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Message from Subspecialty Division

Autism Spectrum Disorders (ASD) consist of a group of clinical behavioral syndromes characterized by both quantitative and qualitative impairments in reciprocal social interaction and communication, and the presence of stereotyped behaviors, interests, and activities[1,2]. Qualitative abnormalities are pervasive, affecting the individual's various domains of development and his/her functioning in almost all aspects of life. Being a complex neuro-developmental disorder with no single etiology and no known "cure", it is both vital and challenging for clinicians to keep abreast of new developments and knowledge on early identification, diagnostic issues, as well as the current state-of-the-art intervention and management approaches, while maintaining a skeptical, scientific and evidence-based attitude.

The current issue discusses the local prevalence and clinical pattern of Autism Spectrum Disorders (ASD) based on data collected from our in-house electronic database, the Child Assessment Service Information System (CASIS) between the year of 2003 to 2005. A special highlight is especially devoted to a critical review and discussion of the recently controversial biomedical treatment approaches to ASD.

CAS Epidemiological Data on Autistic Spectrum Disorders from 2003 to 2005

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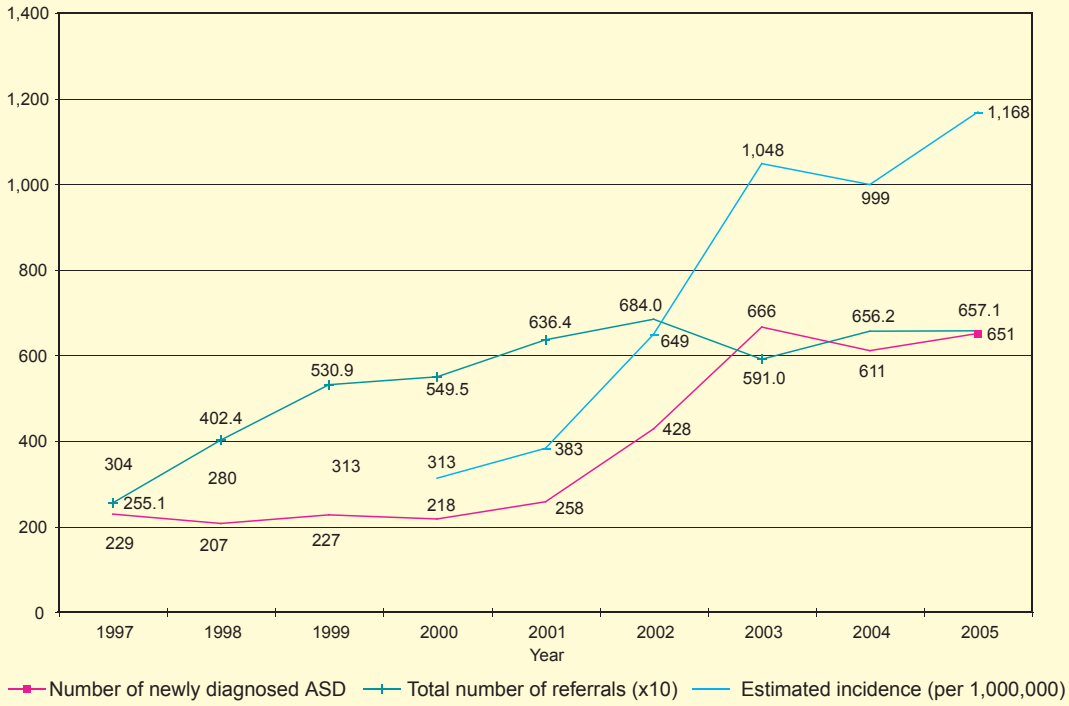
A Rising Incidence Rate

It is evident from many epidemiological studies that there is a rising trend of newly diagnosed cases of ASD both globally and locally in Hong Kong .[3-8] Methodological differences in case definition and case-finding procedures make between-survey comparisons difficult to perform. However, from recent overseas studies, a best estimate between 60 to 93 per 10,000 people can be derived from the prevalence of ASD when taken all forms of ASD into account.[9] There is a lack of academic studies to establish the prevalence of ASD in Hong Kong, but an estimate of 5 per 10,000 in Hong Kong population according to a population-based survey by the Census of Statistics Department was obtained in 2001. According to the special preschool enrolment and waitlist statistics of the Social Welfare Department in 2004, an incidence of 2.3 per 1,000 students was obtained.

This issue gives an overview on the epidemiological data collected from CASIS between the year of 2003 to 2005. Three subgroup conditions within the spectrum were included in this analysis, namely childhood autism (F84.0), atypical autism (F84.1), and

Figure 1. Trend in incidence and number of referrals, 1997-2005



the Asperger's Syndrome (F84.5), using the ICD-10 classification system. Out of the 1,920 incidence cases, 35% were diagnosed to have childhood autism, whereas 65% were diagnosed to have atypical autism and the Asperger's Syndrome, or other ASD conditions in brief.

Table 1 shows the number of cases diagnosed with ASD in Child Assessment Service (CAS) from the year of 1997 through 2005. It is noted that the number of cases seen and diagnosed of ASD have significantly increased over the years. 229 cases were diagnosed with ASD in 1997, whereas 651 cases were diagnosed in 2005, an increase of 184%. A drastic increase of 55% was noted between the year of 2002 and 2003, but the number of newly diagnosed cases tended to be stable between the years 2003-05.

Such drastic increase in figures may be alarming, but should not be over-emphasized. This might due to multitude of reasons, including the presence of more reliable databases, better early identification surveillance programs, increased parents and professional awareness, as well as changing diagnostic criteria, to name but a few.

Sources of Referral

Maternal and Child Health Centres (MCHC) and private practitioners were the major referral sources of ASD cases, representing 69% and 20% respectively of the total referrals (Table 1). A small proportion of referrals (11%) came from the Paediatrics Department of Hospital Authority and other parties including General Out-patient Clinics (GOPC), Student Health Service and Clinical Genetic Services of DH, Education and Manpower Bureau and Social Welfare Department.

Table 1. Number of children with ASD by source of referral, 2003-2005

Source of referral	2003 N (%)	2004 N (%)	2005 N (%)	Total N (%)
Department of Health (DH)	303 (70.0)	333 (68.5)	423 (73.3)	1,059 (70.8)
Family Health Service	296 (68.4)	315 (64.8)	415 (71.8)	1,026 (68.6)
Others units of DH	7 (1.6)	18 (3.7)	8 (1.4)	33 (2.2)
Private Practitioners	94 (21.7)	101 (20.8)	108 (18.7)	303 (20.3)
Hospital Authority (HA)	36 (8.3)	52 (10.7)	46 (8.0)	134 (9.0)

Note: Cases without valid source of referral information are excluded.

Reasons of Referral

The most common reasons for referral were language delay (46%), behavioural and emotional problems (30%) and developmental delay (19%) (Table 2). Other presenting problems such as hearing, speech, articulation, sensory and motor problems, as well as learning problems constitute a small percentage of the total referrals (5%).

Sex Ratio

As reported elsewhere, boys seemed to be more affected by the condition than girls

Table 2. Number of children with ASD by referral reason, 2003-2005

Referral reason	2003 N (%)	2004 N (%)	2005 N (%)	Total N (%)
Language problem	209 (48.0)	213 (43.6)	267 (46.3)	689 (45.9)
Behavioural/emotional problems	140 (32.2)	158 (32.4)	146 (25.3)	444 (29.6)
Developmental delay	64 (14.7)	83 (17.0)	132 (22.9)	279 (18.6)
Learning problem	9 (2.1)	12 (2.5)	13 (2.3)	34 (2.3)
Hearing problem	4 (0.9)	11 (2.3)	15 (2.6)	30 (2.0)
Articulation & speech problem	6 (1.4)	2 (0.4)	2 (0.3)	10 (0.7)
Motor problem	2 (0.5)	4 (0.8)	1 (0.2)	7 (0.5)
Visual problem	1 (0.2)	1 (0.2)	NA	2 (0.1)
At-risk	NA	2 (0.4)	NA	2 (0.1)

Note: Cases without valid referral reason information are excluded.
NA indicates not applicable.

(Table 3). The male to female ratio of all ASD conditions taken together was 7.6 to 1 in children below 12 years of age, which is higher than the figure of 4 to 1 reported elsewhere.[9] Coincidently, the male to female ratio is similar for both childhood autism and other ASD conditions when they were being scrutinized separately. According to some studies in the West, male to female ratio moves closer to 1:1 for children with autism who are profoundly retarded.[10] Because of the small numbers of females with autism and the need to control for intellectual functioning (IQ), small sample sizes have been a major limitation to many studies.

Table 3. Number of children with ASD by sex, 2003-2005

Sex	2003 N (%)	2004 N (%)	2005 N (%)	Total N (%)
Male	580 (87.9)	545 (89.5)	571 (87.7)	1,696 (88.3)
Female	80 (12.1)	64 (10.5)	80 (12.3)	224 (11.7)

Note: Cases without valid sex information are excluded.

Age of Referral

Referrals were made as early as 12 to 24 months old (Table 4). However, the majority of cases, diagnoses were made between 2 to 4 years old, with its peak at the age between 3 to 4 years old when the symptoms might be more notable and pervasive. Cases with full-blown autistic features tended to be referred at younger ages than cases on the milder end of ASD. Similar pattern was noted in cases of high functioning ASD who were referred when they entered school-age under a more demanding social and academic environment. For childhood autism (F84.0), only 10 % of the cases were diagnosed after 6, whereas 17% of cases of other ASD conditions (F84.1 and F84.5) were diagnosed after 6. Continuing work to sharpen parents' and professional's awareness of early indicators of ASD, as well as improvement of the sensitivity of assessment tools, especially for milder ASD cases are deemed imperative.

Table 4. Number of children with ASD by age, 2003-2005

Age group	2003 N (%)	2004 N (%)	2005 N (%)	Total N (%)
Childhood autism				
1 – < 2 years	13 (5.1)	20 (9.3)	19 (8.9)	52 (7.6)
2 – < 3 years	102 (39.8)	91 (42.5)	85 (39.9)	278 (40.7)
3 – < 4 years	53 (20.7)	37 (17.3)	53 (24.9)	143 (20.9)
4 – < 5 years	14 (5.5)	12 (5.6)	21 (9.9)	47 (6.9)
5 – < 6 years	49 (19.1)	26 (12.1)	14 (6.6)	89 (13.0)
6 – < 7 years	19 (7.4)	20 (9.3)	11 (5.2)	50 (7.3)
Above 7 years	6 (2.3)	8 (3.7)	10 (4.7)	24 (3.5)
Other ASD conditions				
0 – < 1 years	1 (0.2)	NA	NA	1 (0.1)
1 – < 2 years	14 (3.4)	21 (5.3)	29 (6.6)	64 (5.1)
2 – < 3 years	127 (31.0)	131 (33.0)	162 (37.0)	420 (33.7)
3 – < 4 years	69 (16.8)	85 (21.4)	100 (22.8)	254 (20.4)
4 – < 5 years	40 (9.8)	39 (9.8)	45 (10.3)	124 (10.0)
5 – < 6 years	78 (19.0)	55 (13.9)	37 (8.4)	170 (13.7)
6 – < 7 years	39 (9.5)	34 (8.6)	21 (4.8)	94 (7.6)
Above 7 years	42 (10.2)	32 (8.1)	44 (10.0)	118 (9.5)

Note: Cases without valid date of birth information are excluded.
NA indicates not applicable.

Common Associated Features

A number of associated features were reported with ASD. One of the commonly known co-morbidities is mental retardation. From the data collected between 2003 and 2005, the children's intellectual functioning was analysed at two points, at diagnosis and at review when pre-primary one assessment was conducted. Among the 666 newly diagnosed cases in 2003, 132 cases finished pre-primary one assessment at the time of data analysis. In CAS a formal assessment with documentation of intellectual functioning is usually conducted by clinical psychologists when the child reaches five years old. For young preschool cases, intellectual functioning is assessed by Paediatricians using developmental scales (e.g. Griffith's Scales of Mental Development).

Table 5. Intellectual functioning level at different developmental stages, 2003-2005

Intellectual functioning	2003 N (%)	2004 N (%)	2005 N (%)	Total N (%)
Childhood autism				
At preschool stage				
With significant global delay	72 (39.6)	88 (55.0)	107 (60.1)	267 (51.3)
Without significant global delay	110 (60.4)	72 (45.0)	71 (39.9)	253 (48.7)
At school stage				
With mental retardation	50 (69.4)	38 (70.4)	22 (62.9)	110 (68.3)
Without mental retardation	22 (30.6)	16 (29.6)	13 (37.1)	51 (31.7)
Other ASD conditions				
At preschool stage				
With significant global delay	46 (18.3)	57 (20.7)	71 (21.1)	174 (20.2)
Without significant global delay	205 (81.7)	219 (79.3)	265 (78.9)	689 (79.8)
At school stage				
With mental retardation	31 (20.0)	20 (16.8)	17 (16.7)	68 (18.1)
Without mental retardation	124 (80.0)	99 (83.2)	85 (83.3)	308 (81.9)

Table 5 shows the intellectual functioning of ASD cases diagnosed from 2003 through 2005. For childhood autism cases diagnosed at preschool stage, 51% had significant global delay while at school age, 68% were found to have mental retardation. For cases of other ASD conditions, regardless of age of diagnosis, around 20% had significant global delay or mental retardation.

The current findings seem to support previous research findings saying the distribution of limited intelligence or lower versus normal intelligence among the whole group of ASD was 70% to 30% respectively.[9] There tends to be a greater proportion of ASD cases to be functioning in the normal range of intelligence when cases of boarder phenotype are included in the analysis. Similar pattern were consistently found in the 132 review cases included in the analysis. For children with other ASD conditions, around 85% were functioning in the normal range of intelligence.

From the data, other common associated features reported were fine and gross motor problems. Epilepsy was encountered only uncommonly as a co-morbidity (1.1%) (Table 6).

Table 6. Types of ASD and associated clinical features, 2003-2005

Associated clinical features	2003 N (%)	2004 N (%)	2005 N (%)	Total N (%)
Childhood autism				
Gross motor problem	10 (3.9)	4 (1.9)	2 (0.9)	16 (2.3)
Epilepsy	NA	2 (0.9)	NA	2 (0.3)
Fine motor problem	15 (5.9)	5 (2.3)	6 (2.8)	26 (3.8)
Atypical autism				
Gross motor problem	15 (3.9)	20 (5.4)	22 (5.3)	55 (4.7)
Epilepsy	NA	1 (0.3)	1 (0.2)	2 (0.2)
Fine motor problem	37 (9.6)	29 (7.9)	35 (8.4)	101 (8.6)
Asperger's Syndrome				
Gross motor problem	10 (40.0)	12 (42.9)	6 (27.3)	28 (37.3)
Fine motor problem	13 (52.0)	11 (39.3)	8 (36.4)	32 (42.7)

Note: NA indicates not applicable.

School Placement

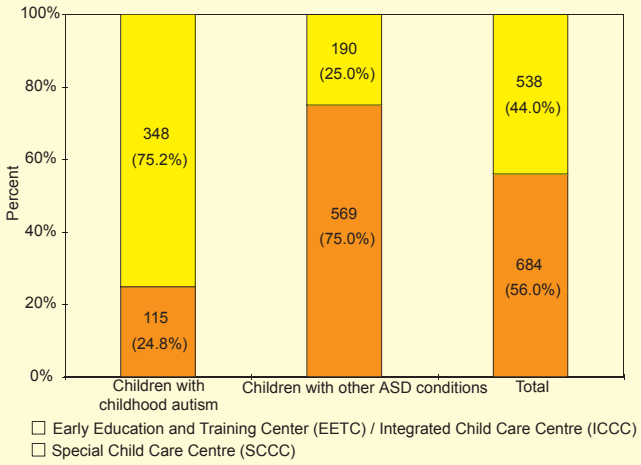
Placement recommendations take into consideration the child's overall cognitive, social adaptive functioning as well as the impact and severity of his/her autistic condition. However, sometimes it is a challenge to strike a balance between professional and parents' views in arriving at the most optimal advice for the child's placement, particularly when the views between the two are widely discrepant. In some cases, the parent's choice played more crucial role than child factors.

Figure 2 shows the distribution of preschool placement from 2003 to 2005 by types of ASD. For childhood autism cases, the ratio of cases enrolled in Special Child Care Centre (SCCC) to cases enrolled in Early Education and Training Centre (EETC)/Integrated Child Care Centre (ICCC) was 3:1. For cases of other ASD conditions, the ratio was reverse as 1:3. The ratio was 1:1.27 when cases of childhood autism and other ASD conditons were considered as a whole.

Figure 3 shows the distribution of preschool case placement from 2003 to 2005 by intellectual functioning. For cases enrolled in EETC/ICCC, only a small fraction (14%) had significant global delay. On the contrary, 55% of cases enrolled in SCCC had significant global delay.

For school-aged placement, placement arrangement seemed to match with the children's intellectual functioning. However, out of the 132 cases, 1 ASD case with moderate grade mental retardation and 1 case with limited intelligence finally opted for special school for mild grade mentally retarded children.10 ASD cases with mild grade mental retardation entered mainstream schools for various reasons, including parents' choice.

Figure 2. Percentage distribution of preschool placement by types of ASD, 2003-2005

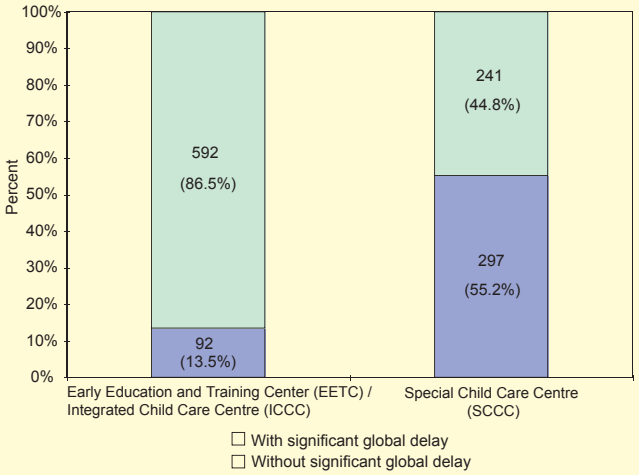


Socio-economic Status

Socio-economic status of the parents in terms of parents' level of education and occupation was analyzed. Majority of the parents' educational level has achieved Secondary School Level (62%), whereas 30% of them have acquired education level of Matriculation or above. As compared with the general population of Hong Kong,[11] with less than half having finished secondary school level (46%), a quarter have matriculation level or above, these statistical figures appear to show that parents of this group of children represent a somewhat

higher educational level than the general population. In terms of parents' occupation, the cases were dispersed across different occupations and socio-economic status. Twelve studies discussed in Fombonne's review paper[9] provided information on the social class of the families. Of these, four studies conducted before the year of 1980 reported an association between autism and social class or parental education. All studies with data collection thereafter provided no evidence for the association.

Figure 3. Percentage distribution of preschool placement by intellectual functioning, 2003-2005



Discussion

From the above analysis of recent statistics of diagnosed ASD cases in Child Assessment Service, we observed trends similar to those found elsewhere, the important ones being the rising trend of newly diagnosed cases, and prevalence of more affected boys than girls, the correlation between pervasiveness of autistic symptoms and mental retardation. The drastic increase in the number of ASD cases by years is striking. However, the prevalence rate of ASD in Hong Kong has not been well determined. On-going effort to collect more reliable information on prevalence and incidence rates of ASD in Hong Kong is important for long-term service planning and policy in Hong Kong. Does the rising incidence rate reflect a real epidemic of the condition? This is a complicated, multi-factorial issue yet to be answered and needs for further in-depth and systematic investigation. A more systematic management and documentation of clinical data in different settings and better agreement among clinicians in deriving diagnosis of ASD pave the first steps in achieving this.

Moreover, we noted that children with childhood autism and other broader phenotypes (i.e. atypical autism and the Asperger's Syndrome) might represent very different subtypes as revealed in their different cognitive profiling and symptomatology. Ongoing research for better understanding of the nature of the conditions, including the genetic, psycho-neurological underpinnings of the children with ASD, better diagnostic differentiation of different subtypes is valuable for devising more suitable intervention approaches for different children on the spectrums.

It should be stressed that the severity of the autistic condition is not always correlated with the level mal-adaptive functioning. In other words, one should not assume that children who are on the autistic spectrum with less autistic features (i.e. atypical autism and the Asperger's Syndrome) might suffer from fewer difficulties in their daily adaptive functioning. In view of the majority of children with high-functioning autism being placed in mainstream schools, there will be a greater challenge for educators to look into effective tailor-made strategies to enhance the learning potential and social adjustment of children in the mainstream. Earlier identification and intervention of children with milder autistic spectrum (broader phenotype) depend on professionals' knowledge, experience, and the availability of reliable screening and assessment tools.

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Biological Treatment for Children with Autism Spectrum Disorders (ASD)

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The treatment of autistic children has been a highly controversial area in recent years. Many complementary and alternative therapies (CAM) purport to address eradication of the cause of ASD, not just the symptoms as in conventionally prescribed treatments. Among the CAM, "biological treatment" that seeks to alter the physiology or processes causing autistic features, was commonly introduced to parents. In this article, some interesting issues on gastrointestinal treatment, nutritional supplements, immunotherapy and chelation therapy will be highlighted.

Gastrointestional Treatment

Food intolerance and elimination diets

Autistic children frequently show idiosyncratic eating habits. The possibility of food intolerance led to the recommendation on special diets that eliminate various substances, hoping to spare the physical discomforts and hence improve their behaviors. So far, no link has been found between gluten sensitivity celiac disease and autism.[1,2] While it would be plausible that some autistic children may have dietary protein intolerance, little evidence shows that such an intolerance is more prevalent within the autistic population. Preliminary studies on the use of elimination diets have failed to show any beneficial effect.[3,4] In recent years, gluten/casein free diet has been most commonly used.[5] It is based on the 'opioid excess theory' which postulates that autistic children have impaired function and permeability of the gastrointestinal system ("leaky gut syndrome") resulting in malabsorption of wheat fragments (gluten) or milk protein (casein) which, in theory, function as endogenous neuropeptides or neurotransmitters that affect brain function.[6] Three small scale clinical trials reported behavioral improvement of children with ASD while on the diet, but their results needed further replication before they could be generalised.[7-10]

Autism and measles-mumps-rubella vaccination (MMR) Some investigators have searched for measles virus infection in children with autism. It was based upon parental report that approximately 2/3 of autistic children referred for GI evaluation, who were subsequently found to have ileal lymphoid hyperplasia, had regressive-onset of their autistic symptoms following MMR vaccination. It was theorized that autistic enterocolitis secondary to viral infection from live-attenuated MMR vaccine might alter the gut permeability to potential neurotoxins, causing the onset of behavioral regression in autistic children.[11] Measles virus RNA has not only been found in ileal biopsy samples of autistic children with ileal lymphoid hyperplasia,[12,13] but also in children with chronic intestinal inflammation.[14] Hence the etiological link between GI inflammation and autism is still uncertain. The safety or efficacy of treatment of autistic children with long-term valacyclovir or other antiviral agents is uncertain, but bone marrow suppression is a concern.[15] In a large number of large scale epidemiological studies, causative relationship between autism and MMR vaccination could not be established.[16-20]

Gastrointestinal factors Gastrointestinal symptoms have been reported to be more prevalent among children with ASD (with a range of 17 to 86%!)[21], but there is no published data to support these claims. Furthermore, sound evidence is also lacking for consistent overgrowth of fungus or bacteria in intestinal tissue.[22]

Nutritional Supplements

Nutritional supplements including vitamins, minerals and other substances considered to be "natural" are available without prescriptions. These substances are believed to enhance neurotransmitter function by increasing availability of substrate or cofactors,[23] and/or to compensate for presumed biochemical deficits that may cause autism.[24] However, the evidence for deficits in the body of various endogenous vitamins and minerals in autistic children has been lacking.[25-27] The doses of supplements typically suggested are grossly higher than recommended daily allowance. There is limited data on long- or short-term side effects, and the clinical usefulness of these substances are in doubt.[15] Also, no consistent abnormality of trace elements has been reported in children with autism[28] and there is no scientific evidence for replacement therapy for these substances either.

Immunotherapy

The immune system has been suggested to play a role in the pathogenesis of autism.[29] The lack of cellular inflammatory infiltrates in the brains of children with autism may speak against the possibility of immune reaction, but the presence of autoantibodies to neural antigens is in favour of it.[30,31] Further research is needed in this area.

Detoxifi cation by Chelation Therapy

Lead poisoning There is no argument that acute lead encephalopathy, now rare in developed countries, significantly damages the immature brain and could be responsible for mental retardation, epilepsy, and behavioral disorders. The Centers for Diseases Control and Prevention of the United States (CDC) recommends that all children with developmental delays be screened for lead poisoning because even low level poisoning has measurable effects on cognition in group studies.[32] Hair analysis is not a reliable means to screen for lead poisoning, which requires a blood test.[33] One study found that the blood lead levels of 18 autistic children were higher than those of controls.[34] However, a more recent analysis was able to show a relationship between lead poisoning and the onset or acceleration of autism in only two out of six children.[35] Treatment of lead poisoning in autistic children is often followed by re-exposure,despite close monitoring of their environment.[36] Furthermore, chelation therapy with Dimercaptosuccinic acid (DMSA) failed to improve developmental function.[37,38]

Mercury poisoning The deleterious effects of high dose mercury poisoning on the brain in both infants and adults are well-known. However, no consistent association between ASD and administration with vaccines containing thimerosal (a ethylmercury derivative for vaccine stabilization) has been found.[39,40] Nevertheless, CDC recommended thimerosal to be removed from vaccines as soon as possible as part of a broader, precautionary effort to decrease overall mercury exposure.[41] With the launching of DTaP/iPV vaccine in Hong Kong in February 2007, all local childhood vaccines do not contain thimerosal. In Hong Kong, a case control study of autistic children showed that there was no significant difference between their hair and blood mercury levels when compared to normal children.[42]

Despite the absence of supportive evidence, some practitioners have started to use DMSA as a detoxifying agent, coupled with various minerals/vitamins/antioxidant supplements and treatment of gut infection/constipation. DMSA could have significant side effects such as bone marrow suppression, liver and kidney toxicity, and its use cannot be recommended. Data related to lead poisoning also indicates that neurological damage could not be affected by chelation at a later date.[43]

Conclusion

To conclude, it is clear that the vast majority of biological treatment modalities for ASD have not been evaluated with robust and well-designed randomized controlled trials. Most of them are scientifically unproven and potentially harmful. More scientifically rigorous research using stringent methodology is urgently needed to evaluate a number of promising approaches mentioned in this review, and novel ones that are yet to come. Lastly, during the counseling of families on complementary and alternative medicine, it is important to maintain a scientific perspective, to provide a balanced view on current status in interventions and therapeutic options, and guard against bias, and to establish and maintain a trusting relationship with families.[44]

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Recent Publications and Scientific Presentations

Publications

Mak RHL, Lam CCC, Ho CCY, **Wong MMY**, editors. A primer in common developmental disabilities: experience at Child Assessment Service, Hong Kong. Hong Kong: Government Logistics Department; 2006.

Leung C, Sanders M, Ip F, Lau J. Implementation of Triple P-Positive Parenting Program in Hong Kong: predictors of programme completion and clinical outcomes. Journal of Children's Services 2006;1(2):4-17.

Tsang SKM, Shek DTL, Lam LL, Tang F, Cheung PMP. Brief report: application of the TEACCH Program on Chinese pre-school children with autism--does culture make a difference? Journal of Autism and Developmental Disorders 2007;37(2):390-6.

Scientific Presentations

The following seminars were conducted at Hong Kong Cantonese Oral Language Assessment Scale (HKCOLAS) seminar and workshop series held on 16-17 September 2006:

- **Administering HKCOLAS and Test of Hong Kong Cantonese Grammar** by *Ng KH*.
- **Textual Comprehension Test** by *Chan BW*.
- **Lexical-Semantic Relations Test and Expressive Nominal Vocabulary Test** by *Chan WK*.
- **Word Definition Test** by *Man YH*.
- **Hong Kong Cantonese Articulation Test: Phonological development** by *Cheung SP*.
- **Nonword Repetition Test** by *Cheung SP*.

Specific language impairment: from infancy to adolescence on 19 October 2006 at the Hong Kong Society of Child Neurology and Developmental Paediatrics Neurodevelopmental Conference by *Man YH*.

Next Issue:

The next issue of CASER will be released in September 2007. The featured topic is on Dyslexia.