

# **PRIMAL HEALTH RESEARCH**

A NEW ERA IN HEALTH RESEARCH

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## **AFTER THE MMR FUSS**

### **AUTISM FROM A PRIMAL HEALTH RESEARCH PERSPECTIVE**

#### **IS THE EPIDEMIC OF AUTISM REAL?**

This is the primary question, since genetic factors have undoubtedly a key role. If the epidemic is real, this implies that environmental factors during the primal period also play an important role.

Until recently, many medical experts claimed that the increased prevalence of autism was simply an artifact of improved diagnostic and greater public awareness. They also emphasized that our understanding of autism has changed over the past decade. One of the changes has been the appreciation that several closely-related disorders exist; they share the same essential features but differ on specific symptoms, age of onset, or natural history. These disorders, which include Asperger syndrome, atypical autism, and disintegrative disorder are now conceptualised as "autism spectrum disorders". This explains why, according to recently published British estimates, the current rates of autism are 16 per 10 000; in fact these rates increase to 63 per 10 000 when all forms of autism spectrum disorders are included.<sup>(1)</sup> Debate remains about the validity and usefulness of a broad definition of autism.

autistic behaviour is associated with several specific genetic disorders, including fragile X disorder. But the mode of transmission does not follow any recognisable pattern, and, although several promising findings are based on candidate gene studies, actual susceptibility genes have not been identified.<sup>(4,5)</sup>

The year 2003 can be seen as a turning point since even public health bodies such as the US Centers for Disease Control (CDC) now acknowledge that we may be in the midst of an autism epidemic. Members of the CDC reported a study of 289,456 children aged 3 to 10 years in the 5 counties of metropolitan Atlanta, Georgia.<sup>(6)</sup> A total of 987 children displayed behaviours consistent with *Diagnostic and Statistical Manual of Mental Disorders for Autistic Disorders* criteria for autistic disorder. The prevalence for autism was 3.4 per 1000. This rate was higher than rates found with the same criteria in earlier studies conducted in the United States in the 1980s and early 1990s. The results of this study are consistent with those of several recent studies in the US and in Western Europe. A report by the California Department of Developmental Services found that 20,377 California children were receiving special services for autism in December 2002 - a 97 percent increase since 1998. According to a British evaluation, the yearly incidence of diagnosed autism among children aged 12 years or younger increased sevenfold between 1988 and 1999.<sup>(7)</sup>

The time has come to offer an overview of autism from a primal health research perspective. This was difficult as long as the MMR-autism obsession was not overcome. Let us recall that the possibility that mumps, measles, and rubella (MMR) vaccine may be related to the risk of autism originated primarily from a publication in 1998 that described 12 cases of children who were diagnosed with a digestive condition ('ileal-lymphoid-nodular hyperplasia') followed by behaviour disorders classified as autism.<sup>(12)</sup> In eight of 12 children the behaviour disorder was 'linked' in time with MMR by the parents or the doctor. These anecdotes were the basis of a theory that has been repeatedly dismissed by epidemiological studies.<sup>(13, 14, 15)</sup> We had to wait until the publication in a prestigious medical journal of a study involving all children born in Denmark from January 1991 through December 1998 (more than half a million children) to convince anyone that the main negative effect of the MMR fuss has been to divert the attentions (and probably the money) from the study of risk factors that might explain the current autism epidemic.<sup>(16)</sup> An accumulation of data suggest that the significant risk factors occur before the age of MMR, which is usually given at 12 months or after.

### A LOOK AT THE PRIMAL HEALTH RESEARCH DATA BANK

The key word 'autism' leads to several studies that detected risk factors in the pre- and peri-natal periods.

My interest in autism started in 1982, when I met Niko Tinbergen, one of the founders of ethology, who shared the Nobel prize with Konrad Lorenz and Karl Von Frisch in 1973. As an ethologist familiar with the observation of animal behaviour, he studied in particular the non-verbal behaviour of autistic children. As a "field ethologist" he studied the children in their home environment. Not only could he offer detailed descriptions of his observations, but at the same time he listed factors which predispose to autism or which can exaggerate the symptoms<sup>(17)</sup>.

He found such factors evident in the period surrounding birth: induction of labour, "deep forceps" delivery, birth under anaesthesia, and resuscitation at birth. When I met him he was exploring possible links between difficulty in establishing eye-to-eye contact among autistic children and the absence of eye-to-eye contact between mother and baby at birth. The work of Tinbergen (and his wife) represents the first attempt to explore autism from a "primal health research" perspective.

It is probably because I met Niko Tinbergen that I read with special attention, in June 1991, a report by Ryoko Hattori, a psychiatrist from Kumamoto, Japan.<sup>(18)</sup> She evaluated the risks of becoming autistic according to the place of birth. She found that children born in a certain hospital were significantly more at risk of becoming autistic. In that particular hospital the routine was to induce labour a week before the expected date of birth and to use a complex mixture of sedatives, anaesthesia agents and analgesics during labour.

The largest study ever published about the perinatal risk factors for autism is dated July 2002.<sup>(19)</sup> The researchers had at their disposal the recorded data from the Swedish nationwide Birth Register regarding *all* Swedish children *born during a period of 20 years* (from 1974 until 1993). They also had at their disposal data regarding 408 children (321 boys and 87 girls) diagnosed as autistic after being discharged from a hospital from 1987 through 1994 (diagnosis according to ICD-9 code 299A). For each case five matched controls were selected, resulting in a control sample of 2040 infants. The risk of

autism was significantly associated with caesarean delivery, a 5-minute Apgar score below 7, maternal birth outside Europe and North America, bleeding in pregnancy, daily smoking in early pregnancy, being small for gestational age, and congenital malformations. Unfortunately the variable 'pre-eclampsia' was not separated from the unprecise framework of 'hypertensive diseases' (increased risk at the limit of statistical significance). Also the variable 'labour induction' could not be taken into account, because it did not appear in the National Birth Register until 1991 (personal correspondence with one of the authors).

Other studies – all of them much smaller than the main Swedish one - have evaluated the rates of birth complications by using 'composite optimality scores'. It also appears from these studies that children with autistic spectrum disorders have higher rates of birth complications. Once more the variable 'labour induction' does not appear in the protocols and the results of such studies.<sup>(20,21,22)</sup> Similar comments are inspired by an American study that used the 'Maternal perinatal scale', a maternal self-report that surveys complications of pregnancies and medical conditions of the mother,<sup>(23)</sup> and by another American study that used the 'Report of Final Natality statistics'.<sup>(24)</sup> The latest study added hyperbilirubinemia (jaundice) to the risk factors mentioned by other researchers, and also the concept of negative risk factors (the risks for the child to become autistic are lower when the mother had vaginal infections and when she did not previously use a contraceptive method). We could not find any study looking at the time when the cord has been clamped. Anyway, early cord clamping was an unchallenged practice 50 years ago, long before the autism epidemics.

Our data bank also includes a Japanese study of the survivors of neonatal intensive care units. The rate of autism in this population is more than twice what we should expect in the overall population; meconium aspiration syndrome appears as a significant risk factor.<sup>(25)</sup>

### **LABOUR INDUCTION EPIDEMIC AND AUTISM EPIDEMIC: IS THERE A LINK?**

There are many reasons why further studies about labour induction as a possible risk factor for autism are urgently needed. The first one is that the authors of the oldest studies included in our database came across risks associated with induction, whereas the most recent studies could not take into account this variable. 'Labour induction' should be explicitly taken into consideration, because it can be associated either with birth by the vaginal route (with or without intervention such as forceps), or with caesarean birth. Another reason is that the epidemic of autism and the epidemic of induction seem to have developed side by side. Most importantly, a third reason is that the results of recent studies suggest that children with autistic disorder show alterations in their oxytocin system.

The first clues came from a study of midday blood samples from 29 autistic and 30 age-matched normal children, all prepubertal.<sup>(26)</sup> It appeared that the autistic group had significantly lower blood oxytocin levels than the normal group. Oxytocin increased with age in the normal but not the autistic children. These results inspired an in-depth inquiry of the oxytocin system of autistic children. In recent years it has become clear that oxytocin can appear in the brain in several forms. There is the nonapeptide oxytocin (OT)

and the 'C-terminal extended peptides', which are described together as OT-X. The OT-X represent intermediates of oxytocin synthesis that accumulate due to an incomplete processing machinery. Twenty eight male children, diagnosed with autistic disorder, were compared with 31 age-matched non psychiatric control children: there was a decrease in blood OT, an increase in OT-X and an increase in the ratio of OT-X/OT in the autistic sample, compared with control subjects.<sup>(27)</sup> In other words autistic children show alterations in the oxytocin system: there are deficits in the processing machinery of oxytocin.

Such findings are of paramount importance at a time when an accumulation of data from animal studies confirm the potent effects of oxytocin (and the parent hormone vasopressin) on social behaviour, communication and rituals. Furthermore we are currently learning that oxytocin brain receptors undergo major changes during development. Among humans, the period surrounding birth is considered a period of dramatic reorganization of central oxytocin binding. We must add that, when reaching a certain degree of maturation, the oxytocin system of the fetus probably participates in the physiological initiation of labour. Artificial induction of labour in general, particularly the use of drips of synthetic oxytocin, create situations that undoubtedly interfere with the development and the reorganization of the oxytocin system in such a critical period. This only fact is a reason for further epidemiological studies focusing on labour induction as a possible risk factor. It would be useful to know also how autistic children release oxytocin. Oxytocin is more effective when released rhythmically, in a succession of fast pulsations. Today it is not impossible to measure the rhythmicity – the pulsatility – of oxytocin release.

### **AUTISM AS AN "IMPAIRED CAPACITY TO LOVE"**

The term "impaired capacity to love" is convenient because it can refer to the capacity to love others and to the capacity to love oneself as well. I use this term to define a sub-group of studies included in our database. Whenever researchers study a disease, a way of being, or a behaviour that can be interpreted as an impaired capacity to love, they always find risk factors in the period surrounding birth. It is noticeable that all the key-words leading to this sub-group are about very important issues, special to our time. This is the case of juvenile criminality, autism, and topical self-destructive behaviours such as suicide of teenagers, drug addiction, anorexia nervosa... It is also noticeable that, despite the publication in authoritative medical and scientific journals, the findings of such studies are shunned by the medical community and the media. They are comparatively unknown and are not taken into account in most subsequent articles. This is a common characteristic between them. I coined the term 'cul-de-sac epidemiology' when referring to such studies, in order to contrast with the term 'circular epidemiology', which refers to a common tendency to constantly repeat the same studies, even when there is no doubt about the results.<sup>(28)</sup> When a study is not politically correct, it leads to 'cul-de-sac epidemiology'.

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