 children studied…and that the data provided further support for a link between autism and vaccination. An additional investigation by Wakefield et al. (1998) in which 12 children were included produced similar results supporting evidence for a possible link between MMR and autism…it was reported that:

> In eight children, the onset of behavioral problems had been linked, either by the parents or by the child's physician, with measles, mumps, and rubella vaccination…Five had had an early adverse reaction to immunization (rash, fever, delirium; and in three cases, convulsions)…In these eight children the average interval from exposure to first behavioral symptoms was 63 days (with a range of 1-14 days) (p. 639).

Singh (2000) related additional evidence in support of a link between the MMR vaccine and autism spectrum disorders. He spoke of research related to autoimmunity and its

explanation for a link between vaccines and autism and other autoimmune diseases. Singh (2000) indicated that he had coined a term "Autoimmune Autism" (AA) to refer to a subset of autism that has autoimmune etiology….and that he believes there are "scientific reasons to think that this subset may indeed be a result of vaccine injuries to children who display autistic regression" (¶2). He further noted that the "autoimmune response is what happens in autoimmune diseases such a lupus,"…and that his research "showed a similar response may account for the brain abnormalities found in people with autism" (¶3). "The hallmark of autoimmune diseases is the organ-specific autoantibodies that have also been identified in people with autistic disorder" (Singh, 2000, ¶4). "A summarization of approximately 400 cases (autistic and controls) found that up to 80% of autistic children have autoantibodies to specific brain structures"…and that "autoantibodies are present quite frequently (60-85%) in autistic children, but only rarely (0-5%) in normal children and other disease controls" (Singh, 2000, ¶4). Based on the belief that autoimmunity is commonly triggered by environmental exposures such as viral infections, Singh (2000) investigated a virus link with autoimmunity and ASD which posed the following questions; 1) Do autistic children have a hyperimmune response (or increase of antibodies) for a specific virus? and 2) Is there a relationship between virus antibodies and brain autoantibodies in autism? Singh's (2000) findings indicated that :

> There was indeed a hyperimmune response to a virus and it was specifically for the measles virus…there was an association between measles virus antibodies and myelin basic proteins autoantibodies (i.e., the higher the measles virus antibody level the greater the chance of brain autoantibody.)" (¶5).

Earlier research by Singh (1998) indicated that many autistic children had antibodies to a specific protein of the measles-mumps-rubella vaccine. These findings led Singh to speculate that autism might be caused by a measles or MMR vaccine-induced autoimmune response. Others have also noted adverse events following MMR vaccination in immunodeficent patients (Kennedy et al., 2004; Krause et al., 2002). It was noted by Kennedy et al. (2004) that certain instances exist in which it is contraindicated for individuals with defective immune systems to receive vaccines. These instances include pregnancy, immune dysfunction, febrile illness, a history of allergic reactions to antibiotics, and HIV.

Additional research conducted by Geier and Geier (2003, 2004, 2005) also indicated a relationship between increasing doses of mercury from thimerosal-containing vaccines and neurodevelopmental disorders such as autism. Specifically, they found a relationship between the thimerosal-containing vaccine DTaP and neurodevelopmental disorders. In their 2004 study, they investigated the effects of administration of tens of millions of doses of thimerosal-containing vaccines to millions of children. Furthermore, Geier and Geier's (2003, 2004, 2005) findings supported earlier studies conducted by Barnard et al. (2001) andBradstreet et al. (2003) which hypothesized that children who were diagnosed with autism spectrum disorders had a decreased ability to expel mercury when compared to normal control groups. This inability to excrete mercury was noted as particularly troubling by Gasset, Motokazu, Yasuo, and Ramer (1975). Gasset et al. (1975) showed that the administration of thimerosal to animals resulted in a high concentration of mercury in the blood and tissue (including the brain), further concluding that thimerosal crosses the blood-brain barrier. Additionally, Bernard et al. (2002) noted

that in his review of the research, preliminary findings suggested that mercury may persist in the tissue of some autistic individuals and may contribute to autistic symptoms.

Perhaps, some of the most fascinating data thus far that is supportive of a possible causal link between the MMR vaccination and ASD comes from the Vaccine Adverse Event Reporting System (VAERS). Kennedy et al. (2004) reported that between January 1990 and January 2001, 291 unique reports from the United States were identified that involved MMR and another poly/multi-valent vaccine and adverse affects such as autism… and that of the 129 reports involving autism, 46% were from the MMR vaccine alone. The evidence is scarce in support of a link between vaccines and ASD in comparison to evidence refuting a link. There are several examples in the literature that indicate a lack of support and/or evidence for a link between the MMR vaccine and autism spectrum disorders. Hilts (2000) indicated that "mainstream medical organizations and leaders in the field of immunization agree that there is not convincing evidence for the theory that the vaccine, MMR, for measles, mumps, and rubella, causes autism" (p. 20).

Several researchers who conducted systematic reviews of the literature found no evidence proposing a link between MMR and ASD (Bower, 1999; DeStefano & Chen, 1999; Klein & Diehl, 2004; Nicoll, Elliman, & Ross, 1998). Jefferson, Price, Demicheli et al. (2003) conducted a review of the literature to evaluate the unintended effects associated with MMR. Jefferson and his colleagues found that MMR was linked, to a varying degree, with conditions such as upper respiratory infections, irritability, and aseptic meningitis but that no link was evident for conditions such as Autism, Crohn's disease, and ulcerative colitis. They concluded that the adverse event could not be

alienated from its role in preventing the intended disease. Time trend analysis were also conducted to assess the association between MMR and the increased prevalence of ASD in the United States (Dales, Hammer, & Smith, 2001), European countries (Taylor et al., 1999) or both (Stehr-Green, Tull, Stellfeld et al., 2003). However, results indicated no causative association or one that is exceedingly rare (Honda, Shimizu, & Rutter, 2005). Makela, Nuroti, and Peltola (2002) conducted a retrospective study involving hospital discharge records in order to assess the possible association between MMR and ASD. They found no clustering of hospitalization for ASD following immunization nor an association between MMR vaccination and ASD. Fombonne and Chakrabarti (2001) tested the claim that there was a new phenotype of ASD (autistic entercolitis) that involved gastrointestinal symptoms but found no support for MMR induced autism or autistic entercolitis. Peltola et al. (1998) conducted a study in which 14 years worth of data from the National Board of Health and National Public Health Institute was reviewed. The findings indicated that a "decades effort to detect all severe adverse events associated with MMR vaccine could find no data supporting the hypothesis that it would cause pervasive developmental disorders" (Peltola et al., 1998, p. 1328). A study conducted by Madsen, Hviid, Vestergaard, Schendel et al. (2002) reviewed records of 537,303 children born in Denmark between January 1991 and December 1998. Of those children, 440,655 had been vaccinated. The authors found that the risk of autism was similar in children who were vaccinated and children who were not as well as that there was no increase in the risk of an autistic disorder among vaccinated compared to unvaccinated children. A large study completed by Taylor et al. (1999) in which approximately 500 children diagnosed with autism were investigated, found no relation

between the children's vaccination dates and the onset of their disease. The study found that although the number of cases of autism disorders had been increasing since 1979, there was no significant increase following the introduction of the multi-valent MMR vaccine. Taylor et al. (1999) also noted that children vaccinated before 18 months of age, after 18 months of age, or not vaccinated, were similar in age at diagnosis, further indicating that vaccination does not appear to result in an earlier onset of autism. Taylor et al. (1999) further notes that these findings "confirm and extend studies from Sweden (Gillberg & Heijbel, 1998), and Finland (Peltola et al., 1998), both of which demonstrated no relationship between MMR vaccination and autism" (p. 2028). Offit (2000), during a government reform hearing, attempted to invalidate proposed theories relating to the association of vaccination and autism. Offit (2000) discussed counter points to theories related to autoimmunity reactions, the use of multi-component vaccines, and the unnatural route/methods by which vaccines are administered.

There is an increasing amount of research presently being conducted into the possible link between autism and vaccinations. Some of this stems not only from concerned parents voicing their experiences related to autism but experiences related to side effects experienced from other vaccines as well. As reported by Hsu (1999) the "US got a wake up call between 1989 and 1991 when measles inoculations lapsed among preschool children in some urban areas…55,000 people got sick and 120 died, most of them children under 5" (p. C1). Additional examples noted by Hsu (1999) included a recent concern over the rotavirus causing a rare and dangerous bowel disorder, seizures as a result of a new strain of the Pertussis vaccine and the chicken pox vaccine, as well as paralization from polio vaccines. In fact, in 1986 the Vaccine Adverse Event Reporting

System (VAERS) was established for parents and/or doctors to report vaccine related injuries and side effects.

This increase in current research has resulted from the elevated incidence of parents claiming that their child's autism was the result of, or compounded by, vaccination. These parents often describe distressing accounts of extremely rapid regression, from perfectly average developing children to children who begin to exhibit severe behavioral and physiological problems. Clinicians, researchers, and parents alike would agree that by the very definition of autism, a period of regression often accompanies the onset of autism, but the timing of vaccinations with autism, by some is simply interpreted as mere coincidence.

A vaccine is intended to help an individual's body establish immunity to a specified disease by creating antibodies, but on occasion it can cause an illness that is unrelated to the actual disease it is created for. Those who dispute the safety of vaccinations indicate their concerns are related to a particular ingredient, thimerosal, an ingredient used as a preservative since the 1930's. The preservatives are used in vaccines to prevent microbial growth and are added during the manufacturing process. "They are used in vaccines to prevent microbial growth in the event that the vaccine is accidentally contaminated, as might occur with repeated puncture of multi-dose vials" (Egan, 2004 section titled Thimerosal Reduction in Vaccines,¶1). Egan (2004) further noted that it is routine to add preservatives to multi-dose vials because when they did not contain preservatives in the past tragic consequences occurred.

Although the level of mercury within any individual vaccine is not harmful, the additive amount of mercury that is contained in the usual dosage of vaccines given during

one visit could allow an excessive amount of mercury, which exceeds government-recommended levels, to be ingested. As of 1999, both the FDA and the American Academy of Pediatrics (AAP) had determined that the typical amount of mercury injected into infants and toddlers via childhood immunizations has exceeded government safety guidelines on an individual (Halsey, 1999) and cumulative vaccine basis (Egan, 1999 in Bernard et al., 2001). Geier and Geier (2005) further noted that the levels of mercury children are exposed to not only exceed the Federal Safety Guidelines but that it also exceeds the United States Environmental Protection Agency's permissible hair mercury limit. showed that exposure to low doses of methyl mercury during the prenatal period was associated with minor neurodevelopmental abnormalities (Cox et al., 1989; Marsh et al., 1987; Redwood et al., 2001). And children are given an aggressive dosage of vaccines throughout their first year of life. Bernard et al. (2001) stated that "exposure to mercury can cause immune, sensory, neurological, motor and behavioral dysfunctions similar to traits defining or associated with autism" (p. 462). Bernard et al. (2001) notes the similarities between ASD and mercury poisoning. Bernard et al. (2001) noted that autism is perceived as a psychiatric disorder and that mercury poisoning, when undetected, is often initially diagnosed as a psychiatric disorder. Commonly occurring symptoms associated with mercury poisoning were noted by Bernard et al. (2001): (a) Extreme shyness, indifference to others, active avoidance of others, or a desire to be alone; (b) depression, lack of interest and mental confusion; (c) irritability, aggression, and tantrums in children and adults, (d) anxiety and fearfulness; and (e) emotional labiality. When Bernard et al. (2001) reviewed the diagnostic criteria for autism and compared it to symptomology associated with mercury poisoning there were several

similarities. They found similarities for impairments in speech/communication, physical movement, and sensory issues.

Additional concerns regarding this notion of vaccinations and their link to the cause of ASD is the claim that a dramatic increase in the number of children identified was seen in relation to the introduction of the multi-component MMR vaccine (Bernard, 2000; Shattock & Savery, 1997; Taylor et al., 1999).

> There is little evidence, even anecdotal evidence, that the older, single component vaccines, could result in such problems as autism. Reports of such problems appear after the introduction of the multi-component MMR vaccine (1988 in the UK)…If these reports are correct it would seem that it is the combination which is responsible for these problems…Given the fact that the Measles virus is known to be immunosuppressant, its inclusion in combination with other disease causing organisms is, in any case, inherently problematic" (Shattock & Savery, 1997, ¶15).

Additionally, as Bernard et al. (2001) noted:

> In studies conducted prior to 1970, autism prevalence was estimated, at 1 in 2000; in studies from 1970 to 1990 it averaged 1 in 1000.…In the early 1990's, the prevalence was found to be 1 in 500, and in 2000 the CDC found 1 in 150 affected in one community, which was consistent with reports from other areas in the country. In the late 1980's and early 1990's, two new thimerosal containing

vaccines, The HIB and Hepatitis B, were added to the recommended schedule (p. 466).

As a result of the controversy, the Food and Drug Administration (FDA) reviewed thimerosal-containing products. In 1999, the FDA discovered that "children could be exposed to an amount of mercury from vaccines that exceeded 1 of 3 existing federal safety thresholds" (Freed et al., 2002, p. 1153). In response to the findings related to safety guidelines being exceeded, the FDA requested that the vaccine manufacturers eliminate thimerosal wherever it was deemed possible. As of 2001, thimerosal in quantities sufficient to act as a preservative was reportedly removed from all vaccines included in the United States childhood immunization schedule, except for some influenza vaccines (FDA, 2003). However, there are still trace amounts of thimerosal present in some vaccines to ensure sterility that are added as a result of the manufacturing process. These trace amounts are reportedly so small that exposure is insignificant (Freed et al., 2003; Parker et al., 2004). Because most multi-dose vials are being replaced with single-dose vials excessive amounts of thimerosal as a preservative are no longer present in most recommended vaccines in the United States, for children younger than 7 (Egan, 2004; Parker et al., 2004). However, thimerosal-containing vaccines continue to be used throughout the world. Furthermore, Organizations such as the Immunization Safety Review Committee of the Institute of Medicine continue to refute any causal relationship between exposure to thimerosal and various neurodevelopmental disorders (Parker et al., 2004) and the World Heath Organization and several vaccine manufacturers continue to advocate for the use of thimerosal in pediatric vaccines (Geier & Geier, 2005).

Factors contributing to the variation in severity of autism spectrum disorders

In addition to researching etiology of ASD, of interest were other factors which may have contributed to the severity or level of symptomology among individuals. While the symptoms associated with ASD often occur with varied intensity it is not completely understood what attributes to these variations among individuals. As Rimland (1964) noted, it was of interest that in several cases of identical twins stricken with autism, the degree of affliction was not identical, suggesting that while genetic factors may predispose toward autism, post-conceptional factors could also be operative. Research is somewhat inconsistent due to the varied methodologies in defining and assessing severity as well as varied classification criteria used over the decades (Glasson et al., 2004). It was highly evident upon review of the literature that the concept of severity has not been well defined; as interpretations varied widely among researchers and clinicians, when it was even recognized. Defining severity, as it pertains to ASD, can include assessment of adaptive behavioral functioning, standard scores from cognitive and/or diagnostic rating scales, or by the number of symptoms exhibited. For the purpose of this study, severity was defined by standard scores on adaptive functioning and specific diagnostic rating scales and referred to as the child's level of autistic symptomology and level of adaptive functioning.

Adaptive skills are involved in coping with day to day demands within the environment and are of particular importance for autistic individuals as they are means of determining the level of supervision needed (Liss, Harel, Fein, et al, 2001). Most children with ASD have some degree of impairment in adaptive functioning (Liss et al., 2001). As well, the degree of diagnostic criteria/symptomology exhibited can be helpful in

determining individual strengths and weaknesses as they relate to adaptive skills. Information related to adaptive functioning and symptomology along with other prognostic data can be helpful in determining the severity of the disorder. But little is known on what variables correlate specifically with adaptive functioning and diagnostic criteria in predicting the severity of ASD.

The literature is significantly lacking in studies that specifically investigate possible predictors of severity (as defined by this study) for ASD. The few studies that do exist did not address the specific question of this study and employed a variety of methodologies. In addition it is noted that the concept of severity was not consistently measured by standardized instruments. Lisset al. (2001) investigated correlates and predictors of adaptive functioning as measured by the Vineland Adaptive Behavior Scales in children with high and low functioning autism. They found that adaptive behavior was strongly correlated with autistic symptomology. Dawson, Meltzoff, Osterling et al. (1998) studied autistic children's performances on neuropsychological task as a predictor of severity. Severity was defined by the frequency of behavioral symptoms exhibited on a structured task. Dawson et al. (1998) found that for children with autism, the severity of autistic symptoms was strongly and consistently correlated with their performance on a task requiring use of the medial temporal lobe. Examination of autistic children has also shown that the severity of autistic disorders correlates with the amount of testosterone present in the amniotic fluid (Geier & Geier, 2004), however the study did not specify how severity was defined and/or measured.

It is noted that the literature that follows makes little reference to severity of ASD, rather the investigators reported on increased occurrences of pre-post natal factors found

among autistic groups. This literature has been included because the variables studied were similar to those investigated in the current study, however, the current study investigated their impact on severity (as defined above) rather than their association with causation. Although not assessing severity, additional researchers found common factors among the medical history of autistic patients. Field, Garland, and Williams (2003) indicated that feeding problems were commonly found among children with ASD as well as other developmental disabilities. Semple (2004) found that prenatal exposure to teratogens/toxins, perinatal difficulties, febrile seizures, severe reactions to medications and/or vaccinations, and a positive family history for autism were reported with greater occurrence among autistic children. Gillberg and Cederlund (2005) found that approximately 50% of all boys with Asperger have had a paternal family history for ASD. A study by Lock, Shapiro, Ross et al. (1986) examined the relationship between the age at which a developmental disability presents itself and factors such as medical illness, motor skills, language skills, and behavioral disturbances. They found that information related to motor, language, and behavior was a better predictor for age of onset than severity of the disorder. Additional researchers have reported significantly higher incidences of pre and post natal difficulties among autistic children. Most commonly investigated factors found to occur with greater incidence included; sleep disturbances (Clements, Wing, & Dunn, 1986; Patzold, Richdale, & Tonge, 1998; Polimeni, Richdale, & Francis, 2005; Rapin, 1991), obstetric complications (Burd, Severud, & Kerbeshian, 1999; Glasson et al., 2004; Park & Bolton, 2001; Wilkerson, Volpe, Dean, et al., 2002), low birth weight (Bhutta, 2002; Indredavik, Vik, Heyerdahl, et al., 2004; Knobloch & Passamanick, 1975; Finnegan & Quarrington, 1979; McCormick, 1997), prenatal

exposure to drugs/prescriptive medications (Deykin & MacMahon, 1980; Walker, Rosenberg, & Balaban-Gil, 1999), maternal age (Tsai & Stewart, 1983) and maternal smoking (Hultman, 2002).

While Patzold et al. (1998), Clements et al. (1986) and Rapin (1991) found that children with autistic disorders exhibited clinically significant levels and patterns of disruptive sleep; Polimeni et al. (2005) found that those with Asperger's exhibited even greater symptoms and types of sleep disturbance than children with autism. Park and Bolton (2001) found that although autistic children had an increased risk of obstetric complications there was no correlation between obstetric adversities and the severity of the disorder. Finegan and Quarrington (1979) examined original medical records of autistic individuals and found that breech presentation during labor, low birth weight, low Apgar scores, and respiratory distress were more frequent among autistic children. Knobloch and Passamanick (1975) found an increased incidence of low birth weight and toxemia/bleeding in the birth histories of autistic children. Wilkerson et al. (2002) investigated the association of prenatal complications and autism by having parents of autistic and non-autistic children complete the Maternal Perinatal Scale (MPS). They found that factors such as prescription drugs used during pregnancy, length of labor, viral infection, abnormal presentation at delivery, low birth weight, urinary infection, high temperature and maternal depression occurred with greater frequency among the autistic group. Although sparse, findings have suggested maternal smoking (Hultman, et al., 2002) and maternal age (Tsai & Stewart, 1983) as possible risk factors for autism.

Nearly all children in the United States are immunized, yet only a small proportion actually develop autism. The etiology of autism has not yet been linked to any

one cause. There are several hypotheses proposed for the etiology of autism spectrum disorders that have been investigated throughout the last 60 years. While a genetic link has been established by research it is likely that both genetic and environmental factors attribute to its cause. Concerns dating back to the early 1960's focused on questions related to an infectious etiology as one possible cause for these disorders. This questionable link has once again surfaced as a result of both an increase in prevalence of autism spectrum disorders and reported causal links of autism to immunization administration. In addition to the proposed link of vaccination to the cause of ASD, is the question of additional pre-and postnatal factors that attribute to the variation of symptomology and adaptive functioning and therefore severity among autistic children. Given the variability in ASD, even in groups of children who evidence the same disorder, it seems likely that environmental factors play an important role in the development of these disorders as well as influence severity.

This study investigated whether exposure to various environmental events during pre-, peri-, or postnatal periods predict the onset of autism and severity of autism spectrum disorders. Specifically, it investigated whether parent risk characteristics (a family history positive for psychological and learning disorders, length of gestational period, and maternal illness during pregnancy) and the presence of child risk characteristics (e.g., physical sensitivity, impaired social interaction, developmental regression and stereotypical/unusual behaviors) to a marked degree during the first five years of life predict an individuals current level of autism symptomology and adaptive functioning.

CHAPTER III

METHODOLOGY

Overview, Statement of Questions and Hypotheses

Research related to the etiology of ASD indicates both genetic and environmental components may be important causal factors. However, predicting the importance of each of these factors has been challenging for researchers. Nevertheless, it is likely that autism has a multifactor origin. There is evidence indicating pre- and postnatal exposure factors, genetic predisposition, and environmental catalyst, are in part responsible for the onset and severity of the disorder. This study investigated the relationship of multi-valent and thimerosal-containing childhood vaccinations (particularly MMR), the child's state of health at the time of immunization and the onset of ASD. The relationship of various environmental events during pre-, peri-, or postnatal periods with the levels of current autism symptomology and adaptive functioning was also examined. The following questions and hypotheses were proposed:

Question 1: Does exposure to thimerosal-containing vaccines during scheduled vaccination(s) predict the onset of an autism spectrum disorder?

Hypothesis 1: The exposure to thimerosal-containing vaccines during scheduled vaccination(s) does predict the onset of an autism spectrum disorder.

Question 2: Does exposure to a multi-valent and thimerosal-containing vaccination, particularly MMR, predict the onset of an autism spectrum disorder?

Hypothesis 2: The exposure to a multi-valent and thimerosal-containing vaccination, particularly MMR, does predict the onset of an autism spectrum disorder.

Question 3: Does the child's state of health at the time of vaccination predict the onset of an autism spectrum disorder?

Hypothesis 3: The child's state of health at the time of vaccination does predict the onset of an autism spectrum disorder.

Question 4: Do child risk factor characteristics (physical sensitivity, impaired social interaction, developmental regression, and stereotyped or unusual behaviors) displayed to a marked degree during the first five years of life predict current levels of autism symptomology?

Hypothesis 4: Child risk factor characteristics (physical sensitivity, impaired social interaction, developmental regression, and stereotyped or unusual behaviors) displayed to a marked degree during the first five years of life do predict current levels of autism symptomology.

Question 5: Do child risk factor characteristics (physical sensitivity, impaired social interaction, developmental regression, and stereotyped or unusual behaviors) displayed to a marked degree during the first five years of life predict current levels of adaptive functioning in children with ASD?

Hypothesis 5: Child risk factor characteristics (physical sensitivity, impaired social interaction, developmental regression, and stereotyped or unusual behaviors) displayed to a marked degree during the first five years of life do predict current levels of adaptive functioning in children with ASD.

Question 6: Do parent risk characteristics (maternal or paternal family history of psychological disorder or learning problems, length of gestational period, and maternal illness during pregnancy) predict current levels of autism symptomology?

Hypothesis 6: Parent risk characteristics (maternal or paternal family history of psychological disorder or learning problems, length of gestational period, and maternal illness during pregnancy) do predict current levels of autism symptomology.

Question 7: Do parent risk characteristics (maternal or paternal family history of psychological disorder or learning problems, length of

gestational period, and maternal illness during pregnancy) predict current levels of adaptive functioning?

Hypothesis 7: Parent risk characteristics (maternal or paternal family history of psychological disorder or learning problems, length of gestational period, and maternal illness during pregnancy) do predict current levels adaptive functioning.

Participants

Participants were children diagnosed with an autism spectrum disorder (autism, Asperger's, or pervasive developmental disorder) who were born after 1971. Participants born prior to 1971 were excluded from the study because the multi-component MMR immunization was not utilized in the United States until after this time. Participants ranged from 2 to 23 years of age, with the average age being 9.17 years (4.6 SD). Information regarding developmental, medical, family, and diagnostic history, as well as details of immunizations was obtained. Assessment information related to adaptive behavior functioning and the child's autism spectrum disorder was also obtained to determine the level of the autistic disorder symptomology and adaptive behavior functoining. Participants were considered to have ASD if the parent reported the child had been diagnosed through a multidisciplinary evaluation within the public school setting or by a licensed psychologist. Demographic data including age, gender, education, and race of both the participant and his/her parents were requested. Demographic data are summarized in Table 5.

Independent Variables

Multi-Valent and Thimerosal-Containing Immunizations

The receipt of multi-valent and thimerosal-containing immunizations was the first independent variable. All immunizations were included as thimerosal is used as a preservative in these vaccines. Models were created with each set of immunizations received at the proposed age comprising a block. Five blocks were created; Block 1 = Immunizations received at 2 months: DTP, HepB, Polio, Influenza; Block 2 = Immunizations received at 4 months: DTP, HepB, Polio, Influenza; Block 3 = Immunizations received at 6 months: DTP, Influenza; Block 4 = Immunizations received at 12-15 months: DTP, HepB, Polio, MMR, Varicella; and Block 5 = Immunizations received at 4-6 years: DTP, Polio, MMR. Receipt of vaccination was determined from immunization history requested on the developmental and medical history form questionnaire.

Measles-Mumps-Rubella Immunization

The receipt of the multi-valent and thimerosal-containing MMR vaccine was the second independent variable. This immunization is received by children between the ages of 12-15 months and again between 4-6 years of age. Receipt of the MMR immunization was determined from immunization history requested on the developmental and medical history form questionnaire.

State of Health at the time of Immunization

The child's state of health at the time of vaccination was the third independent variable. In addition to requesting information related to immunization history, parents were asked to indicate whether their child was sick or healthy at the time of

immunization. Sick at the time of immunization was defined as the child experiencing a compromised state of health (e.g., suffering from a cold, virus, infection, or fever). Models were created for state of health (sick vs. healthy) with each set of immunizations received at the proposed age comprising a block. Five blocks were created; Block 1 = Sick at the time of immunizations received at 2 months: DTP, HepB, Polio, Influenza; Block 2 = Sick at the time of immunizations received at 4 months: DTP, HepB, Polio, Influenza; Block 3 = Sick at the time of immunizations received at 6 months: DTP, Influenza; Block 4 = Sick at the time of immunizations received at 12-15 months: DTP, HepB, Polio, MMR, Varicella; Block 5 = Sick at the time of immunizations received at 4-6 years: DTP, Polio, MMR. State of health at the time of immunization was determined from immunization history requested on the developmental and medical history form questionnaire.

Child Risk Characteristics

Independent variables related to child risk characteristics were also examined in relation to current levels of ASD symptomology and adaptive functioning. These included the presence of a sibling diagnosed with ASD or other medical or psychological conditions, achievement of developmental milestones (e.g., sitting, rolling, crawling, walking, speaking, dressing independently), and experience of various factors to a marked degree during the first five years of life (e.g., high fevers, poisoning, illness, behavioral oddities). A detailed questionnaire was utilized to obtain information related to these characteristics. A copy of the developmental and medical history form is included in the appendix. Correlations among each of the dependent variable rating scales standard scores and the independent variables were calculated to determine which of the

independent variables were most related to the dependent variables. Items were chosen based on theoretical framework and their significance at the .05 and .01 levels. This exploratory technique was used to reduce the original number of variables; 1) physical sensitivity, 2) impaired social interaction, 3) developmental regression, and 4) stereotypical/unusual behaviors. Physical sensitivity was comprised of items related to the child's difficulty being calmed, dislike of being held, and general sensitivity. Impaired social interaction was comprised of items relating to poor eye contact, starring, and difficulty interacting with others. Developmental regression was comprised of items endorsing or refuting a slowness to speak and roll over, and an observable loss of developmental skills. Stereotypical/unusual behaviors was comprised of questions related to a child's display of rocking, toe walking, hand flapping, clumsiness and unusual or odd behaviors.

Parent Risk Characteristics

Parent risk characteristics were also examined in relation to current levels of ASD symptomology and adaptive functioning. These included the presence of a family history positive for various medical, psychological, and learning problems, and exposure to various factors during pregnancy (e.g., drugs, prescription or over the counter medications, alcohol, tobacco, illness, trauma, toxic chemicals). A detailed questionnaire was utilized to obtain information regarding medical and birth history. Correlation was used to examine and reduce the original number of variables into three categories, 1) parent history of psychological disorders/learning problems, 2) length of gestation, and 3) illness during pregnancy. Parent's psychological history was comprised of items related to the family medical history of both parents. Parents of the participants were asked to

report whether there was a positive family history for themselves or someone within their family for various disorders. The following disorders were included in this variable: anxiety, depression, learning disability, and speech-language disorder. Length of gestation and illness during pregnancy were comprised from single items/variables. Length of gestation was reported in weeks with the average gestation established by the medical community as 36 weeks.

Instrumentation

Dependent Variables

Age of Onset

The first dependent variable in this study was the child's age when autism spectrum characteristics/symptoms were first noted by parents. This variable was referred to as the onset of autism. For the purpose of this study, an individual was considered to be autistic if s/he met criteria for an autism spectrum disorder (autism, Asperger's, or PDD) as specified by the DSM-IV.

ASD Symptomology

The second dependent variable in this study was the level of the individuals' autistic symptomology. Level of symptomology was defined by an individuals overall standard score obtained on an autism rating scale (Gilliam Autism Rating Scale (GARS) or Asperger's Syndrome Disorder Scale (ASDS)).

The GARS is a forty-two item standardized behavioral rating scale developed to identify and diagnose persons who are autistic. It is used to distinguish children with autism in the low to moderate range from children with autism in the moderate to high range. The GARS assessed the child from the parents' point of view. The forty-two

GARS items are divided into three subtests (Stereotyped Behaviors, Communication, and Social Interaction) that describe specific, observable, and measurable behaviors. The items were rated using a frequency based rating of 0 to3 (0 = never observed, 1 = seldom observed, 2 = sometimes observed, and 3 = frequently observed). Fourteen additional items are included for parents to contribute data about their child's development during the first three years of life, however, the completion of these items was not required as the subject matter was covered within the developmental and medical history form.

The GARS was normed on a sample of 100 individuals from 21 states, with regard for gender, age, ethnicity, and geographic location. Internal consistency for the subtests Stereotyped Behaviors, Social Interaction and Autism Quotient yielded coefficient alphas of .90 or above, while the Communication subtest alpha was .89 and the Developmental Disturbance subtest alpha was .88. The test-retest reliability was found to be beyond the .01 level of significance for all subtest. The parent-parent interrater reliability subtests coefficients were found to be the weakest of all examined but were still significant ($p < .01$). The parent-parent interrater reliability was found to be .83 for the Autism Quotient.

Content validity was obtained for the following scales: Stereotyped Behaviors .61, Communication .65, Social Interaction .69, and Developmental Disturbances .61. Criterion-related validity was also found to discriminate the autistic from nonautistic sample at a 90% accuracy rate.

The ASDS is a fifty item standardized behavioral rating scale developed to identify and diagnose persons with Asperger's syndrome. It is used to distinguish children with Asperger's in the low to moderate range from children with Asperger's in

the moderate to high range. The ASDS assesses the child from the parents' point of view. The fifty GARS items are divided into five subtests (Language, Social, Maladaptive, Cognitive, and Sensorimotor) that describe specific, observable, and measurable behaviors. The items are rated using a rating of 0 or 1 (0 = never observed and 1 = observed).

The ASDS was normed on a sample of 100 individuals from 21 states, with regard for gender, age, ethnicity, and geographic location. Internal consistency for the subtests were lower than the alpha for the Asperger Syndrome Quotient (ASQ) (.83). The parent-parent interrater reliability was found to be 96.36 ($p < .01$) for the ASQ.

Content validity was obtained for the following scales: Language .55, Social .59, Maladaptive .57, Cognitive .47, and Sensorimotor .67. Criterion-related validity was also found to discriminate the Asperger from non-Asperger sample at a 85% accuracy rate.

Adaptive Behavioral Functioning

The third dependent variable in this study was level of the autistic individuals' adaptive functioning. Level of adaptive functioning was defined by an individuals standard score obtained on an adaptive behavior scale (Scales of Independent Behavior - Revised: Short Form (SIB-R)).

The SIB-R Short Form is a forty item standardized adaptive behavior rating scale developed to assess independent living skills. The adaptive behavior scale was used to assess information related to the following areas: motor skills, social interaction and communication skills, personal living skills, and community living skills.

Norming data for the SIB-R was obtained from 2,182 individuals from 15 states, with regard for gender, age, ethnicity, occupational status and level, geographic location,

and type of community. Reliability for the SIB-R was determined using the split-half procedure and corrected by the Spearman-Brown formula (Bruininks, Woodcock, Weatherman et al., 1996). Internal consistency for the SIB-R Short Form yielded a coefficient of .76. The test-retest reliability coefficient for the SIB-R Short Form was .97. The interrater reliability among parents was found to be .93. Construct validity was obtained by comparison of the SIB and SIB-R using Rasch item calibration. The SIB-R Short Form yielded a correlation of .99.

Developmental and Medical History Form

The developmental and medical history form was developed to obtain demographic information, family medical history, and information related to pregnancy/birth, developmental achievement, and immunizations received. The questionnaire was a compilation of existing clinical intake forms previously used by the author. Items included were based on a review of the current literature as well as interest of new variables to be examined in the current study.

Procedure

Participants were solicited through special education programs in Oklahoma and parent support groups from across the United States. The directors of special education programs and autism support groups/organizations were contacted by phone and/or e-mail and asked to disseminate information to the parents/members related to participation requirements of the study. A cover letter was sent via mail or e-mail to directors/group leaders explaining the study which was then disseminated to potential participants. Demographic data along with detailed developmental, medical, diagnostic, and immunization history were obtained through questionnaire format that was sent and

returned via mail. A child was considered for participation in the study if s/he had received the majority of immunizations according to the recommended U.S. schedule. It is noted that some participants did not receive subsequent immunizations after 15 months of age (particularly the MMR shot) after the onset of autism was noted by parents. In regard to the questions related to family medical history and exposure to medication and toxins during pregnancy, not all known diagnoses and medications could be included, therefore space was provided for respondents to provide information. Information not readily available from the participant that needed to be obtained from school/medical records was received after a medical release of information form was signed. Each participant received a packet containing an informed consent sheet, release of information form, the Gilliam Autism Rating Scale (GARS) or Asperger Syndrome Diagnostic Scale (ASDS), an adaptive behavior rating scale (SIB-R Short Form), and a detailed developmental and medical history questionnaire requesting the above-mentioned information. Participants were guaranteed privacy and anonymity regarding the information relayed for the purpose of the study. Participants were not identified by name. Identification numbers were used for demographic information, the developmental health history form, and the rating scales. All data was secured in a locked file cabinet. The autism and Asperger's rating scales were estimated to take approximately 10-15 minutes to complete while the developmental and medical history questionnaire was estimated to take approximately 20 minutes to complete. For individuals who had not completed a GARS or ASDS for their child within a 12-month period one was provided for their completion.

CHAPTER IV

RESULTS

This study examined the relationship between various environmental events during pre-, peri-, or postnatal periods and the onset and severity of autism spectrum disorders. The onset of autism, the severity of symptomology, and the level of adaptive functioning were used as the dependent variables while the receiving of the MMR immunization, the individual's state of health at the time of vaccination, and various factors related to medical, family, and developmental history were used as independent variables. The Statistical Package for Social Sciences version 12.0 (SPSS, 2003) was used to conduct statistical analysis of the data.

Both continuous and categorical variables were included in the study. Dummy coding was used to code the categorical data obtained from the developmental and medical history form, indicating the presence or absence of each variable (e.g., 1= yes, 2= no). Descriptive statistics were calculated to describe the participants and are summarized in Table 5. Descriptive statistics were also calculated for the dependent variables and are summarized in Table 6. Correlations among each of the dependent variable rating scales standard scores and the independent variables were calculated to determine which of the independent variables were most related to the dependent variables. Items were chosen based on theoretical framework and their significance at the .05 and .01 levels. The component variables of parent and child risk characteristics were developed. This exploratory technique was used because there were too many independent variables to

select for regression models and the literature did not allow for strong a priori hypotheses to be developed with specific independent variables. Simple linear regression equations were calculated to analyze the relation among independent variables and the dependent variables (onset of ASD, Level of ASD symptomology, Level of Adaptive Functioning.)

Characteristics of the 114 participants included in the study are summarized in Table 5. A proportionately larger amount of the participants were male and Caucasian rather than female and other ethnicities. The sample is representative of what would be found in the general population. Approximately 60% of the individuals included in the study were between 4 and 9 years of age with the average age being 9.17 years(4.6 SD). Slightly more than half (55.3%) of the participants had a diagnosis of autism versus Asperger's (28.9%) or Pervasive Developmental Disorder (15.8%). Over half (51.3%) of the participants included in the study experienced the onset of autism and received a diagnosis by the age of three (47 months). Parents of participants diagnosed with PDD were given the option of which autism rating scale was more appropriate for their child. The majority (15 of 18) completed the GARS and are therefore categorized with the autism group.

Table 5

Characteristics of Participants

Characteristic	n	Percent
Gender		
Male	94	82.46
Female	20	17.54
Age in months		
1-47 (1-3 years)	7	6.14
48-83 (4-6 years)	38	33.33
84-119 (7-9 years)	30	26.32
120-155 (10-12 years)	17	14.91
155-179 (13-15 years)	9	7.89
180-231 (16-18 years)	9	7.89
$\geq$ 232 ($\geq$ 19 years)	4	3.51
Race		
African American	2	1.77
Caucasian	101	89.38
American Indian	3	2.65
Hispanic	1	0.88
Asian	1	0.88
Other	5	4.42
Diagnosis		
Autism	63	55.26
Asperger's	33	28.95
PDD	18	15.79
Onset of Symptoms/Age of Parental Concerns Noted: in months		
1-24 (1-2 years)	76	68.47
25-48 (3-4 years)	26	23.42
60-96 (5-8 years)	9	8.11
Age at Diagnosis: in months		
1-47 (1-3 years)	58	51.33
48-83 (4-6 years)	31	27.43
84-119 (7-9 years)	11	9.73
120-155 (10-12 years)	11	9.73
155-179 (13-15 years)	1	0.88
180-231 (16-18 years)	1	0.88
$\leq$ 232 ($\geq$ 19 years)	0	

Mean Age of Onset = 24.16 months Standard Deviation = 18.38 months
Mean Age of Diagnosis = 56.95 months Standard Deviation = 37.81 months

Table 6

Means and Standard Deviations of Dependent Variables

Dependent Variable	Mean	SD
Age of Onset (in months)	24.16	18.38
Level of Symptomology (GARS SS/Autism Quotient)	92.20	19.84
Level of Adaptive Functioning (SIB-R SS/Broad Indep)	54.37	34.00

Onset of Autism Spectrum Disorder

The mean age at which parents initially noted concerns for their child's development and the onset of an autism spectrum disorder was approximately 24 months (2 years) of age, whereas the mean age at which a diagnosis was determined was 56 months (4.6 years) of age. Of the 114 participants, a high percentage of them were administered the recommended vaccinations between 2 and 15 months of age, but a significant decrease was noted for the number of participants who received immunizations at 4-6 years of age. Data on influenza was the exception, as some states have different policies regarding the requirement of this particular immunization. Participant's immunization participation is summarized in Table 7.

Table 7

Immunizations (U.S. Schedule) Received by Participants

Immunization	n	Percent
Diptheria/Tetanus/Pertusis (DTP)		
2 months	113	99.12
4 months	112	98.25
6 months	109	95.61
12-15 months	106	92.98
4-6 years	84	73.68
Hepatitis B		
2 months	101	88.60
4 months	101	88.60
12-15 months	99	86.84
Polio		
2 months	110	96.49
4 months	109	95.61
12-15 months	107	93.86
4-6 years	88	77.19
Influenza		
2 months	79	69.30
4 months	78	68.42
6 months	77	67.54
Measles/Mumps/Rubella (MMR)		
12-15 months	110	96.49
4-6 years	79	69.30
Vericella		
12-15 months	96	84.21

A series of simple linear regression analyses were completed to assess the relation between childhood vaccinations, particularly the MMR vaccination, and the participants state of health at the time of vaccination with the onset of an autism spectrum disorder. A p-value of 0.05 was retained for statistical significance. The single-variable regression models confirmed no association between MMR vaccinations and the onset of an autism spectrum disorder. However, one variable did approach significance when analyzing its effect on the onset of autism; MMR vaccination administered at 4 years of age yielded an overall R of .182, F (1,106) = 3.647, p = .059. These findings are summarized in Table 8. Table 8 displays the R, R^2, adjusted R^2, F, degrees of freedom, and p value for the regression equations. It is noted that analysis was not possible for the independent variable Diptheria/Tetanus/Pertusis at 2 months of age (DPT-2months) as there was no variance. Variables were entered as blocks with each set of immunizations received at the proposed age comprising a block (e.g., Block 1 = Immunizations received at 2 months: DTP, HepB, Polio, Influenza; Block 2 = Immunizations received at 4 months: DTP, HepB, Polio, Influenza; Block 3 = Immunizations received at 6 months: DTP, Influenza; Block 4 = Immunizations received at 12-15 months: DTP, HepB, Polio, MMR, Varicella; and Block 5 = Immunizations received at 4-6 years: DTP, Polio, MMR). No significant associations were found among each of the blocks and the onset of ASD. These regressions are summarized in Table 9.

Table 8

Regressions Predicting the Onset of ASD and MMR Immunization

	R	R^2	Adjusted R^2	F	*df*	P
Onset of ASD						
Predictor						
Measles/Mump/Rubella (MMR)						
12-15 months	.030	.001	-.008	.099	1,107	.754
Onset of ASD						
Predictor						
Measles/Mump/Rubella (MMR)						
4-6 years	.182	.033	.024	3.647	1,106	.059*

Note: * approached significance

Table 9

Regressions Predicting Onset of ASD and Thimerosal-Containing and Multi-Valent Immunizations

	R	R^2	Adjusted R^2	F	*df*	P
Onset of ASD						
Predictors						
Immunizations Received						
Block 1: 2 months	.206	.043	.014	1.483	3,100	.268
Block 2: 4 months	.227	.051	.013	1.352	4,100	.256
Block 3: 6 months	.085	.007	-.012	.376	2,104	.687
Block 4: 12-15 months	.168	.028	-.022	.566	5,98	.726
Block 5: 4-6 years	.231	.053	.026	1.957	3,104	.125

Note: Block 1 = Immunizations received at 2 months: DTP, HepB, Polio, Influenza; Block 2 = Immunizations received at 4 months: DTP, HepB, Polio, Influenza; Block 3 = Immunizations received at 6 months: DTP, Influenza; Block 4 = Immunizations received at 12-15 months: DTP, HepB, Polio, MMR, Varicella; and Block 5 = Immunizations received at 4-6 years: DTP, Polio, MMR

The participant's state of health at the time of vaccination and the onset of an autism spectrum disorder were also examined. Variables were entered as blocks with state of health (sick) and each set of immunizations received at the proposed age

comprising a block (e.g., Block 1 = Sick at the time of immunizations received at 2 months: DTP, HepB, Polio, Influenza). Table 10 summarizes the percentage of participants who were sick at the time of immunization. No significant associations were found among each of the blocks and the onset of ASD. These regressions are summarized in Table 11.

Table 10

Percentage of Participants who were Sick at the time of Immunization

Variable	n	Percent
Sick at the time of Immunization		
2 Months		
DTP	111	97.36
HepB	100	87.72
Polio	110	96.49
Influenza	77	67.54
4 Months		
DTP	110	96.49
HepB	100	87.72
Polio	109	95.61
Influenza	77	67.54
6 Months		
DTP	108	94.73
Influenza	75	65.78
12-15 Months		
DTP	104	91.22
HepB	98	85.96
Polio	107	93.86
MMR	108	94.73
Vericella	94	82.45
4-6 Years		
DTP	83	72.80
Polio	88	77.19
MMR	77	67.54

Table 11

Regressions Predicting Onset of ASD and State of Health at the time of Immunization

	R	R^2	Adjusted R^2	F	*df*	P
Onset of ASD						
Predictors						
Immunizations Received						
Block 1: 2 months (sick)	.102	.010	-.018	.370	2,70	.692
Block 2: 4 months (sick)	.175	.030	.03	1.115	2,71	.333
Block 3: 6 months (sick)	.038	.001	-.012	.102	2,72	.750
Block 4: 12-15 months (sick)	.122	.015	-.046	.244	5,81	.942
Block 5: 4-6 years (sick)	.038	.001	-.013	.09	1,68	.757

Note: Block 1 = Sick at the time of immunizations received at 2 months: DTP, HepB, Polio, Influenza; Block 2 = Sick at the time of immunizations received at 4 months: DTP, HepB, Polio, Influenza; Block 3 = Sick at the time of immunizations received at 6 months: DTP, Influenza; Block 4 = Sick at the time of immunizations received at 12-15 months: DTP, HepB, Polio, MMR, Varicella; Block 5 = Sick at the time of immunizations received at 4-6 years: DTP, Polio, MMR.

Level of Current ASD Symptomology and Adaptive Behavioral Functioning

Independent variables related to risk characteristics displayed by a child within the first five years of life were analyzed using linear multiple regression to determine their relationship to the participant's current level of ASD symptomology and adaptive functioning. Correlations among each of the rating scales standard scores and the independent variables were calculated in order to reduce the original number of variables analyzed and create the following component variables; physical sensitivity, impaired social interaction, developmental regression, and stereotyped/unusual behaviors.

Parent risk characteristics were also analyzed using linear multiple regression to determine their relationship to the participant's current level of autistic symptomology and adaptive functioning. Correlations among each of the rating scales standard scores and the independent variables were calculated in order to reduce the original number of

variables analyzed and create the following component variables; family history positive for psychological and learning problems, length of gestation, and maternal illness during pregnancy.

Tables 12, 13 and 14 show the correlations of the independent variables with each of the rating scales. Only participants with a diagnosis of Autism or PDD who completed the GARS and/or the SIB-R were included in the final analysis related to severity. Those diagnosed with Asperger's and who completed the ASDS were excluded because of the small sample size. Although participants who completed the ASDS were excluded, the variables parent history of psychological disorders/learning problems and physical sensitivity displayed by the child were found to correlate with the ASDS standard score at the .05 level.

Table 12

Correlations among the Independent Variables and the GARS Autism Quotient Standard Score

Independent Variable	GARS Autism Quotient
Parent Risk Characteristics	
Psychological Disorders/Learning Problems	.259*
Length of Gestation	-.305**
Illness during Pregnancy	-.030
Child Risk Characteristics	
Physical Sensitivity	.304**
Impaired Social Interaction	.136
Developmental Regression	.156
Stereotyped/Unusual Behaviors	.420**

Note: *Significant at the p=.05 level, ** Significant at the p=.01 level.,

Table 13

Correlations among the Independent Variables and the SIB-R Broad Independence Standard Score

Independent Variable	SIB-R Broad Independence
Parent Risk Characteristics	
Psychological Disorders/Learning Problems	.144
Length of Gestation	.072
Illness during Pregnancy	-.004
Child Risk Characteristics	
Physical Sensitivity	-.061
Impaired Social Interaction	-.292**
Developmental Regression	-.319**
Stereotyped/Unusual Behaviors	-.196*

Note: *Significant at the p=.05 level, ** Significant at the p=.01 level.,

Table 14

Correlations among the Independent Variables and the ASDS Asperger's Syndrome Quotient Standard Score

Independent Variable	ASDS Asperger's Syndrome Quotient
Parent Risk Characteristics	
Psychological Disorders/Learning Problems	.394*
Length of Gestation	.005
Illness during Pregnancy	.055
Child Risk Characteristics	
Physical Sensitivity	.376*
Impaired Social Interaction	.007
Developmental Regression	-.076
Stereotyped/Unusual Behaviors	-.018

Note: *Significant at the p=.05 level, ** Significant at the p=.01 level.,

Current Level of ASD Symptomology as Assessed by the GARS

Parent Risk Characteristics

Parent risk characteristics (presence of a psychological or learning disorder within the family history, length of gestation, and illness during pregnancy) and the level of autistic symptomology were examined. All parent characteristic variables were entered into the equation and referred to as block 1. A significant association was found for parent risk characteristics and current level of ASD symptomology. These regressions are summarized in Table 15.

In block 1 the variable psychological or learning disorder within the parent's family history accounted for a large portion of the variance. The zero-order correlation value for the variable is .263. The variable (Psychological/Learning Disorders) in the regression accounts for 26.3% of the overall variance in the model The variable related to gestation also accounted for a significant amount of variance. The zero-order correlation for length of gestation is -.305, indicating it accounts for 30.5% of the overall variance in the model. The variable illness during pregnancy accounted for less than one percent.

Table 15

Regression Predicting Current Level of ASD Symptomology and Parent Risk Characteristics

	R	R^2	Adjusted R^2	F	*df*	P
Level of ASD Symptomology (GARS) Predictors						
Block 1: Parent Char.	.402	.161	.126	4.553	3,71	.006

Note: Parent Char. = Parent Characteristics (Psychological and/or Learning Problems, Length of Gestation, Illness during Pregnancy).

Child Risk Characteristics

Child risk characteristics (physical sensitivity, impaired social interaction, developmental regression, and stereotypical/unusual behaviors) and the level of autistic symptomology were examined. All child characteristic variables were entered into the model (block 2). A significant association was found for child characteristics and current level of ASD symptomology. These regressions are summarized in Table 16.

In block 2 the variables physical sensitivity and stereotypical/unusual behaviors each accounted for a large portion of the variance. The zero-order correlation value for the variable physical sensitivity is .304 while the zero-order correlation value for stereotypical/unusual behavior is .420. These two variables in the regression collectively account for approximately 72% of the overall variance in the model The variables impaired social interaction and developmental regression account for 13% and 15 % of the overall variance in the model.

Table 16

Regression Predicting Current Level of ASD Symptomology and Child Risk Characteristics

	R	R^2	Adjusted R^2	F	*df*	P
Level of ASD Symptomology (GARS) Predictors						
Block 2: Child Char.	.453	.205	.162	4.779	4,74	.002

Note: Child Char. = Child Characteristics (Physical Sensitivity, Impaired Social Interaction, Developmental Regression, Stereotypical/unusual behaviors).

Parent and Child Characteristics

A statistically significant relationship was also noted among the dependent variable, current level of symptomology as assessed by the GARS, and all seven independent variables (Psychological/Learning Disorders, Length of Gestation, Physical Sensitivity, Impaired Social Interaction, Developmental Regression, and Stereotypical/Unusual Behavior), yielding an overall R of .555, F (7, 67) = 4.256, $p < .01$. This model was referred to as block 3. The presence of both child and parent risk characteristics within a participant's history accounted for a significant amount of variance in the current level of ASD symptomology. The R^2 value for the model is .308. The independent variables in the regression collectively account for 30.8% of the variance in the dependent variable. Examination of the zero-order correlations indicated each of the following variables attributed significantly to the overall variance of the model: Psychological/Learning Disorder = 26.3%, Physical Sensitivity = 29.6%, Length of Gestation = 30.5%, and Stereotypical/Unusual Behaviors = 44.4%. Table 17 summarizes the regression.

Table 17

Regression Predicting Current Level of ASD Symptomology and the Presence of Both Parent and Child Risk Characteristics

	R	R^2	Adjusted R^2	F	*df*	P
Level of ASD Symptomology (GARS)						
Predictors						
Block 3: Parent/Child Char.	.555	.308	.235	4.256	7,67	.001

Note: Parent/ Child Char. = Parent and Child Characteristics (Psychological and/or Learning Problems, Length of Gestation, Illness during Pregnancy, Physical Sensitivity, Impaired Social Interaction, Developmental Regression, Stereotypical/unusual behaviors).

Current Level of Adaptive Functioning for Individuals with ASD as Assessed by the SIB-R

Parent Risk Characteristics

No statistically significant relationship among current level of adaptive functioning, as assessed by the SIB-R, was found for the predictor variables related to parent characteristics (block 1). Table 18 shows the regression.

Table 18

Regression Predicting Current Level of Adaptive Functioning and Parent Risk Characteristics

	R	R^2	Adjusted R^2	F	*df*	P
Level of Adaptive Functioning (SIB-R) Predictors						
Block 1: Parent Char.	.161	.026	-.002	.926	3,104	.431

Note: Parent Char. = Parent Characteristics (Psychological and/or Learning Problems, Length of Gestation, Illness during Pregnancy).

Child Risk Characteristics

A statistically significant correlation was noted among the dependent variable, current level of adaptive functioning, and the independent variables related to child risk characteristics (block 2). Table 19 presents the regression. The variable developmental regression accounts for 31.9% of the variance in the overall model while the variable impaired social interaction accounts for 29.2% of the variance in the overall model. The variable stereotypical/unusual behaviors accounts for 19.6% and physical sensitivity accounts for 6.1% of the overall variance in the regression model.

Table 19

Regression Predicting Current Level of Adaptive Functioning and Child Risk Characteristics

	R	R^2	Adjusted R^2	F	*df*	P
Level of Adaptive Functioning (SIB-R) Predictors						
Block 2: Child Char.	.391	.153	.122	4.926	4,109	.001

Note: Child Char. = Child Characteristics (Physical Sensitivity, Impaired Social Interaction, Developmental Regression, Stereotypical/unusual behaviors).

Parent and Child Risk Characteristics

A statistically significant relationship was found between current level of adaptive functioning and all the predictor variables related to child and parent risk characteristics (block 3), yielding an overall R of .456, F (7,100) = 3.740, $p < .01$. The presence of both child and parent risk characteristics within a participant's history accounted for a significant amount of variance in the current severity/level of adaptive functioning for those with ASD. The R^2 value for the model is .207. The independent variables in the regression collectively account for 20.7% of the variance in the dependent variable. Table 20 summarizes the regression. Examination of the zero-order correlations indicated each of the following variables attributed significantly to the overall variance of the model: Impaired Social Interaction = 30.7%, Developmental Regression = 35.2%, and Stereotypical/Unusual Behaviors = 22.6%.

Table 20

Regression Predicting Current Level of Adaptive Functioning and the Presence of Both Parent and Child Risk Characteristics

	R	R^2	Adjusted R^2	F	*df*	P
Level of Adaptive Functioning (SIB-R) Predictors						
Block 3: Parent/Child Char.	.456	.207	.152	3.740	7,100	.001

Note: Parent/ Child Char. = Parent and Child Characteristics (Psychological and/or Learning Problems, Length of Gestation, Illness during Pregnancy, Physical Sensitivity, Impaired Social Interaction, Developmental Regression, Stereotypical/unusual behaviors).

CHAPTER V

DISCUSSION

Several factors provided the impetus for this research, predominantly the notable increase in the prevalence of ASD over the past decade and a lack of a definitive and unified theory regarding the etiology. Secondly, of interest was the wide variation and severity of symptoms endured by each individual diagnosed with an autism spectrum disorder. Current sources estimate the frequency of ASD to be from 10 to 60 per 10,000 (Baird, Charman, Baron-Cohen et al., 2000; Bertrand, Mars, Boyle et al., 2001; Chakarabarti & Fombonne, 2001; Horton, 2004; Medical Research Council, 2001 as cited in Purssell, 2004; Yeargin-Allsopp, 2003). Autism spectrum disorders (autism, Asperger's and PDD) impact a wide range of adaptive attributes. All these disorders are characterized by varying degrees of impairment in communication skills, social interactions, and restricted, repetitive and stereotyped patterns of behavior. The onset of autism is typically noted during the second year of life when significant developmental milestones such as speech and socialization become more evident. Although the precise cause of ASD is unknown it is probable that it is not the result of a single etiological factor. It is a syndrome that appears to have multiple etiologies and is likely due to underlying genetic factors and the interaction of these factors with the environment. The likelihood of a multifactor cause in the onset of ASD is a common theme throughout the literature. The theory that a combination of genetic and environmental factors playing a role in the etiology of ASD is both distressing and reassuring. While additional research is needed to

determine specific contributing factors, it indicates that the presence of a genetic vulnerability alone is not enough to cause ASD. It could therefore be rationalized that adequate health and a safe pre and postnatal environment could assist in decreasing the chance of ASD occurring in some instances.

Research related to the etiology of ASD has been inconsistent and controversial. A small portion of the increase can likely be attributed to better identification by clinicians and more definitive diagnostic criteria. A genetic component has been well established with the publication of family and twin studies, however as noted by Wassink et al. (2005) no gene has been conclusively identified. While these studies have clearly demonstrated that genetics play a role in the etiology of ASD they do not account for the increased prevalence. Research has established that ASD has a genetic base, however, exposure to particular stimuli during pre and post natal periods of development have also been suspected in attributing to the cause and differences in severity among individuals. While the symptoms associated with ASD often occur with varied intensity it is not completely understood which factors attribute to these variations among individuals.

This study specifically investigated whether multi-valent and thimerosal-containing childhood vaccinations (particularly MMR) as well as the child's state of health at the time of immunization were related to the onset of ASD. No primary link between immunization and the onset of autism was found, however, it is hypothesized that genetic and nongenetic factors may establish a predisposition whereby adverse effects of vaccines occur only in some children. It was also investigated whether parent risk characteristics (a family history positive for psychological and learning disorders, length of gestational period, and maternal illness during pregnancy) as well as the

presence of child risk characteristics (e.g., physical sensitivity, impaired social interaction, developmental regression and stereotypical/unusual behaviors) to a marked degree during the first five years of life predict an individuals current levels of autism symptomology and adaptive functioning.

Vaccination programs are under particular scrutiny due to reports by parents whose children began to demonstrate autistic behaviors shortly after being immunized. There were initial reports both in the United States and in the United Kingdom that the introduction of the poly/multi-valent MMR vaccine coincided with the apparent increase in cases of autism spectrum disorders. However, the majority of researchers have found no convincing evidence to suggest that MMR vaccination increases the risk of autism spectrum disorders. In fact, despite the mounting research efforts, it appears that little is still clearly known about the causation of autism which could explain the reason for suggesting MMR as a possible cause. The current study explored the suggestion that MMR vaccination could act as a possible catalyst for the onset of autism and found neither that MMR, nor any other childhood vaccination was associated with the onset of an autism spectrum disorder. The findings of no increased risk for the onset of autism for individuals who are administered the MMR vaccine was consistent with several previous studies that showed no temporal relationship between MMR vaccination and the onset/development of autistic symptoms (Dales et al., 2001; Honda et al., 2005; Stehr-Green et al., 2003; Taylor et al., 1999). Children receive their first MMR vaccination during their second year of life, the age autism generally manifests itself, chance alone dictates that some cases will appear shortly after vaccination. The significant amount of

inconsistency among the research related to MMR and ASD indicates the additional research is required before thimerosal is vindicated.

While it is impossible to mention all potential variables, it is of particular interest that over the past decade there has been in increase in autism and autoimmune disorders. As Semple (2004) noted, there has been an increase in immune dysfunction and autoimmune disorders over the past 25 years and that these disorders have been tied to environmental causes. A cumulative effect for environmental exposures is certainly a strong possibility, particularly if autism were found to be a disorder of immune dysfunction. The condition of an individual's immune system when immunized and the relationship to the onset of autism has also been investigated by Singh (1998, 2000). While the majority of the studies have not proved a solid link, they certainly provide sufficient circumstantial evidence which should not be ignored. It is likely that our knowledge of the immune system is not yet fully understood. In the current study no association was found between the participant's state of health at the time of vaccination and the onset of an autism spectrum disorder. These findings are consistent with the majority of the current literature. Perhaps the lack of statistically significant findings suggest that genetic factors are more significant in predicting the onset of ASD than originally thought.

While there is not much one can do to prevent perinatal trauma, greater control can be exerted to ensure adequate pre-and postnatal environments. Although children who endure pre- and postnatal difficulties have a greater chance of surviving than they did in previous decades, they are at greater risk of suffering from life long neurodevelopmental difficulties such as autism. Findings related to pre-, peri- and

postnatal factors should be considered in conjunction with increased prevalence and severity of ASD. Although the results of this study could not definitively determine causality, findings do suggest that some factors related to parent risk characteristics and child risk characteristics present to a marked degree prior to the age of five have a greater impact on predicting the level of ASD symptomology and level of adaptive functioning than generally expected.

Despite the lack of significant findings for the dependent variable related to onset of autism, variables were found to predict the current level of autism symptomology and level of adaptive functioning. It was not a significant surprise that the variables related to child risk characteristics within the first five years of life were found to have a significant effect on current level of symptomology and level of adaptive functioning. The variables that comprised these models are highly associated with diagnostic criteria of ASD. These significant findings also indicate validity and reliability of the rating scale used in the study. Because the independent variables are closely related to diagnostic criteria for ASD and were found to be significant predictors of ASD symptomology it indicated that the GARS adequately measured information it was designed to assess. The variables related to parent risk characteristics were also found to be predictors of current levels of ASD symptomology but not with current levels of adaptive functioning . This was not surprising as the literature has shown strong genetic associations with family and twin studies. Gillberg and Cederlund (2005) found that approximately 50% of all boys with Asperger's have a paternal family history of autism spectrum disorder and that one in four individuals with Asperger's experienced pre- and perinatal risk factors. As the disorders that comprised the parent risk characteristics (anxiety, depression, speech-

language disorder, learning disorder) are thought to have a genetic basis it seems logical that the presence of psychological disorders within one's family history could potentially exacerbate an individual's level of ASD symptomology. The presence of both parent and child risk characteristics were also found to be significant predictors of current ASD symptomlogy and adaptive functioning. These significant findings also indicate validity and reliability of the rating scales used in the study. Because the independent variables are closely related to diagnostic criteria for ASD as well as adaptive behavioral skills and were found to be significant predictors of ASD symptomology and adaptive functioning it indicated that the GARS and SIB-R adequately measured information they were designed to assess. Moreover, findings of the current study would suggest that early presence of ASD symptomology predicts that these symptoms/characteristics will be pervasive and stable across time. The parent risk characteristic related to length of gestational period was shown to have an inverse relationship with the severity of ASD. The correlation indicated a longer gestational period was associated with less ASD symptomology. Although this variable was found to be statistically significant it may not be of clinical significance in that shortened gestational periods are more commonly associated with a risk of neurodevelopmental and medical difficulties. The parent characteristic variable of illness during pregnancy as well as other factors such as exposure to teratogens in utero have been shown to be associated with various psychological and medical disorders in children (Cox et al., 1989; Geier & Geier, 2003; Marsh et al., 1987; Redwood et al., 2001; Verdoux, 2004).

The examination of pre-, peri-, and postnatal factors and their ability to predict current levels symptom severity and adaptive functioning was not readily found in the

literature. The current study appears to be one of a few to date to investigate factors associated with severity of ASD symptoms and has brought attention to environmental factors more commonly examined in relation to the onset of ASD rather than severity of the disorder.

Limitations

A few limitations have been noted for this study. The sample size was limited and only contained 114 participants. The size and power of this sample may not have been sufficient to explain the associations found. The sample was more heterogeneous, including individuals with autism, Asperger's and/or PDD. However, it has been noted by Szatmari (1999) that autism is likely to be etiologically heterogeneous. In addition, a control/comparison group was not included. Data were obtained from parent report and no children were individually examined. Although no verification of diagnosis was conducted, most respondents, although not specifically requested, sent copies of their child's diagnostic evaluation/report. The majority of requested data was obtained from retrospective parental reports. While the validity of these accounts, particularly where precise dating was requested could be questioned, most participants within the sample were still fairly young when data was collected and the respondents inaccurate recall of information should have been kept to a minimum.

Implications for the Future

Although the debate is ongoing as to whether autism has a genetic or environmental cause or both, most would agree that the prevalence has increased. The question is whether the observed increase is due to better diagnosis of autism spectrum disorders or other factors such as thimerosal-containing vaccinations. If MMR were a

significant cause of autism, it would be expected that a cluster of cases would have been seen promptly after the introduction of the poly/multi-valent MMR vaccine, but such a cluster has yet to be evidenced among the many researchers who have examined the data. Additional concern that poly/multi-valent vaccinations might result in immunosupression is also unwarranted as Miller et al (2003) noted, there is no increase in invasive bacterial infections in children immediately after MMR vaccination…therefore it would indicated that a polyvalent immunization such as MMR would not have an adverse effect on an individuals' immune system.

There is a natural tendency for all of us to seek out explanations for occurrences that are uncertain, painful, and unexplained, such as the onset of autistic symptoms in a young child. Perhaps this is even more so for parents of children who suddenly experience a regression or complete loss of previously learned skills. Parents base their beliefs on their own experiences, observations, and the temporal association between vaccination and the onset of symptoms. Concerns regarding the development of autistic characteristics or atypical developmental patterns typically occur before 24 months and usually during the second year (De Giacomo & Fombonne, 1998; Rogers & DiLalla, 1990; Short & Schopler, 1988; Volkmar et al, 1985). When one considers that children receive a high number of vaccinations, including the MMR vaccine, during the second year of their life, when autism typically manifests itself; chance alone would determine that some cases will appear shortly after immunization has occurred. Although the initial symptoms of autism are typically discernible at the age one receives the MMR vaccination, there is not sufficient epidemiological evidence that immunizations cause autism. Determining the onset of autism is difficult even under ideal circumstances.

Despite negative findings related to thimerosal and the fact that it is recognized by some as a health hazard, many nations continue to add it to their vaccines. Vaccination has been and will continue to be a necessity that helps control the outbreak of deadly diseases. Vaccines are intended to protect both the individual and society. Those in the United States who are adversely affected by the MMR or any vaccination should report their experiences and adverse reactions to the Vaccine Adverse Events Reporting System (VAERS) database so that information can continue to be generated in relation to the safety or lack of safety related to vaccines.

In the 1970's immunization concerns were of lower priority and case-based information was minimal. Coordinators were non-existent and vaccination rates appeared to slump because of the lack of assigned responsibility. The pertussis experience should not be repeated with current vaccinations, particularly MMR. While no vaccination can come without risk, the risk must be weighed against the advantages of protection against debilitating diseases. Concerns exist among parents and will likely continue to grow and spread. Most would agree that there is certainly a need for greater understanding of vaccine contraindications and precautions before a specific risk intervention can be developed. Those with the task of advising patients and families have the responsibility to make sure that their decisions can be based on hard scientific evidence. Keeping an open mind about causation and continuing to explore new hypotheses is important, but a task of higher importance is forprofessionals to remain skeptical about claims of association that might fall short of strict scientific criteria.

Irrespective of conclusions from various organizations and researchers that there is no relationship between the thimerosal-containing MMR vaccine and autism, and their

belief that no further studies are necessary to evaluate the relationship, it is evident from the conflicting pool of data from recent years that additional research should be carried out and should focus on thimerosal-containing/mercury associated exposure. For research to be successful in this domain, researchers from clinical and epidemiological fields will need to make concerted efforts to combine their scientific strategies. Collaboration among these fields is necessary as there appears to be a multi-factor etiology to ASD. With out collaborative efforts it will be difficult to determine which combination of genetic and environmental factors may be contributing to the onset and severity of ASD.

Findings have strongly supported the hypothesis that the perinatal period is a crucial neurodevelopmental stage in which exposure to deleterious environmental events may increase vulnerability (Verdoux, 2004). Although a link has been shown between some variables and the severity of ASD it appears to be weak and possibly nonspecific, with these factors more likely being consequences of the disorder. The literature is sparse in studies investigating factors impacting the severity of ASD among individuals. As well, the operational definitions of severity are widely varied and the methodologies lack the use of standardized instruments and measurable outcomes. Although the few investigations that exist have not been fruitful in identifying a means of preventing ASD or lessening the severity of the disorder it is still appropriate to continue examining pre and postnatal factors. The current study contributed to the literature by providing clearly defined and measurable variables related to severity, which could be replicated for future research. Identification of these risk factors could be useful for early detection and intervention planning while ultimately alleviating the potential severity of the disorder over ones lifetime.

There is no disputing that this disorder has taken a toll on the families of affected children, the children themselves, and the school districts and agencies serving them. Higher functioning children with ASD report feelings of anger, depression, and frustration from trying to communicate and function socially in a world that requires these skills to survive (Semple, 2004). Because the research is inconclusive, parents are often victims of proposed cures that are nothing more than empty promises. The public schools and state agencies are up against the rising cost of caring for the growing number of individuals afflicted with ASD. Current and promising treatments often include costly intensive one on one therapy for the areas of speech and language, behavior, socialization, and fine and gross motor skills. Continued research into the etiology of ASD could potentially lead to earlier detection, effective early intervention, prevention and the hopes of someday finding a cure.

Despite the growing amount of literature to date, it appears we still know far too little about ASD for anyone to make a final or definitive conclusion regarding the etiology and severity. Autism has been bewildering researchers and clinicians for several decades. This complex disorder includes a broad variety of symptoms which typically manifest before the age of three. Nothing will likely simplify the search for ASD causes but every possible risk factor that is identified alleviates some of the mystery associated with the search. Continued research from all disciplines could help alleviate the life long devastation associated with this disorder. Consistent and appropriate designs and methods with clearly defined and measurable variables are critical to achieving meaningful and applicable results. Although biological and environmental risk will never be completely eradicated, it is not unreasonable to strive for prevention and reduce the occurrence of

adverse outcomes. For that reason, prevention of avoidable pre-, peri-, and postnatal risks should be of highest priority.

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APPENDICES

Appendix A: Cover Letter

AUTISM STUDY Spring/Summer 2005 Investigator: Jennifer Aldridge-Sumner, M.Ed.

Autism is a pervasive developmental disorder due to the fact that it impacts a wide range of areas in an individual's life (e.g., language, communication, social interactions, cognitive functioning, and behavior). The prevalence of Autism is estimated to affect 6 individuals per 1000. The purpose of the research study is to investigate whether the effects of childhood immunizations on the onset of Autism Spectrum Disorders as well as additional medical history that might affect the severity of Autism Spectrum Disorders. This study is my dissertation and the final component to completing my doctoral degree in school psychology at Oklahoma State University. Your participation would be greatly appreciated.

Participants will be asked to complete a brief and detailed developmental history form along with an adaptive behavior rating scale and/or Autism rating scale (if one has not been recently completed). The developmental history form will inquire about demographics, pregnancy, birth, developmental milestones, immunizations, diagnosis and other pertinent medical information. Information not readily available from the participant that may need to be obtained from school records will be sought through the signing of a medical release form/consent form. Permission to access school records will be for the purpose of obtaining ***only*** information pertaining to the student's immunization history and psycho-educational testing (e.g., to obtain a score if the Autism rating scale has recently been completed).

Your participation is completely voluntary and there is no penalty for not choosing to participate. Your participation will be kept completely confidential as your information will only be identified through codes/numbers. Your participation in the study may help researchers and other professionals who work with children understand factors related to the etiology of Autism Spectrum Disorders.

If you are willing to participate in the study or if you have any questions please e-mail me at Jifsumner@aol.com or call 918-749-1840 (Tulsa). Packets will be sent to you through the mail with a self-addressed/stamped envelope for their return.

Sincerely,

Jennifer Aldridge-Sumner, M.Ed.

Appendix B: Informed Consent Form

Consent Form

Spring/Summer 2005 Study: An Investigation of the Effects of Childhood Immunizations on the Onset of Autism and Risk Factors that Predict Current Levels of Autistic Symptomology and Adaptive Functioning

I, _____, hereby authorize or direct Jennifer Aldridge-Sumner and/or Dr. Terry Stinnett to perform the following procedure:

Present to me a developmental health history form an Autism rating scale (Gilliam Autism Rating Scale or Asperger's Syndrome Diagnostic Scale) and an Adaptive Behavior Scale.

Details of the Study:
Participants will be parents of children (ages 3to 29) who have been diagnosed with an Autism Spectrum Disorder and identified through various autism support groups across the United States. Participants will be asked to volunteer and those who choose to participate will be asked to sign an informed consent form. There is no risk to the participants and confidentiality will be maintained.

Demographic information along with detailed developmental, medical, diagnostic, and immunization history will be requested through questionnaire format. Information not readily available from the participant that may need to be obtained from school records will be sought through the signing of a medical release form. Participants will be guaranteed privacy and anonymity regarding the information relayed for the purpose of the proposed study.

I understand that participation is completely voluntary, there is no penalty for not choosing to participate, that I may withdraw from the study at any time with no negative consequences to me or my child and that participation and responses will be kept completely confidential. There is minimal risk or possible discomfort associated with participation. I understand this study may help researchers and other professionals who work with children understand factors related to the etiology of Autism Spectrum Disorders.

As part of this study, I understand that by signing this consent form I give permission for the examiners to access my child's school records to obtain *only* information pertaining to his/her immunization history and psycho-educational testing. Access to his/her file is only necessary if I am unable to provide the above listed information (i.e., immunization records, psycho-educational evaluation, and a current/recently completed Gilliam Autism Rating Scale) to the examiner at this time.

I may contact Dr. Terry Stinnett at Oklahoma State University at (405) 744-9456 or Jennifer Aldridge-Sumner at (918) 749-1840. I may also contact Dr. Sue Jacobs, IRB Chair, 415 Whitehurst, Oklahoma State University, Stillwater, OK 74078: (405) 744-1676.

I have read and fully understand the consent form. I sign freely and voluntarily. A copy has been given to me.

Date:_____

Time:_____ (a.m./p.m.)

Signed:_____

I certify that I have personally explained all of the elements of this form to the participant before requesting him or her to sign it.

Signed:_____
Project Director or Authorized Representative

#_____

Developmental and Medical History Form

FAMILY AND SOCIAL HISTORY

Child's Information:

Gender: M F Birth Date: _____ Current Age: _____

Race: (circle one) African American, Caucasian, American Indian, Hispanic, Asian, Other _____

Education:

Highest Grade Completed (1-12) _____ High School Graduate / GED (circle one)

Highest Degree Awarded: (circle one) High School Bachelors Masters Doctorate

Diagnosis:(circle one) Autism Disorder Asperger's Disorder Pervasive Developmental Disorder

Age at initial diagnosis:_____

Parents Information:

Mother: (circle one) Biological, Adoptive, Step, Foster, Legal Guardian

Age: _____

Race: (circle one) African American, Caucasian, American Indian, Hispanic, Asian, Other _____

Education:

Highest Grade Completed (1-12) _____ High School Graduate / GED (circle one)

Highest Degree Awarded: (circle one) High School Bachelors Masters Doctorate

Father: (circle one) Biological, Adoptive, Step, Foster, Legal Guardian

Age: _____

Race: (circle one) African American, Caucasian, American Indian, Hispanic, Asian, Other _____

Education:

Highest Grade Completed (1-12) _____ High School Graduate / GED (circle one)

Highest Degree Awarded: (circle one) High School Bachelors Masters Doctorate

Additional Children in the Family:

Gender	Age	Relation (biological, step, foster, adoptive)	Medical or Psychological Problems?
M / F		B S F A	
M / F		B S F A	
M / F		B S F A	
M / F		B S F A	
M / F		B S F A	
M / F		B S F A	

Is there any history of the following?
(Use the following: M=mother, F=father, S=sister, B=brother, GM=grandmother, GF=grandfather, U=uncle, A=aunt, C=cousin)

Biological Mother's Side of the Family

_____Learning Problems
_____Speech/Language Problems
_____Mental Retardation
_____Seizures/Epilepsy
_____Attention/Concentration Problems
_____Hyperactivity
_____Anxiety
_____Obsessive-Compulsive Disorder
_____Unreasonable Fears (i.e., phobias)
_____Depression
_____Alcoholism/Drug Abuse
_____Autism Spectrum Disorder
_____Psychiatric Hospitalization
_____Other Psychiatric Disorder

_____Other_____

Biological Father's Side of the Family

_____Learning Problems
_____Speech/Language Problems
_____Mental Retardation
_____Seizure/Epilepsy
_____Attention/Concentration Problems
_____Hyperactivity
_____Anxiety
_____Obsessive Compulsive Disorder
_____Unreasonable Fears (i.e., phobias)
_____Depression
_____Alcoholism/Drug Abuse
_____Autism Spectrum Disorder
_____Psychiatric Hospitalization
_____Other Psychiatric Disorder

_____Other_____

PREGNANCY AND BIRTH HISTORY

1. How many weeks did pregnancy last (normal 38-42 weeks) _____

2. Was any medication used during pregnancy (circle one) Yes No
If yes, please list medications taken during pregnancy (include vitamins, all prescription drugs and over the counter drugs)

Medication	Months Taken (of 9)	Dose	Reason for Taking

3. Was alcohol consumed during pregnancy? YES NO

4. Was smoking or tobacco used during pregnancy? YES NO

5. Were any other drugs (not prescribed) used during pregnancy? YES NO

6. Were there any illnesses during pregnancy? YES NO
If YES, please describe

_____

7. Were there any traumas during pregnancy? YES NO
If YES, please describe

_____

8. Was there any exposure to chemicals, toxic substances or people with infections during the pregnancy? YES NO
If YES, please describe

_____

Child's birth weight: _____pounds _____ounces

DEVELOPMENTAL PROGRESSION

At what age did you become concerned about your child's development? _____

At what age was your child diagnosed? ____ Diagnosis (circle one): Autism or Asperger's

Developmental Milestones: (List age in months for each milestone achieved –average is listed in parenthesis)

	Slower	Average	Faster
Rolled Over (2-5 months)			
Sat Alone (5-8 months)			
Crawled (7-8 months)			
Walked alone (11-14 months)			
First words (9-13 months)			
Put words together/Sentences (15-18 months)			
Toilet Trained (24-36 months)			
Rode a tricycle (21-36 months)			
Dressed self independently (36-42 months)			

Were any of the following present to an unusual degree during the first five years of life?

Y	N	High Fevers
Y	N	Pneumonia
Y	N	Meningitis
Y	N	Poisoning/Toxic Exposure
Y	N	Colic
Y	N	Poor Weight Gain
Y	N	Disrupted Sleep
Y	N	Difficult to Calm/Pacify
Y	N	Did not Like to be Held
Y	N	Irritability/Easily Agitated
Y	N	Clumsy/Uncoordinated
Y	N	Difficulty Making Eye Contact
Y	N	Staring at or Avoiding Looking at Others
Y	N	Rocking, Spinning, or Head Banging
Y	N	Walking on Tiptoes or Flapping Hands
Y	N	Unusual Play Behaviors
Y	N	Difficulty Interacting/Playing with Others
Y	N	Slow to Roll, Crawl, or Walk
Y	N	Slow to use Words or Sentences
Y	N	Loss of Abilities/Regression
Y	N	Sensitivity to Sounds/Sights/Touch/Taste

IMMUNIZATION/VACCINATION HISTORY

Please provide the following information regarding your child's immunization history (the typical immunization schedule followed in the United States is in parenthesis)

Immunization	Sick or Healthy at time of Immunization		Adverse Reactions?
Diptheria/Tetanus/Pertusis			
2 months	S	H	Illness / Loss of skills
4 months	S	H	Illness / Loss of skills
6 months	S	H	Illness / Loss of skills
12-15 months	S	H	Illness / Loss of skills
& 4-6 years	S	H	Illness / Loss of skills
Hepatitis B			
2 months	S	H	Illness / Loss of skills
4 months	S	H	Illness / Loss of skills
& 12-15 months	S	H	Illness / Loss of skills
Polio			
2 months	S	H	Illness / Loss of skills
4 months	S	H	Illness / Loss of skills
12-15 months	S	H	Illness / Loss of skills
& 4-6 years	S	H	Illness / Loss of skills
Influenza			
2 months	S	H	Illness / Loss of skills
4 months	S	H	Illness / Loss of skills
& 6 months	S	H	Illness / Loss of skills
Measles/Mump/Rubella			
12-15 months	S	H	Illness / Loss of skills
& 4-6 years	S	H	Illness / Loss of skills
Vericella			
(12-15 months)	S	H	Illness / Loss of skills

EVALUATION

Please refer to your child's most recent psycho-educational evaluation to complete the following section. Please see the examiner for help with this section if necessary.

Which test was used to assess your child's intellectual functioning? What scores were obtained?

Date Administered?_____

a. WISC-III: PIQ=_____ VIQ=_____ FSIQ=_____

b. WISC-IV: VCI=_____ PRI=_____ WMI=_____ PSI=_____ FSIQ=_____

c. DAS: Verbal=_____ Nonverbal Reasoning=_____ Spatial=_____ General Cognitive Ability=_____

d. Leiter/Leiter-R: Full IQ=_____ Brief IQ=_____

e. TONI-3: TONI-3 Quotient=_____

f. Other: _____

If you have completed one of the following adaptive behavior rating scales within the last year please report the following scores. If it has been more than one year or you have not completed one of the following rating scales listed below, please see the examiner at this time.
Date Administered?_____

a. Scales of Independent Behavior-Revised (SIB-R): Broad Independence=_____

Subtest standard scores: Motor Skills ____ Social Interaction/Communication Skills_____

Personal Living Skills_____ Community Living Skills_____

b. Vineland Adaptive Scales (Vineland): Adaptive Behavior Composite=_____

Subtest standard scores: Communication____ Daily Living Skills _____ Socialization _____

Motor Skills _____

If you have completed one of the following autism rating scales within the last year please report the following scores. If it has been more than one year or you have not completed one of the following rating scales listed below, please see the examiner at this time.
Date Administered?_____

a. Gilliam Autism Rating Scale (GARS): Autism Quotient=_____ Probability of Autism=_____

Subtest standard scores: Stereotyped Behaviors_____ Communication _____ Social Interaction _____

b. Gilliam Asperger's Disorder Scale (GADS): Asperger's Disorder Quotient=_____

Probability of Asperger's=_____

Subtest standard scores: Social Interaction ____ Restricted Patterns of Behavior ____ Cognitive Patterns_____

Pragmatic Skills _____

c. Asperger's Syndrome Diagnostic Scale (ASDS): Asperger's Syndrome Quotient=_____

Probability of Asperger's=_____

Subtest standard scores: Language ____ Social _____ Maladaptive _____ Cognitive ____ Sensorimotor ____

Oklahoma State University
Institutional Review Board

Protocol Expires: 3/21/2005

Date: Monday, March 22, 2004 IRS Application No ED0483

Proposal Title: An Investigation of the Effects of Childhood Immunizations on the Onset of Autism

Principal
Investigator(s):
,,,,/'

Jennifer Aldridge-Sumner
244 E. 27th Place
Tulsa, OK 74114

Terry Stinnett
445 Willard Stillwater,
OK 74078

Reviewed and
Processed as: Expedited (Spec Pop)

Approval Status Recommended by Reviewer(s): Approved

Dear PI :

Your IRB application referenced above has been approved for one calendar year. Please make note of the expiration date indicated above. It is the judgment of the reviewers that the rights and welfare of individuals who may be asked to participate in this study will be respected, and that the research will be conducted in a manner consistent with the IRB requirements as outlined in section 45 CFR 46.

,As Principal Investigator, it is your responsibility to do the following:

1. Conduct this study exactly as it has been approved. Any modifications to the research protocol must be submitted with the appropriate signatures for IRB approval.
2. Submit a request for continuation if the study extends beyond the approval period of one calendar year. This continuation must receive IRB review and approval before the research can continue.
3. Report any adverse events to the IRB Chair promptly. Adverse events are those which are unanticipated and impact the subjects during the course of this research; and
4. Notify the IRB office in writing when your research project is complete.

Please note that approved protocols are subject to monitoring by the IRB and that the IRB office has the authority to inspect research records associated with this protocol at any time. If you have questions about the IRB procedures or need any assistance from the Board, please contact me in 415 Whitehurst (phone: 405-744-5700, colson@okstate.edu).

Sincerely,

~(Q~

Carol Olson, Chair
Institutional Review Board

VITA

Jennifer Otoka Aldridge-Sumner

Candidate for the Degree of

Doctor of Philosophy

Thesis: THE EFFECTS OF IMMUNIZATIONS ON THE ONSET OF AUTISM SPECTRUM DISORDERS AND RISK FACTORS THAT PREDICT CURRENT LEVELS OF AUTISTIC SYMPTOMOLOGY AND ADAPTIVE FUNCTIONING

Major Field: Educational Psychology

Biographical:

Education: Graduated from Jenks High School, Tulsa, Oklahoma May 1990; received Bachelor of Science degree in Psychology from Oklahoma State University, Stillwater, Oklahoma in May 1994; received Masters of Education in Counseling from The University of Central Oklahoma, Edmond, Oklahoma in May 1996. Completed the requirements for the Doctor of Philosophy with a major in School Psychology at Oklahoma State University in May 2006.

Experience: Raised in Tulsa, Oklahoma; employed by Oklahoma State University, School of Applied Health and Educational Psychology as a graduate assistant, 1998-1999, as a psychological associate 1996-2000. Employed by Union Public Schools, Tulsa, Oklahoma as an intern 1999-2000. Employed by Primary Childrens Medical Center, Salt Lake City, Utah 2000-2001. Employed by Union Public Schools, Tulsa, Oklahoma as a School Psychologist 2000-2004.

Name: Jennifer Otoka Aldridge-Sumner Date of Degree: May 2006

Institution: Oklahoma State University Location: Stillwater, Oklahoma

Title of Study: THE EFFECTS OF IMMUNIZATIONS ON THE ONSET OF AUTISM SPECTRUM DISORDERS AND RISK FACTORS THAT PREDICT CURRENT LEVELS OF AUTISTIC SYMPTOMOLOGY AND ADAPTIVE FUNCTIONING

Pages in Study: 129 Candidate for the Degree of Doctoral Philosophy

Major Field: Educational Psychology

Scope and Method of Study: Autism spectrum disorders (autism, Asperger's, PDD) are devastating neurological disorders characterized by varying degrees of impairment in communication skills, social interactions, and restricted, repetitive and stereotyped patterns of behavior. This study investigated the use of multi-valent and thimerosal-containing childhood vaccinations (particularly MMR) as well as the child's state of health at the time of immunization and their possible link to the onset of ASD. It was also investigated whether the presence of one or more parent and child risk characteristics predict current level of autistic symptomology and adaptive functioning. Parents of 114 participants diagnosed with an autism spectrum disorder completed a detailed developmental history form along with the Scales of Independent Behavior: Short Form and an Autism rating scale (Gilliam Autism Rating Scale or Asperger's Syndrome Diagnostic Scale). The developmental history form inquired about demographics, pregnancy, birth, developmental milestones, immunizations, diagnosis and other pertinent medical information.

Findings and Contributions: The results of this study confirmed no association between neither childhood immunizations nor the participant's state of health at the time of vaccination and the onset of an autism spectrum disorder. A statistically significant correlation was noted among the dependent variable, current level of autism symptomology and all independent variables (parent risk characteristics; family history noted to include psychological and/or learning disorders and length of gestation and child risk characteristics: the presence of the following to a marked degree during the first fives years of life, physical sensitivity, impaired social interaction, developmental regression, and stereotypical/unusual behaviors). A statistically significant correlation was also noted among the dependent variable, current level of adaptive functioning and child risk characteristics as well as for the model including both parent risk characteristics and child risk characteristics.

Advisor's Approval: Terry A. Stinnett, Ph.D.