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The MMR-Vaccination & Autism Controversy

(Word Count = 2080)

1.0 INTRODUCTION

Autism is a neuropsychiatric disorder that was first described in 1943 by Kanner. This disorder is characterised by early signs of impairments in socialisation and communication (refer to appendix 1.0). However, no two autistic cases are the same. It is generally found that symptoms occur along a spectrum which includes children and adults across the range of severity and intellectual ability, from severely impaired to high-functioning. Consequently, the term Autistic Spectrum Disorders (hereafter known as ASD) has been employed in an attempt to describe the diversity of the condition. Onset is seen generally before the age of 3 years old (Volkmar & Pauls, 2003). Having said this, due to the nature of the condition, diagnoses may not be made up until five years in severe cases of the spectrum or up until adulthood in mild cases. There have been many claims of cures and successes at various symptoms have been made with treatment options, however, the disorder is a life-long disability requiring substantial amounts of care, affection and attention as part of continual maintenance. According to the National Autistic Society, there are currently 500,000 families affected by ASD in the UK.

Autism was once considered a rare disorder before the late 1980's. However, since the introduction of the triple measles, mumps and rubella vaccination (hereafter known as MMR) the number of cases of autism appears to have risen (Kaye *et al*, 2001). *Is this a coincidence or a significant factor?*

Wakefield *et al* noticed this increase in incidence and attributed a causal relationship between the administration of MMR and the onset of autism. In 1998, he published a report of eight children in the United Kingdom with regressive autism following the receipt of MMR-vaccine (Offit & Coffin, 2003). The implications of this controversial statement led to a drop in the MMR-immunisations rate from 94 to 75% across England (Scalon, 2002; Boseley, 2001). The concerns about MMR also spread to the United States.

Wakefield *et al* hypothesised that a series of events that explained how MMR causes autism. According to the group, the result of the actual components of the MMR-vaccine is intestinal inflammation. Consequently, there is a change in the

permeability of the intestinal barrier function allowing the passage of gut-derived peptides that exert an 'opioid effect' on the brain. Such peptides dysregulate the endogenous opioid system and thus subsequently disrupt normal brain development (Offit & Coffin, 2003).

The media seized upon Wakefield's hypotheses and, as it was politically favourable, a frenzy of research was commenced investigating the link between MMR and Autism. Further research has since failed to replicate Wakefield's findings and also heavily criticised his work on methodological grounds.

Epidemiological studies into this area are mostly retrospective, looking back at past medical notes of large samples in an attempt to correlate any relationship between the incidence of autism and MMR administration. Statistical analyses are then applied to the results in an attempt to determine any significant correlations.

1.1 AIM

This paper will investigate into a sample of studies examining the causal relationship between MMR-vaccination and autism in an attempt to determine whether there is a link.

An attempt will be made to answer the following question:

Is the Aetiology of Autism linked to the Administration of MMR-Vaccination? Or Are Parents Fears Unfounded?

2.0 METHOD

Studies were acquired for recruitment to this investigation by means of electronic journal search engines. The following search engines were used:

1. Science Direct
2. Ingenta Journal
3. British Medical Journal (search across multiple journals option)
4. PsychInfo
5. New England Journal of Medicine
6. The Lancet

7. Medline central

Several searches were conducted using the following search terms within the 'title', 'abstract', 'keywords' fields:

- "Autism"
- "Autism AND MMR"
- "Aetiology of Autism"

The searches were conducted to include all relevant scientific information between the dates of 1942 to 2003.

A selection criterion was then applied to the results of the journal search in an attempt to recruit papers with reliable and comparable results. This criterion included:

- Retrospective or prospective studies on individuals up to the age of 15 years, published between 1969-2003
- Cohort, time-series or ecological studies
- Samples above 50
- Controlled studies
- Single-sex or dual sex studies
- Peer-reviewed published research within a medical journal

The criteria were developed before the searches were conducted to eliminate experimenter bias and reduce the risk of rejecting a paper blindly.

3.0 RESULTS

3.1 SEARCH RESULTS

The initial searches conducted revealed in total 113 hits. Of these only 8 articles were relevant studies, of which four studies were recruited:

3.1.1 Table to Show Studies Recruited for Investigation

Name (+ date) of Study	Sample size
Fombonne *et al*, 2001	**n=262**
Madsen *et al*, 2002	**n=527,303**
Taylor *et al*, 2002	**n=473**
Dales *et al*, 2001	**n=305**

Also included for comparison was the original study linked to the hypotheses that Wakefield proposed in 1998 – Wakefield *et al*, 1998 n=12. According to the criterion used to recruit papers to this investigation, Wakefield's study would have been rejected.

3.2 RESULTS OF EACH STUDY

3.2.1 Fombonne *et al*, 2001

Hypothesis proposed: "There is a link between MMR-vaccine and a form of Autism that is a combination of developmental regression and gastrointestinal symptoms that occur shortly after immunisation".

Thus not only is there a link between MMR and autism but that there is a new phenotype of the disorder that is induced by administration.

Methods Used: Three samples were used:

1. 96 children immunised with MMR who had a pervasive developmental disorder (known as post-MMR sample)
2. 98 autistic children (pre-MMR)
3. 68 autistic children (post-MMR)

Data regarding age of parental concern, developmental regression, bowel symptoms and immunisation dates were analysed.

Main Results:

- Rate of developmental regression reported in the post-MMR group was not different from the pre-MMR group
- Subset of autistic children with regression had no other developmental or clinical characteristics which could be used to argue a specific aetiologically different phenotype

Conclusions:

- No evidence was found to support a distinct syndrome of MMR-induced autism or of 'autistic enterocolitis'
- Failure to find support an association between MMR and autism at population level

- Current findings do not argue for changes with current immunisation programs and recommendations

3.2.2 Masden *et al*, 2002

Hypotheses: "It has been suggested that the measles, mumps and rubella vaccine causes autism"

Methods Used: Retrospective cohort study of all children born in Denmark between Jan 1991 and Dec 1998 = 537,303 children of which 82% received the MMR-vaccine Immunisation status, autistic diagnoses and other confounding information was then analysed.

Main Results:

- Relative risk of autistic disorder for MMR-group was 0.92% compared with unvaccinated group
- Relative risk of another autistic-spectrum disorder was 0.83%
- For either disorder no significant difference between non-vaccinated group and vaccinated group

Conclusion:

- This study provides strong evidence against the hypothesis that MMR-vaccination causes autism

3.2.3 Taylor *et al*, 2002

Hypotheses: "To investigate whether measles, mumps and rubella vaccination is associated with bowel problems and developmental regression in children with autism, looking for evidence of a 'new-variant' form of autism"

Methods Used: Population study of 278 core autistic children and 195 atypical autistic children from five health districts in London. Information regarding immunisation status, age of reported regression of child's development and bowel symptoms were analysed.

Main Results:

- Proportion of children with developmental regression (25% overall) or bowel symptoms (17% overall) did not change significantly during the 20 years from 1979, a period which included the introduction of MMR-vaccination in Oct 1998
- No significant difference was found in rates of bowel symptoms or regression in children who received MMR after such concern as compared to those who had not received it
- A possible association between non-specific bowel problems and regression in children with autism was seen but this was not related to MMR-vaccination

Conclusions

- Failure to support an MMR-associated 'new-variant' form of autism with developmental regression and bowel problems
- This study adds further evidence against involvement of MMR-vaccine in the initiation of autism

3.2.4 Dales *et al*, 2001

Hypotheses: "To determine if a correlation exists in secular trends of MMR-immunisation coverage among young children and autism occurrence"

Methods Used: Retrospective analyses of MMR-immunisation coverage rates and autism diagnoses. Main outcome measures were MMR coverage rates as of ages 17 months and 24 months and numbers of Department of Developmental Services system enrolees diagnosed with autism, grouped by birth

Main Results:

- No correlation observed between secular trend of early childhood MMR-rates in California and the secular trend in numbers of children with autism
- A marked sustained increase in autism case numbers of children with autism but changes in MMR coverage over the same time period were much smaller and of shorter duration

Conclusion:

- These data do not suggest an association between MMR-immunisation among young children and an increase in autism occurrence

3.2.5 Wakefield *et al*, 1998

Hypotheses: No specific questions found, "We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder"

Methods Used: 12 children between 3-10 years referred to paediatric gastroenterology unit with history of normal development followed by a loss of acquired skills. Children underwent gastroenterological, neurological and developmental assessment.

Main Results:

- Onset of behavioural symptoms was associated, by the parents, with MMR-vaccination in 8 of 12 children
- Behavioural disorders included 9 with autism, 1 with disintegrative psychosis and 2 with possible postviral or vaccinal encephalitis

Conclusion:

- Gastrointestinal disease and developmental regression in a group of previously normal children is associated with possible environmental triggers
- In most cases onset of symptoms was after MMR-immunisation

4.0 DISCUSSION

Any conclusion drawn by this investigation should only be taken as a possible truth since only the conclusions drawn by each study examined have been taken into consideration. No independent statistical testing has been applied to the results making the significance difficult to estimate.

In addition to this, the sample of papers reviewed is subject to a restricted constraint. Despite the search criteria of papers up to 2003 was included, the search was limited financially since only 'free-to-view' papers were recruited. Most search engines do not release papers on 'free-to-view' 6 months to a year after publication.

In conjunction with this issue, it cannot be certain that the sample included all investigations conducted in this area since a lot of material may be unpublished or rejected from journals for political reasons (see below). Such material can only be

accessed from unsupervised websites where it is difficult to ascertain the validity of results owing to the lack of academic peer-review.

One limitation of all the studies recruited is their source of financial support. Although this was not investigated formally, most studies appeared to have financial backing from the Government. Such support immediately introduced researcher bias since the experimenter may be under pressure to produce favourable results in line with the guidelines set out by the Government.

Another limitation is the design of the studies recruited. Most of them employ a retrospective design looking back at data already collated. This poses problems with standardisation of information, falsification of data and corrupted or missing files. A lot of information may be lost or damaged without the knowledge of the researcher. In essence, to eliminate this problem a better design may involve a prospective experiment of a large sample involving a clear control group (unvaccinated children) and an experimental group (vaccinated children) with follow-ups up to 3 years after vaccination.

The flaws briefly discussed above are a few of many. There *are* other limitations of both this study and the studies recruited for examination.

5.0 CONCLUSIONS

This review suggests that there is *no* link between the aetiology of autism and the administration of MMR-vaccine. With the exception of Wakefield's report, all the studies recruited for review fail to find support for such a theory.

Wakefield's work has been heavily criticised on methodological grounds in terms of sampling and also design study. In November 2003, Murch (one of Wakefield's original team) approached the press claiming *no* link between MMR and autism after a review of research conducted into this area as a consequence to his original research.

However, an answer has to be found regarding the aetiology of autism, if MMR-vaccine is not a causative factor then what is? And can it be prevented? With increasing numbers of Autistics, there is a mounting pressure to determine cures or preventative measures. It is clear that a substantial amount of continuing research in this area is required.

6.0 REFERENCES

6.1 JOURNAL ARTICLES

Boseley S (2001) Fear of Measles Epidemic as Jab Rate Drops. London, UK: *The Guardian*; 5 January 2001

Dales L, Hammer S J, Smith N J (2001) Time Trends in Autism and in MMR Immunization Coverage in California. *JAMA* **322**:460-3p

Fombonne E, Chakrabarti S (2001) No Evidence for New Variant of Measles-Mumps-Rubella-Induced Autism. *Pediatrics* **108**:4:1-8p

Kanner L (1943) Autistic Disturbances of Affective Contact. *Nervous Child* **2**:217-50p

Kaye J A, Melero-Montes M d M, Jick H (2001) Mumps, Measles and Rubella Vaccine and the Incidence of Autism Recorded by General Practitioners: A Time Trend Analysis. *British Medical Journal* **322**:460-3p

Offit P A, Coffin S E (2003) Communicating Science to the Public: MMR Vaccine and Autism. *Vaccine* **22**:1-6p

Scalon T (2002) MMR Vaccine Uptake May Be Lower Than Reported Because of Manipulation of Target Groups. *British Medical Journal* **324**:724p

Volkmar F R, Pauls D (2003) Autism. *The Lancet* **362**:1133-41p

Wakefield A J, Murch S H, Anthony A, Linnell J, Casson D M, Malik M, Berelowitz M, Dhillon A P, Thomson M A, Harvey P, Valentine A, Davies S E, Walker-Smith J A (1998) Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, and Pervasive Developmental Disorder in Children. *The Lancet* **351**:637-41p

6.2 Electronic Resources

British Medical Journal: www.bmj.com *dates accessed 09/11/2003, 10/11/2003,12/11/2003*

Ingenta Journals: www.bids.ac.uk *date accessed 12/11/2003*

Medline Central: www.nlm.nih.gov *dates accessed 09/11/2003, 10/11/2003, 11/11/2003*

National Autistic Society: www.nas.org.uk *date accessed 09/11/2003*

New England Journal of Medicine: www.nejm.com *date accessed 09/11/2003*

PsychInfo Journals: www.bids.ac.uk *date accessed 12/11/2003*

Science Direct: www.sciencedirect.com *dates accessed 09/11/2003, 12/11/2003*

The Lancet: www.thelancet.com *dates accessed 09/11/2003, 10/11/2003, 11/11/2003*

Appendices

1.0 Taken from Volkmar & Pauls (2003)

Features and Sample Behaviours Required for Diagnosis of Autism	
Qualitative Impairment in Social Interaction	Impaired eye gaze, lack of social reciprocity, poor or absent joint attention, limited or absent peer relationships
Qualitative Impairments in Communication	No language (no alternative compensatory means used to communicate), if language spoken involved echolalia and difficulties in pragmatic language, lack of appropriate imaginative play
Restricted Patterns of Behaviour, Interests	Abnormal pre-occupations interests and activities, difficulties with change, stereotyped mannerisms
Onset Before Age of 3 Years	Problems in social interaction, communication or pl ay