26 The epidemiology of autism

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26.1 Introduction

Autism has been described in the lay press as 'the hidden epidemic.' It is an 'epidemic' because of the dramatic increase in prevalence over the past 20 years – in the most recent surveys in the United States, the prevalence among school-aged children was greater than 1% [1, 2] – and 'hidden' because those who advocate for people with autism do not believe that it has received sufficient attention or funding. This chapter reviews our current knowledge of the epidemiology of autism.

26.2 Background

A popular conception exists that the United States and other countries are experiencing an epidemic of autism [3–6]. A glance at Figure 26.1, which graphs the number of people with autism spectrum disorder (ASD) enrolled in the California Department of Developmental Services delivery system between 1987 and 2007 [7] seems to support this notion. These increases have impacted health and education services across the country. Even Figure 26.2, which shows the cumulative prevalence of ASD corrected for population, age of child and birth cohort [8], shows a dramatic increase in autism for each subsequent cohort. However, closer scrutiny of the data raises major questions about the apparent 'epidemic'. This chapter will address the epidemiology of autism and current views regarding its occurrence and aetiology.

26.3 Definition and diagnosis

The ASD includes three major categories: autistic disorder, Asperger's syndrome and pervasive developmental disorder, not otherwise specified (PDD-NOS). Leo Kanner first described children with autism in the 1940s [9] and categorised them as having impaired social relationships and a preoccupation with sameness. In the 1970s Michael Rutter added impaired language to these two criteria [10], developing the three core criteria used by most definitions since. While Kanner was describing children now labelled as having 'autistic disorder', Hans Asperger was describing children who had impaired social relationships and unusual behaviour, but were higher functioning. Although they often have difficult with the pragmatics of language, people with Asperger's syndrome do not have the same degree of speech and language delay seen in other people on the spectrum. His work remained largely unread in this country until it was translated into English in the 1990s [11]. While autistic disorder and Asperger syndrome have specified criteria, PDD-NOS is a subthreshold diagnosis. Figure 26.3 describes these three conditions.

Autism has been viewed both as a spectrum, with continuously varying traits (like social reciprocity) and levels of severity, as well as a heterogeneous collection of discrete entities with different aetiologies sharing a common presentation – that is a final common pathway. For example, disparate conditions like tuberous sclerosis, fragile X syndrome, congenital rubella, prenatal exposure to valproic

Textbook of Psychiatric Epidemiology, Third Edition. Edited by Ming T. Tsuang, Mauricio Tohen and Peter B. Jones.

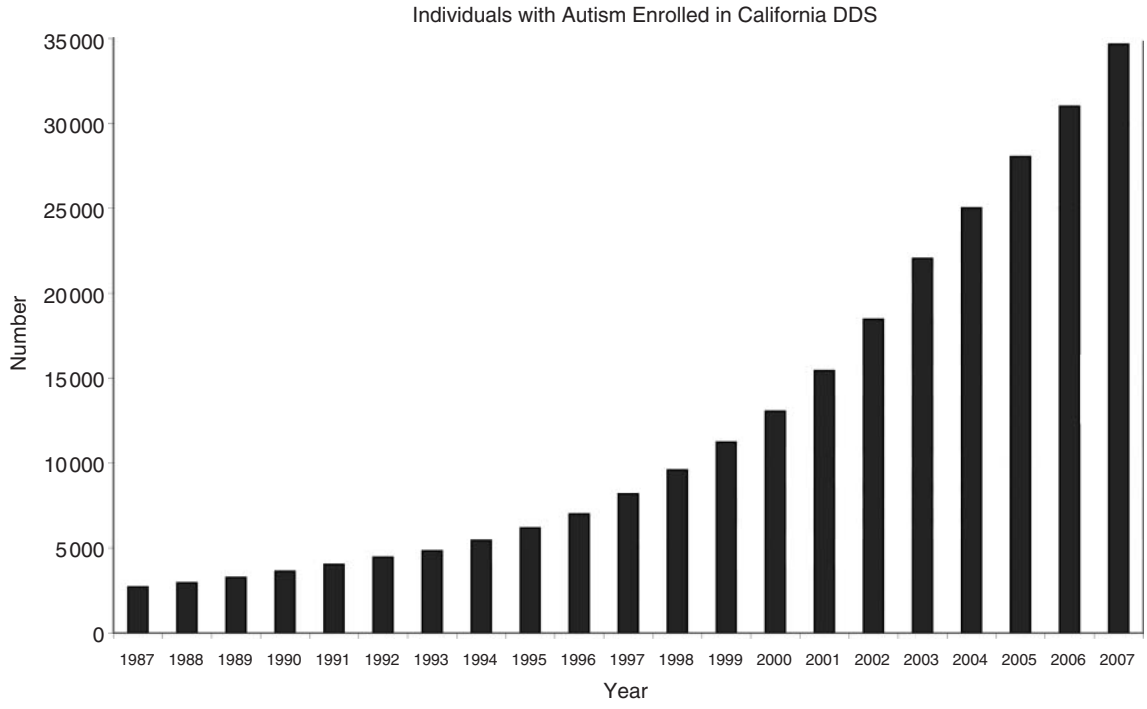

Fig 26.1 Number of people with autism spectrum disorder enrolled in the California Department of Developmental Services (DDS) delivery system between 1987 and 2007.

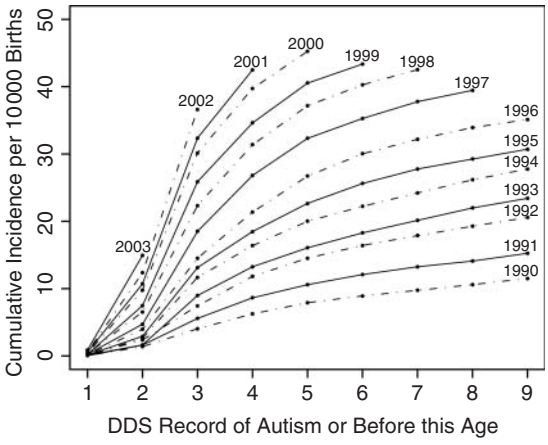

Fig 26.2 Cumulative incidence of individuals with autism spectrum disorder (ASD) enrolled in the California Department of Developmental Services (DDS) delivery system by age and by birth cohort.

acid, phenylketonuria (PKU) and Joubert syndrome (hypoplasia of the cerebellar vermis) all can present with signs and symptoms of autism. As Waterhouse stated, 'it is unlikely that a single cause or pathophysiological mechanism will be described that applies to most individuals currently diagnosed with autism' [12]. This chapter deals with 'idiopathic' autism, that is not linked to a specific known condition.

The definition of autism has changed over time. For example, the first studies used Kanner's criteria. By 1980 the American Psychiatric Association's diagnostic manual (*Diagnostic and Statistical Manual of Mental Disorders* (DSM)-III) [13] required individuals to meet six of six criteria for an autism diagnosis. Neither PDD-NOS (added in 1987) nor Asperger's syndrome (added in 1994) were included in that definition. The 1994 version (DSM-IV), which is currently in use [14], requires individuals to meet only 8 of 16 criteria and includes PDD-NOS as well as Asperger's syndrome. Thus, the definition of ASD has changed to become more expansive. The

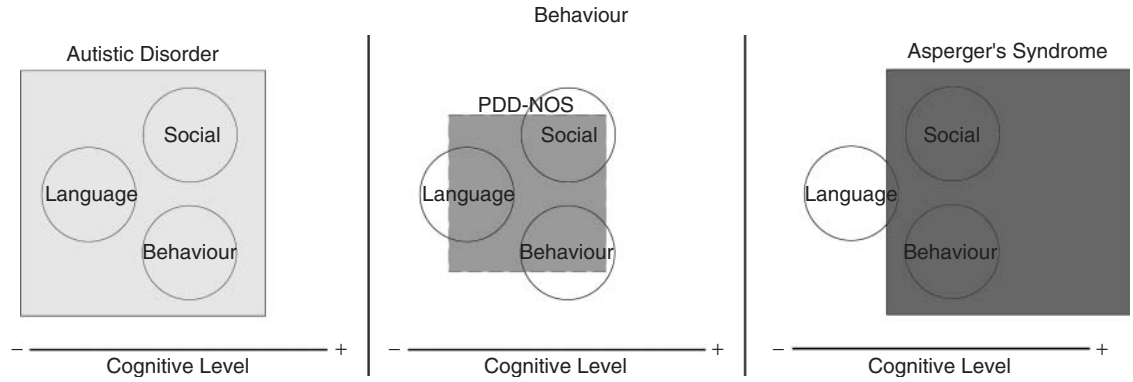

Fig 26.3 Conceptualisation of autistic disorder, pervasive developmental disorder, not otherwise specified (PDD-NOS) and Asperger syndrome in terms of their position with cognitive level, social abilities, language and behaviour.

characteristics of individuals diagnosed with ASD has changed over time. For example, data from California show that in 1992 72% of individuals had mental retardation. By 2005 this had fallen to 36%; similarly the rate of epilepsy decreased from 16 to 7% [7]. This suggests that the current group of individuals labelled with ASD are higher functioning and less involved medically than they were 15–20 years ago [15].

In addition to the changing criteria for ASD, many have argued that diagnostic substitution is occurring, which increases the prevalence as well. For example, Shattuck [16] used administrative data from the US Department of Education from 1994 to 2003. The prevalence of ASD among children increased from 0.6 to 3.1 per 1000 by 2003. At the same time, the prevalence of mental retardation and learning disabilities decreased by 2.8 and 8.3 per 1000, respectively. Higher ASD prevalence was associated with corresponding declines in the prevalence of mental retardation and learning disabilities. In a Canadian study, diagnostic substitution accounted for one-third of the increase in autism prevalence over the study period [17]. Thus individuals who in the past would have been categorised as having mental retardation and other conditions are now being classified as having ASD.

In addition to changes in the definition of ASD, changes in reporting have occurred. For example, schools are required to report data on students who receive special-education services, but autism was not added as a category until the 1991–1992 school year. In 1990, the new Individuals with Disabilities Education Act (PL 101-476) added autism to its list of categories of children and youth served under the act. This led to growing awareness and increased reporting by school districts [18]. Thus, a significant amount of the increase in reported prevalence has been attributed to changes in diagnostic criteria, increased awareness and reportingand diagnostic substitution. Finally, in some communities having a diagnosis of an ASD allows a child to receive more services in school. Some have argued that this motivates physicians and psychologists to diagnose ASD in children who do not fulfil all the criteria of ASD in order to help them get services. This hypothesis has not been formally studied.

The diagnosis of an ASD is made on the basis of a constellation of behavioural symptoms rather than on any biological markers. The Autism Diagnostic Observation Schedule (a standardised observation of communicative and social behaviour) [19] is considered by many to be the gold standard for diagnosing autism clinically [20, 21]. However, because it takes 45–60 minutes to administer, it has limitations for epidemiological prevalence or incidence studies in large samples. Therefore, many other varied methods have been used to ascertain cases of ASD. For example, the Centers for Disease Control (CDC) [22] has developed a multiple-source, population-based, active system using a records-based approach from both educational and clinical sources; they employ a common case definition (from the *Diagnostic and Statistical Manual of Mental Disorders*, 4th

edition, Text Revision (DSM-IV-TR)) [23], standardised data abstraction and clinician review of records to define a case. In their most recent survey [1], they found an overall prevalence estimate among 8-year-old children of 1 per 110 population (confidence interval $(CI)_{95} = 6.3–6.8$). Other studies have used administrative datasets [24] or employed identification by clinicians or parents [25]. In a study comparing two different methods of ascertainment, Barbaresi *et al*. [26] evaluated children who had been diagnosed with ASD from a research study, which was based on a structured record review and determined whether or not they had had a clinical diagnosis of ASD. Only 47% of research-identified cases had received a clinical diagnosis of ASD. Mattila [27] found different rates of autism in the same sample when using different standards. These findings highlight the difficulty in validly identifying individuals with autism in epidemiologic studies.

Children and youth with ASD frequently have associated conditions, including intellectual and developmental disability (mental retardation), anxiety (including obsessive compulsive disorder), epilepsy and attention deficit hyperactivity disorder (ADHD). Since children who have low cognitive skills typically have less well developed social and communication abilities, behavioural overlap occurs between children with mental retardation and children with ASD, making the diagnosis of ASD more challenging in this group [28].

Early diagnosis of ASD has several theoretical advantages. Earlier therapy, for example with applied behaviour analysis (ABA), has been advocated as being more effective than later therapy [29], (although the evidence for this argument is not optimal). In addition, earlier diagnosis can help families plan for subsequent pregnancies, since the rate of recurrence for ASD or the 'broader autism phenotype' (qualitatively similar but milder features of autism) is significantly increased (see below) once a family has an affected child. Finally, communities can help plan for resources, for example preschool and kindergarten programmes, if they know the current prevalence. Over time the average age of diagnosis of ASD has been decreasing. However, many have argued that ASD should be diagnosed earlier than it is now. In a 2004 survey of children the mean age of diagnosis was 3.1 years for children with autistic disorder, 3.9 years for PDD-NOS and 7.2 years for Asperger's syndrome [30]. Rural children received a diagnosis 0.4 years later than urban children. In this study, near-poor children received a diagnosis 0.9 years later than those with incomes above the poverty level.

Because of the theoretical value of early diagnosis, the American Academy of Pediatrics has recommended that primary care physicians screen all children for ASD at 18 and 24 months of age [31]. Similar recommendations for universal screening in Great Britain have not been implemented [32]. Using specific criteria, the UK National Screening Committee has argued that the diagnosis of ASD is still uncertain; no valid screening test has been developed for use in a population setting, and insufficient evidence is available regarding the effectiveness of interventions.

26.4 Natural history

The natural history of ASD has not been thoroughly studied. Although most infants with ASD demonstrate developmental disabilities consistently throughout childhood, a substantial group appear to develop normally until 12–24 months of age and then show regression in language and social skills [33]. Because this regression occurs at around the time of the measles, mumps and rubella (MMR) vaccine, some have attributed the regression to the vaccine. A study by Wakefield *et al*. [34] identifying antigens to the MMR components in the intestines of individuals with ASD heightened anxiety about this vaccine. The validity of Wakefield's study has been questioned [35, 36]; however, many families still believe that vaccines lead to autism. For instance, in a recent survey, 24% of individuals surveyed said that because vaccines may cause autism it was safer not to have children vaccinated at all. Another 19% were not sure [37].

A small per cent of children who have autistic characteristics as toddlers seem to improve clinically by the time they enter school [38, 39]; thus it is important to have a comparison group whenever conducting an intervention study on these children. The development of children with ASD in middle childhood depends in part on the types of services

being received by the child. During adolescence, behaviour may deteriorate, with increasing aggression (felt by many to be the effects of changing hormones). Individuals with non-verbal intelligence quotients (IQs) below 70 usually live dependently as adults; few of them live alone, have close friends or permanent employment. Communication generally is impaired, reading is poor and restricted or repetitive behaviours or interests persist [40]. The death rate is somewhat higher for those who have ASD, especially with mental retardation. In California the overall standardised mortality rate (SMR) for people with ASD was 2.6 [41]; for those with moderate or worse mental retardation it was 3.1; the SMR was 22.6 for those with mild or no MR who had seizures [42].

Autism has no cure. Table 26.1 lists some behavioural and educational interventions that have been utilised in the treatment of individuals with ASD as well as their level of evidence [43]. A higher grade does not mean that the intervention is more effective. It simply means that higher quality evidence has been published regarding its efficacy or effectiveness. Right now, ABA has the most peer-reviewed evidence regarding its effectiveness and efficacy; however, even for ABA most of the studies are not optimal. In addition, in most studies, the ABA is applied for many hours per week – as high as 40 – which is very difficult to do in most real-life situations, especially because individuals trained to administer ABA are not that available in most communities; in addition, it is difficult to get payment for those services. Psychoactive medications like atypical neuroleptics (risperidone, aripiprazole, etc.) and selective serotonin reuptake inhibitors (e.g. fluoxetine and venlafaxine) are used to treat specific behavioural problems like repetitive behaviour, obsessive–compulsive symptoms, hyperactivity and aggression [44]. Because no effective allopathic treatment for autism is available, many families use complimentary and alternative treatments, which have very little evidence either refuting or supporting their efficacy [45].

26.5 Prevalence

Figure 26.4 shows the reported prevalence of ASD by year of actual data collection and specific test used to identify cases in studies conducted since 1962. While prevalence has increased over time, it also has increased as newer criteria have been used to ascertain cases. The most widely cited pediatric prevalence rate for the United States is 1 in 152, which was determined in the CDC study [22]. In a Canadian study the prevalence of autistic disorder was 21.6 per 10 000; for PDD-NOS 32.8 per 10 000 and for Asperger's syndrome 10.1 per 10 000 [46]. Williams *et al*. [47] analysed prevalence studies using meta-regression. They found a significant increase in prevalence over time. However, the variation by year was so closely linked to changes in diagnostic criteria that the two could not be examined separately. The age of the children screened was strongly associated with the prevalence estimates, with studies of younger children having higher rates. Prevalence rates also were higher in urban areas and studies done in certain countries like Japan. They concluded that 61% of the variation among prevalence studies was explained by a model that included specific diagnostic criteria, age of children screened and study location.

26.6 Risk factors

Specific conditions like Fragile X syndrome and tuberous sclerosis increase the probability that the affected person will be diagnosed with autism. The remainder of this discussion will refer to 'idiopathic' autism. ASD is more common in males. For Asperger disorder the ratio is approximately 6 : 1, while for autistic disorder it is 4 : 1. The lower the IQ the lower the male : female ratio becomes [48]. In some studies the prevalence of autism is higher in whites than in blacks [49] and has raised the issue of racial disparity in diagnosis. However, a lower prevalence for blacks due to genetic differences is an alternate explanation. In other studies, this apparent racial disparity has not been found [50]. Latinos have been found in some studies to have lower rates as well, although this has not been confirmed in all studies. In one California study [51], Hispanic women had a corrected relative risk similar to that for whites for having a child with autism (RRc = 1.1). In another study from California [52], however, the prevalence of autism identified by the Department of Developmental Services was 7.5 per 10 000 for Hispanics while the rate for whites was 12.5 per

Table 26.1 Some behavioural and educational interventions used in individuals with ASD.

Intervention	Description/rationale	Evidence[a]
Applied behaviour analysis (ABA)	Intensive one-on-one method of shaping behaviour using a system of rewards. Uses discrete trials – antecedent, behaviour (response) and consequence to the behaviour. Parents are taught as cotherapists	B
Denver method	Intensive, eclectic, developmental play-based approach, based on Piaget's theory of how children explore their worlds to learn concepts. It enhances functional communication in the context of naturally occurring activities. It also uses behaviour analytic techniques to reduce aberrant behaviours	C
DIR (Developmental, individual, difference, relationship – based)/ floortime/Greenspan method	One-on-one, child-directed play periods based on the premise that an exchange of emotional signals forms the basis for learning in childhood. Parents and teachers get down on the floor to enter the child's world, helping turn repetitive acts into playful interactions. Focus is on social skills and language. Child is moved up a symbolic ladder from shared attention, engagement, simple and complex gestures and problem solving to ideas and abstract thinking. Key elements: (i) self-regulation and shared attention, (ii) engagement and relating, (iii) two-way intentional communication, (iv) purposeful complex problem solving communication, (v) creating and elaborating symbols (ideas) and (vi) building bridges between symbols (ideas)	D
Treatment and Education of Autistic and related Communication – handicapped CHildren (TEACCH)	Special education programme. Development of instruction and supports based on each individual's skills, interests and needs. Teachers create activities and environments that are organised to emphasise meaningfulness. (1) Focuses on structural teaching, especially independent work skills. (2) Emphasises strategies to enhance visual processing, including (i) the physical structure of the classroom, (ii) the use of visual activity schedule to help children anticipate future events, (iii) visual organisation of the work materials to teach the tasks and their sequences and (iv) a visual system to teach complicated skills such as language and imitation. (3) Involves the teaching of a communication system based on gesture, pictures, signs or printed words. (4) Teaches preacademic skills (colours, numbers, shapes, drawing, writing and assembly). (5) Encourages parents to work as co-therapists with their child in the home using the same techniques and materials	C
Alternative communication		
Picture exchange communication system (PECS)	PECS: Based on behavioural principles of stimulus, response and reward, to help facilitate functional communication. Children give the picture of a desired item to a 'teacher' who exchanges the card for the actual item requested, for example a banana	C
Facilitated communication (FC)	FC: Children learn to communicate by typing on a keyboard or pointing at letters, images or other symbols to represent messages with the direct help of an aid. FC includes physical and emotional support to an individual who has difficulties with speech and with intentional pointing (i.e. unassisted typing). Most evidence suggests that the facilitator (though usually unintentionally) is responsible for the messages, and not the child	B

Table 26.1 (cont.)

Sensory integration therapy	Sensory integration is the neurological process that allows an individual to organise internal and environmental sensations in order to regulate and function efficiently in the environment. Sensory integration therapy focuses on improving the child's abilities to take in and process sensory information, and to have more appropriate behavioural responses. Activities may include swinging, dancing to music, playing in boxes filled with beans, crawling through tunnels, building with clay or Play-Doh, hitting swinging balls, spinning on a chair and balancing	C
Social skills training		
Social stories (SS)	SS: Short, individualised narratives, written to help a student understand an activity and its associated behavioural expectations. Gives the child positive examples of what to do in a given situation, rather than what not to do	C
Social skills peer groups (SSPGs)	SSPG: Uses cognitive and behavioural approaches. Includes didactic instruction, role-playing, feedback, social stories and visual supports	C

[a]Levels of Evidence [43]
A – based on high-quality randomised controlled trials (RCTs) or high-quality quantitative systematic review(s).
B – based on non-randomised clinical trial, lower quality RCT or other type of study (like case-control or cohort).
C – based on some evidence, for example case series.
D – based on expert opinion.

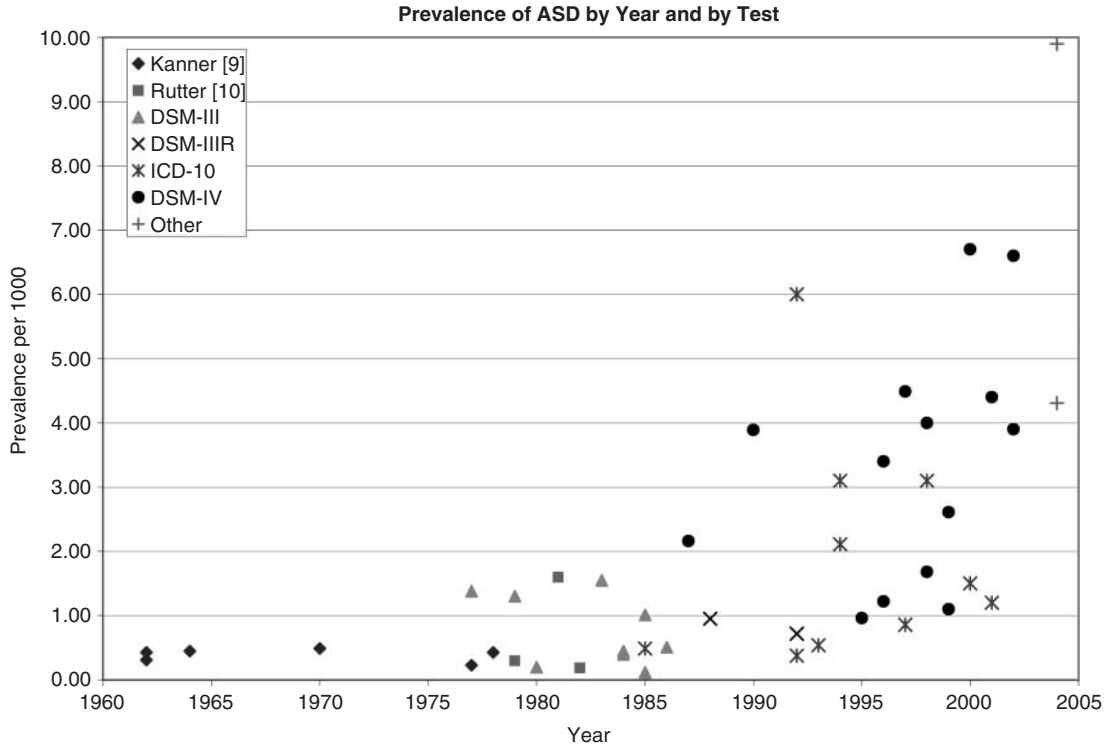

Fig 26.4 Reported prevalence of ASD by year of actual data collection and specific test used to identify cases.

10 000. Autism also is higher in children who were born prematurely, who had birth injury including hypoxic ischaemic encephalopathy [53], and who were born after prenatal maternal stress [54].

Earlier studies reported a higher prevalence of autism among children from higher socioeconomic status (SES). It is not clear whether this association reflects a link to aetiology or a link to case identification (ascertainment bias). In a case–control study from Atlanta, higher maternal education and higher median family income were significantly associated with autism without MR, but not associated with autism with MR [55]. In one study based on parent-identified ASD, poor children appeared to be diagnosed at a later age than children whose families were above the poverty level [56]. However, other studies, including one from Denmark where access to health care is universal and free, have found no differences based on SES [57].

26.7 Genetic factors

ASD has a large genetic component. For instance, concordance in monozygotic twins is as high as 70% (and is close to 0 in dizygotic twins) [58]. The prevalence of autistic disorder among siblings of individuals with autistic disorder ranges from 2 to 14% [59]. This is 20 times higher than in the general population, but much lower than in single-gene conditions. When the 'broader autism phenotype' [60] is considered, about 20% of siblings who have ASD will have this phenotype [61]. Parents of children with ASD also are more likely to have this broader phenotype [62]. In addition, parents who have bipolar disorder or schizophrenia are more likely to have children on the spectrum, which some believe is related to copy number variations affecting the same genes [63]. The male dominance in ASD has not been explained by genetic studies and may be related to the effects of prenatal testosterone on the developing brain [64].

ASD is a heterogeneous group of disorders with comorbid conditions like mental retardation. This makes it difficult to determine whether any associations between genetic risk factors and ASD are specific to more homogeneous subgroups such as children with ASD and mental retardation. The genetic mechanisms leading to changes in neurologic mechanisms have not been elucidated. More than 25 different loci that may be considered autism susceptibility candidate genes have been identified and many more implicated loci are under investigation [65]. However, all together they only account for 10% of individuals with ASD [66].

26.8 Public health impact

ASDs are common, affecting more than 1% of school-aged boys. Children with ASD use more health and educational resources than those without ASD. They also lead to lost opportunities for their families, such as the mother who cannot return to work because she has to watch her child. Montes and Halterman estimated that the average loss of annual income associated with having a child with ASD was $6200 for an American family [67]. These researchers also found that 39% of the parents of children with ASD reported that child care problems had greatly affected their employment decisions; this effect was three times larger than the effect of poverty [68].

Assuming a prevalence of 5 per 10 000, Järbrink and Knapp [69] estimated the annual societal cost of autism for the United Kingdom in 2001 to exceed £1 billion. The lifetime cost for a person with autism exceeded £2.4 million; the main costs were for living support and day activities. In a subsequent study in Sweden, Järbrink [70] estimated that the additional annual societal cost due to autism was €50 000 per child. Parents of these children spent about 1000 hours per year additional time caring for and supporting them. Ganz estimated that the lifetime per capita incremental societal cost of autism in the United States was $3.2 million in 2003 [71].

One treatment, ABA, which has been studied the most, has been shown to be effective in improving cognition, and social skills while decreasing behavioural problems. However, it requires intensive one-to-one intervention with the child. In the original studies, Lovaas *et al.* [72] children received 40 hours of intervention per week. This utilises significant community resources. A recent intervention using the Denver model (an amalgam of ABA and other interventions) was estimated to cost $50,000 per year

per child [73]. Children in schools with ASD use resources including special education, therapy services (e.g. speech and occupational therapy), aides and psychologists. Some individuals with more severe ASD move to institutional settings, especially when they become adults. This increases costs to society as well. In one study of institutionalised people in Sweden more than 13% had autism [74]. Many adults with ASD are unemployed, which also has economic costs to society.

Another public health impact of the increase in children diagnosed with autism has been a decrease in immunisation rates. Parents are choosing to delay vaccination of their children or follow alternate vaccine schedules. In the United Kingdom the rate of immunisation with MMR has decreased significantly; in 1998 56 cases of measles were reported; in 2007 1348 cases were reported [75]. Unlike undervaccinated children, unvaccinated children are more likely to be white, live in higher income households and have a married mother with a college education [76]. They choose not to have their children vaccinated, mostly because they fear that the vaccines will cause autism.

26.9 Associations and causal factors

Prenatal conditions including maternal infection with rubella, and exposure to valproic acid, thalidomide and misoprostol have been linked to ASD in the offspring. Congenital disorders of the cerebellum and brainstem like Joubert's syndrome and Moebius sequence also have been associated with ASD. Disorders of immunity in the affected individual have been suggested as aetiological factors for autism, which formed the basis of the studies on MMR vaccine. Several large epidemiological studies have shown no association between MMR vaccines and ASD. A Cochrane review of the MMR vaccine [77] concluded that exposure to MMR was unlikely to be associated with autism. The Institute of Medicine (IOM) issued a statement indicating that no reliable information linked MMR vaccine in the majority of individuals to ASD [78]. The possibility that other types of inflammations or autoimmunity are involved in ASD continues to be investigated.

Significant variation in the rates of autism among US states has suggested the possibility of an environmental trigger. Exposure to toxins, including mercury, have been suggested as causes of ASD. Several vaccines given to children contained methyl mercury (thimerosal) and were felt by some to contribute to the increase in ASD. In 1999 thimerosal was removed from most commonly given vaccines (except for killed influenza and RhoGam). Despite this, the prevalence of ASD has continued to rise [79]. Prenatal exposure to thimerosal-containing anti-D immune globulins (RhoGam) has been shown not to increase the risk of autism [80]. The IOM also stated that mercury was not a factor in the occurrence of ASD [78]. Several studies implicating exposure to pesticides have been published [81, 82]. One study has linked ASD with annual rainfall in three US states [83], although the likelihood of ecological fallacies in this study has been raised. For example, rates of medical specialists were higher in the areas of greater rainfall; these areas also were more likely to be urban, which is a factor previously associated with higher rates of autism [47].

26.10 Future directions

Epidemiology provides data that are vital for the prevention and control of disease. It has a public health function – to monitor and reduce the burden of disease on the community; and it has a scientific function – to understand the causes of a condition. ASDs are a heterogeneous group of conditions that have shown a dramatic increase in occurrence. However, our knowledge of aetiologies and therapies regarding ASD is unsatisfactory. Epidemiology can help clarify our understanding and monitor the impact of ASD. However, the studies need to be scientifically rigorous. Well accepted criteria for a sound prevalence study include the following: specification of the target population, valid sampling, adequate sample size, adequate response rate, information on non-responders, valid and reliable disease definition, measurement with valid instruments and consistency of measurement across sites with reduction of observer bias [83].

Many of the current studies of ASD do not meet these criteria, especially with regard to valid and

reliable disease definition, which have changed over time. ASDs represent a continuum of behaviourally defined conditions that are diagnosed through clinical observations. The complex nature of these behaviourally defined disorders, coupled with the current lack of genetic or biological markers for early and consistent identification, make epidemiologic investigation challenging. One future step that could dramatically improve these studies would be to find biological markers (biomarkers) like messenger RNA, genetic differences or patterns of enzymes and proteins (proteomics) that could help identify individuals who have ASD. Technological improvements in molecular genetics have made the collection of samples for DNA, including high-resolution DNA microarray, feasible in large field studies using cheek scrapings or small blood samples from finger sticks. They also have made testing for candidate genes economically feasible for large samples.

Yet, because of the heterogeneity of ASD, it is likely that even when biological or genetic markers are found they will not be present in all individuals with ASD. Breaking down samples into subgroups with specific patterns (endophenotypes) such as people who have autistic disorder with mental retardation and a history of regression, or people with high-functioning Asperger's syndrome and deficits in attention, motor control and perception (DAMP) [85] may allow more consistent identification and new discoveries into the aetiology of the conditions.

Current work to develop multiple source surveillance networks [86], and large cohort or case–control studies [87] can help in the near future by yielding more reliable information. Work for the more distant future includes developing international studies using a variety of techniques, such as records-based approaches with structured services and school records, registry-based approaches and screening – even to the extent of going door-to-door – in less developed countries. Finally, it is critical to use the information obtained in a way that will convince parents that the benefits of vaccines outweigh the risks.

26.11 Summary

The number of individuals with ASD has increased dramatically, which has increased the burden of care for schools, preschool programmes and healthcare facilities. Epidemiological studies to monitor the changes in prevalence and provide insight into the causes and impact of ASD have been limited by methodological problems. Some of the increase in prevalence can be attributed to (i) intentionally broadened diagnostic criteria, (ii) greater public awareness and (iii) improved case finding. While these factors explain more than half the excess of cases, they do not completely explain the observed increases. It appears that ASDs are increasing with no sign yet of levelling off. Earlier low-powered studies to provide insights on aetiology have implicated the measles and MMR vaccines as well as thimerosal. Even though subsequent studies have not supported these earlier scientifically weak findings, the confidence of the public has been shaken and fewer individuals are being adequately immunised. Future studies that better define ASDs and examine subgroups should help monitor the impact of these conditions and provide insight into aetiologies. If information from these studies is used wisely, it could restore faith in vaccines as well as improve the lives of people with ASD.

References

[1] Autism and Developmental Disabilities Monitoring Network Surveillance Year 2006 Principal Investigators; Centers for Disease Control and Prevention (CDC). (2009) Prevalence of autism spectrum disorders - Autism and Developmental Disabilities Monitoring Network, United States, 2006. *MMWR Surveill Summ*. 18, **58** (10), 1–20.

[2] Kogan, M.D., Blumberg, S.J., Schieve, L.A., *et al*. (2009) Prevalence of parent-reported diagnosis of autism spectrum disorder among children in the US, 2007. *Pediatrics*, **124** (5), 1395–403.

[3] 107th Congress House Hearings (2002) The Autism Epidemic – is the NIH and CDC Response Adequate? Hearing before the Committee on Government Reform House of Representatives, One Hundred Seventh Congress, Second Session, April 18, 2002. Serial No. 107-74. From the US Government Printing Office via GPO Access [Internet]. Available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_house_hearings&docid=f:80356.wais (accessed 1 October 2010).

[4] Masland, M. (2005) Autism: the Hidden Epidemic; More US Families in the Grip of

Autism. MSNBC February 23. Available at: http://www.msnbc.msn.com/id/6844737/ (accessed 1 October 2010).

[5] KCTS9 (2008) Autism Epidemic, December 5. Available at: http://www.kcts9.org/video/autism-epidemic (accessed 1 October 2010).

[6] Pangorn, J. and Baker, S. (2005) *Autism: Effective Biomedical Treatments (Have We Done Everything We Can For This Child?): Individuality in an Epidemic*, Autism Research Institute, San Diego.

[7] Cavagnaro, A.T. (2009) *Autistic Spectrum Disorders: Changes in the California Caseload. An Update: June 1987–2007*, Department of Developmental Services, California Health and Human Services Agency, Sacramento, CA, Available at: www.dds.ca.gov (accessed 1 October 2010).

[8] Hertz-Picciotto, I. and Delwiche, L. (2009) The rise in autism and the role of age at diagnosis. *Epidemiology*, **20** (1), 84–90.

[9] Kanner, L. (1943) Autistic disturbances of affective contact. *Nerv. Child.*, **2**, 217–250.

[10] Rutter, M. (1978) Diagnosis and definition of childhood autism. *J. Autism. Child. Schizophr.*, **8**, 139–161.

[11] Frith, U. (1991) Asperger and his syndrome, in *Autism and Asperger Syndrome* (ed. U. Frith), Cambridge University Press, Cambridge, pp. 1–36.

[12] Waterhouse, L. (2009) Autism is a Portmanteau syndrome. *Neuropsychol. Rev.*, **19** (2), 275–276.

[13] American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders*, revised 3rd edn, American Psychiatric Association, Washington, DC.

[14] American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn, American Psychiatric Association, Washington, DC.

[15] Gernsbacher, M.A., Dawson, M. and Goldsmith, H.H. (2005) Three reasons not to believe in an autism epidemic. *Curr. Dir. Psychol. Sci.*, **14**, 55–58.

[16] Shattuck, P.T. (2006) The contribution of diagnostic substitution to the growing administrative prevalence of autism in US special education. *Pediatrics*, **117** (4), 1028–1037.

[17] Coo, H., Ouellette-Kuntz, H., Lloyd, J.E. *et al.* (2008) Trends in autism prevalence: diagnostic substitution revisited. *J. Autism Dev. Disord.*, **38** (6), 1036–1046.

[18] Palfrey, J.S. and Rodman, J.S. (1999) Legislation for the education of children with disabilities, in *Developmental-Behavioral Pediatrics*, 3rd edn (eds M.D. Levine, W.B. Carey and A.C. Crocker), W. B. Saunders, Philadelphia, PA, pp. 869–872.

[19] Lord, C., Risi, S., Lambrecht, L. *et al.* (2000) The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J. Autism Dev. Disord.*, **30** (3), 205–223.

[20] Luyster, R., Gotham, K., Guthrie, W. *et al.* (2009) The Autism diagnostic observation schedule-toddler module: a new module of a standardized diagnostic measure for autism spectrum disorders. *J. Autism Dev. Disord.* **39** (9), 1305–1320.

[21] Battaglia, A. and Carey, J.C. (2006) Etiologic yield of autistic spectrum disorders: a prospective study. *Am. J. Med. Genet. C Semin. Med. Genet.*, **142C** (1), 3–7.

[22] Centers for Disease Control and Prevention (2007) Prevalence of autism spectrum disorders – Autism and developmental disabilities monitoring network, 14 sites, United States, 2002. Surveillance summaries, February 9, 2007. *Morb. Mortal. Wkly. Rep.*, **56** (SS-1), 12–27.

[23] American Psychiatric Association (2000) *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn, text revision, American Psychiatric Association, Washington, DC.

[24] Newschaffer, C.J., Falb, M.D. and Gurney, J.G. (2005) National autism prevalence trends from United States special education data. *Pediatrics*, **115** (3), e277–e282.

[25] Centers for Disease Control and Prevention (2006) Parental report of diagnosed autism in children aged 4–17 years – United States, 2003–2004. *Morb. Mortal. Wkly. Rep.*, **55**, 481–485.

[26] Barbaresi, W.J., Colligan, R.C., Weaver, A.L. *et al.* (2009) The incidence of clinically diagnosed versus research-identified autism in Olmsted County, Minnesota, 1976–1997: results from a retrospective, population-based study. *J. Autism. Dev. Disord.*, **39** (3), 464–470.

[27] Mattila, M.L., Kielinen, M., Jussila, K. *et al.* (2007) An epidemiological and diagnostic study of Asperger syndrome according to four sets of diagnostic criteria. *J. Am. Acad. Child Adolesc. Psychiatry*, **46** (5), 636–646.

[28] de Bildt, A., Sytema, S., Kraijer, D. *et al.* (2005) Prevalence of pervasive developmental disorders in children and adolescents with mental retardation. *J. Child Psychol. Psychiatry*, **46** (3), 275–286.

[29] McConachie, H. and Diggle, T. (2007) Parent implemented early intervention for young children with autism spectrum disorder: a systematic review. *J. Eval. Clin. Pract.*, **13** (1), 120–129.

[30] Mandell, D.S., Novak, M.M. and Zubritsky, C.D. (2005) Factors associated with age of diagnosis among children with autism spectrum disorders. *Pediatrics*, **116** (6), 1480–1486.

[31] Johnson, C.P. and Myers, S.M., American Academy of Pediatrics Council on Children With Disabilities (2007) Identification and evaluation of children

with autism spectrum disorders. *Pediatrics*, **120** (5), 1183–1215.

[32] Williams, J. and Brayne, C. (2006) Screening for autism spectrum disorders: what is the evidence? *Autism*, **10** (1), 11–35.

[33] Wiggins, L.D., Rice, C.E. and Baio, J. (2009) Developmental regression in children with an autism spectrum disorder identified by a population-based surveillance system. *Autism*, **13** (4), 357–374.

[34] Wakefield, A.J., Murch, S.H., Anthony, A. *et al.* (1998) Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet*, **351** (9103), 637–641.

[35] Deer, B. (2009) Hidden records show MMR truth; A *Sunday Times* investigation has found that altered data was behind the decade-long scare over vaccination. *Sunday Times (Lond.)*, 6–7 http://www.timesonline.co.uk/tol/life_and_style/health/article5683671.ece.

[36] Murch, S.H., Anthony, A., Casson, D.H. *et al.* (2004) Retraction of an interpretation. *Lancet*, **363** (9411), 750.

[37] Florida Institute of Technology (2008) Survey Confirms Parents' Fears, Confusion Over Autism, October 03. Available at http://www.fit.edu/newsroom/news/3705/florida_tech_dedicates_scott_center_for_autism_treatment/ (cited October 27, 2010).

[38] Cox, A., Klein, K., Charman, T. *et al.* (1999) Autism spectrum disorders at 20 and 42 months of age: stability of clinical and ADI-R diagnosis. *J. Child Psychol. Psychiatry*, **40** (5), 719–732.

[39] Kleinman, J.M., Ventola, P.E., Pandey, J. *et al.* (2008) Diagnostic stability in very young children with autism spectrum disorders. *J. Autism Dev. Disord.*, **38** (4), 606–615.

[40] Howlin, P., Goode, S., Hutton, J. *et al.* (2004) Adult outcome for children with autism. *J. Child Psychol. Psychiatry*, **45** (2), 212–229.

[41] Pickett, J.A., Paculdo, D.R., Shavelle, R.M. *et al.* (2006) 1998–2002 update on 'Causes of death in autism'. *J. Autism Dev. Disord.*, **36** (2), 287–288.

[42] Shavelle, R.M., Strauss, D.J. and Pickett, J. (2001) Causes of death in autism. *J. Autism Dev. Disord.*, **31** (6), 569–576.

[43] Centre for Evidenced Based Medicine (2009) Oxford Centre for Evidence-based Medicine–Levels Of Evidence, March. Available at: http://www.cebm.net/index.aspx?o=1025 (accessed 1 October 2010).

[44] Myers, S.M. and Johnson, C.P., American Academy of Pediatrics Council on Children With Disabilities (2007) Management of children with autism spectrum disorders. *Pediatrics*, **120** (5), 1162–1182.

[45] Levy, S.E. and Hyman, S.L. (2008) Complementary and alternative medicine treatments for children with autism spectrum disorders. *Child. Adolesc. Psychiatry Clin. N. Am.*, **17** (4), 803–820.

[46] Fombonne, E., Zakarian, R., Bennett, A. *et al.* (2006) Pervasive developmental disorders in Montreal, Quebec, Canada: prevalence and links with immunizations. *Pediatrics*, **118** (1), e139–e150.

[47] Williams, J.G., Higgins, J.P. and Brayne, C.E. (2006) Systematic review of prevalence studies of autism spectrum disorders. *Arch. Dis. Child.*, **91** (1), 8–15.

[48] Fombonne, E. (1995) Epidemiological studies of pervasive developmental disorders, in *Handbook of Autism and Pervasive Developmental Disorders* (eds F. Volkmar, R. Paul, A. Klin, and D. Cohen), John Wiley & Sons, Inc., New York, pp. 42–69.

[49] Mandell, D.S., Listerud, J., Levy, S.E. and Pinto-Martin, J.A. (2002) Race differences in the age at diagnosis among medicaid-eligible children with autism. *J. Am. Acad. Child Adolesc. Psychiatry*, **41** (12), 1447–1453.

[50] Nicholas, J.S., Charles, J.M., Carpenter, L.A. *et al.* (2008) Prevalence and characteristics of children with autism-spectrum disorders. *Ann. Epidemiol.*, **18** (2), 130–136.

[51] Croen, L.A., Grether, J.K. and Selvin, S. (2002) Descriptive epidemiology of autism in a California population: who is at risk? *J. Autism Dev. Disord.*, **32** (3), 217–224.

[52] Croen, L.A., Grether, J.K., Hoogstrate, J. *et al.* (2002) The changing prevalence of autism in California. *J. Autism Dev. Disord.*, **32** (3), 207–215.

[53] Brimacombe, M., Ming, X. and Lamendola, M. (2007) Prenatal and birth complications in autism. *Matern. Child Health J.*, **11** (1), 73–79.

[54] Kinney, D.K., Miller, A.M., Crowley, D.J. *et al.* (2008) Autism prevalence following prenatal exposure to hurricanes and tropical storms in Louisiana. *J. Autism Dev. Disord.*, **38** (3), 481–488.

[55] Bhasin, T.K. and Schendel, D. (2007) Sociodemographic risk factors for autism in a US metropolitan area. *J. Autism Dev. Disord.*, **37** (4), 667–677.

[56] Liptak, G.S., Benzoni, L.B., Mruzek, D.W. *et al.* (2008) Disparities in diagnosis and access to health services for children with autism: data from the National Survey of Children's Health. *J. Dev. Behav. Pediatr.*, **29** (3), 152–160.

[57] Larsson, H.J., Eaton, W.W., Madsen, K.M. *et al.* (2005) Risk factors for autism: perinatal factors, parental psychiatric history, and socioeconomic status. *Am. J. Epidemiol.*, **161** (10), 916–925.

[58] Steffenburg, S., Gillberg, C., Hellgren, L. *et al.* (1989) A twin study of autism in Denmark, Finland, Iceland, Norway and Sweden. *J. Child Psychol. Psychiatry*, **30**, 405–416.

[59] Bailey, A., Palferman, S., Heavey, L. *et al.* (1998) Autism: the phenotype in relatives. *J. Autism Dev. Disord.*, **28**, 369–392.

[60] Losh, M., Adolphs, R., Poe, M.D. *et al.* (2009) Neuropsychological profile of autism and the broad autism phenotype. *Arch. Gen. Psychiatry.*, **66** (5), 518–526.

[61] Piven, J., Palmer, P., Jacobi, D. *et al.* (1997) Broader autism phenotype: evidence from a family history study of multiple-incidence autism families. *Am. J. Psychiatry*, **154**, 185–190.

[62] Smith, C.J., Lang, C.M., Kryzak, L. *et al.* (2009) Familial associations of intense preoccupations, an empirical factor of the restricted, repetitive behaviors and interests domain of autism. *J. Child Psychol. Psychiatry*, **50** (8), 982–90.

[63] O'Donovan, M.C., Craddock, N.J. and Owen, M.J. (2009) Genetics of psychosis; insights from views across the genome. *Hum. Genet.* **126** (1), 3–12.

[64] Knickmeyer, R.C. and Baron-Cohen, S. (2006) Fetal testosterone and sex differences in typical social development and in autism. *J. Child Neurol.*, **21**, 825–845.

[65] Bill, B.R. and Geschwind, D.H. (2009) Genetic advances in autism: heterogeneity and convergence on shared pathways. *Curr. Opin. Genet. Dev.*, **19** (3), 271–278.

[66] Muhle, R., Trentacoste, S.V. and Rapin, I. (2004) The genetics of autism. *Pediatrics*, **113** (5), e472–e486.

[67] Montes, G. and Halterman, J.S. (2008) Association of childhood autism spectrum disorders and loss of family income. *Pediatrics*, **121** (4), e821–e826.

[68] Montes, G. and Halterman, J.S. (2008) Child care problems and employment among families with preschool-aged children with autism in the United States. *Pediatrics*, **122** (1), e202–e208.

[69] Järbrink, K. and Knapp, M. (2001) The economic impact of autism in Britain. *Autism*, **5** (1), 7–22.

[70] Järbrink, K. (2007) The economic consequences of autistic spectrum disorder among children in a Swedish municipality. *Autism*, **11** (5), 453–463.

[71] Ganz, M.L. (2007) The lifetime distribution of the incremental societal costs of autism. *Arch. Pediatr. Adolesc. Med.*, **161** (4), 343–349.

[72] Lovaas, O.I., Schreibman, L. and Koegel, R.L. (1974) A behavior modification approach to the treatment of autistic children. *J. Autism Child. Schizophr.*, **4** (2), 111–129.

[73] Dawson, G., Rogers, S., Munson, J. *et al.* (2010) Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. *Pediatrics*, **125** (1), e17–23.

[74] Anckarsater, H., Nilsson, T., Saury, J.M. *et al.* (2008) Autism spectrum disorders in institutionalized subjects. *Nord. J. Psychiatry*, **62** (2), 160–167.

[75] Choi, Y.H., Gay, N., Fraser, G. *et al.* (2008) The potential for measles transmission in England. *BMC Public Health*, **8**, 338.

[76] Omer, S.B., Salmon, D.A., Orenstein, W.A. *et al.* (2009) Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. *N. Engl. J. Med.*, **360** (19), 1981–1988.

[77] Demicheli, V., Jefferson, T., Rivetti, A. *et al.* (2005) Vaccines for measles, mumps and rubella in children. *Cochrane. Database Syst. Rev.*, (4), (Art. No. CD004407, DOI: 10.1002/14651858.CD004407.pub2).

[78] Institute of Medicine (2004) Immunization Safety Review: Vaccines and Autism, May 17. Available at http://www.iom.edu/CMS/3793/4705/20155.aspx (accessed 1 October 2010).

[79] Offit, P.A. (2007) Thimerosal and vaccines – a cautionary tale. *N. Engl. J. Med.*, **357** (13), 1278–1279.

[80] Croen, L.A., Matevia, M., Yoshida, C.K. *et al.* (2008) Maternal Rh D status, anti-D immune globulin exposure during pregnancy, and risk of autism spectrum disorders. *Am. J. Obstet. Gynecol.*, **199** (3), 234.e1–234.e6.

[81] McGovern, V. (2007) Autism and agricultural pesticides. Integrating data to track trends. *Environ. Health Perspect.*, **115** (10), A504.

[82] Ritvo, E.R., Mason-Brothers, A., Freeman, B.J. *et al.* (1990) The UCLA-University of Utah epidemiologic survey of autism: the etiologic role of rare diseases. *Am. J. Psychiatry*, **147** (12), 1614–1621.

[83] Waldman, M., Nicholson, S., Adilov, N. *et al.* (2008) Autism prevalence and precipitation rates in California, Oregon, and Washington counties. *Arch. Pediatr. Adolesc. Med.*, **162** (11), 1026–1034.

[84] Radulescu, M., Diepgen, T.L., Weisshaar, E. *et al.* What Makes a Good Prevalence Survey? Updated .http://www.blackwellpublishing.com/medicine/bmj/dermatology/pdfs/prevalence_survey.pdf (accessed 1 October 2010).

[85] Sturm, H., Fernell, E. and Gillberg, C. (2004) Autism spectrum disorders in children with normal intellectual levels: associated impairments and subgroups. *Dev. Med. Child Neurol.*, **46** (7), 444–447.

[86] Van Naarden, B.K., Pettygrove, S., Daniels, J. *et al.* (2007) Evaluation of a methodology for a collaborative multiple source surveillance network for autism spectrum disorders–Autism and Developmental Disabilities Monitoring Network, 14 sites, United States, 2002. *MMWR Surveill. Summ.*, **56** (1), 29–40.

[87] Hertz-Picciotto, I., Croen, L.A., Hansen, R. *et al.* (2006) The CHARGE study: an epidemiologic investigation of genetic and environmental factors contributing to autism. *Environ. Health Perspect.*, **114** (7), 1119–1125.