

Brain Damage caused by Vaccination - By Alan Challoner MA (Phil) MChS

That vaccinations are helpful to society is without question; however, that some individuals suffer permanent and damaging sequelae to vaccinations is also well documented. The purpose of this paper is to offer a mechanism by which vaccination-induced neuronal damage in some individuals can be understood.

History of Suspected Neurological Events in Association with Pertussis Vaccines

Whole-cell pertussis vaccine was first used on a large scale by Madsen, during a 1925 epidemic in the Faroe Islands. The possibility that pertussis immunisation might cause adverse neurologic events resulting in permanent brain injury was first raised following a report of two cases by Madsen (1933). Madsen reported that manifestation of pertussis among vaccinated cases was less severe than among unvaccinated cases (Madsen, 1925).

Madsen's 1933 report of the death of two infants following pertussis vaccination was among the first published accounts of serious adverse effects associated with the vaccine. Both infants had received initial subcutaneous injections within eight days of birth, leading Madsen to recommend against vaccination of infants under 1 month old. Both infants exhibited cyanosis prior to death; one infant experienced convulsions (Madsen, 1933).

In 1948, Byers and Moll presented a watershed case series of adverse reactions to pertussis vaccine. This report was crucial to practitioner recognition of the possibility that adverse risks could be associated with pertussis vaccination.

Retrospective chart reviews revealed 15 such cases of children, ages 5 to 18 months at time of inoculation, who were admitted or treated as outpatients at Children's Hospital between 1938 and 1947. 14 of the 15 cases identified experienced severe reactions, and had no notable medical history.

The common event to neurologic complications was pertussis vaccination, although variation included: time from injection to reaction (mean time 13.3 hours); administration; manufacturer; and duration of reaction. All cases experienced convulsions and changes in consciousness. While follow-up varied, 11 of the 13 surviving children suffered from recurrent convulsions more than one year after vaccination; six children were suffering from cerebral palsy.

Recommendations included review or modification of the vaccine or inoculation practices (Byers and Moll, 1948). At the time this study was published, approximately one dozen pharmaceutical companies were manufacturing DPT vaccines (Coulter and Fisher, 1985).

Early case series and case reports on serious adverse reactions to pertussis vaccine document neurological complications ranging from convulsions and behavioural changes to recurrent seizures, paralysis, cerebral palsy, and death.

Toomey acknowledged the difficulty with references to encephalopathy as an outcome and attempts to restrict outcomes in his own case series to seizures.

This review traces the most groundbreaking case series, which in many instances; involve presentation of both clinical symptoms as well as use of the term encephalopathy (Toomey, 1949).

Page 1 of 17

Subsequent descriptions of encephalopathies of various types occurring at differing time periods after pertussis immunisation were given: (e.g., Berg, 1958; Malmgren et al., 1960; Sutherland, 1953). The report by Globus and Kohn is particularly significant. They documented the reactions of two male infants who experienced convulsions and unresponsiveness subsequent to pertussis vaccination. One infant (9 months old) continued to experience convulsive episodes at follow-up; the second infant, experienced convulsions, became comatose, and subsequently died; autopsy revealed evidence of degenerative processes in the brain. The authors concluded that an allergic form of encephalopathy was caused by an antigen-antibody reaction (Globus and Kohn, 1949).

On the basis of these reports, Strom (1960) questioned whether the risk of adverse neurologic effects following immunisation might be more of a concern than the risk of pertussis itself, a view reiterated in reports by Aicardi and Chevrie (1975), Cavanagh et al. (1981).

Feldman¹ reported that there are two absolute contraindications to DTP and DTaP: an immediate anaphylactic reaction and encephalopathy within 7 days.^{2, 3} The latter is defined as a severe, acute central nervous system disorder unexplained by another cause, which may be manifested by major alterations of consciousness or by generalized or focal seizures that persist for more than a few hours without recovery within 24 hours.

Precautions for immunization are to be aware of potential adverse events that were formally contraindications but now require careful consideration before administration of additional doses. (Pickering & Atkinson de m) These reactions have not proven to cause permanent sequelae. They are:

1. Seizure with or without fever, occurring within 3 days of immunization with DTP or DTaP;
2. Persistent, severe, inconsolable screaming or crying within 3 days for 3 or more hours within 48 hours;
3. Collapse or shock-like state (hypotonic-hypo-responsive episode) within 48 hours;
4. Temperature $\geq 40.5^{\circ}\text{C}$ (104°F), unexplained by another cause, within 48 hours. [1, 2]

The reader is referred to the Red Book (Report of the Committee on Infectious Diseases by the American Academy of Pediatrics) for a detailed discussion on DTP and children with underlying neurologic disorders and children with a family history of seizures.⁴

More light was thrown on this problem when Professor W. Ehrengut in Hamburg, reported that signs of severe brain damage began to appear in some children soon after adverse reactions to triple vaccine. Ehrengut (1977, 1980).

The importance of the paper by Kulenkampff et al (1974) was that it showed results from a clustering of complications following DPT vaccination which occurred in the first 24 hours after inoculation. The authors believed that this

1 - Medscape Pediatrics. 2002;4(1)<http://www.medscape.com/viewarticle/420703>

2 - Pickering L, ed. Report of the Committee on Infectious Diseases. 25th ed. Elk Grove, Ill: American Academy of Pediatrics; 2000:435-448.

3 - Atkinson W, Wolfe C, Humiston S, Nelson R, eds. Centers for Disease Control. Epidemiology and Prevention of Vaccine -- Preventable Diseases. 6th ed. Atlanta, Ga: Centers for Disease Control; 2000:67-83.

4 - Pickering L, ed. Report of the Committee on Infectious Diseases. 25th ed. Elk Grove, Ill: American Academy of Pediatrics; 2000: 68

Page 2 of 17

suggested a causal rather than a coincidental relation. Stewart (1977, 1979), consistently drew attention to the toxicity of the DPT vaccine.

In the late 1970s, a number of reports appeared in the Press from different parts of the UK about children who were previously well but had become mentally retarded or paralysed soon after receiving triple vaccine. The Government, on the advice of its advisory committees, responded to these reports by re-affirming the efficacy and safety of pertussis vaccine and by insisting that the pertussis component be retained in triple vaccine. They insisted also that a high level of vaccination among children of all ages must be maintained if epidemics were to be averted.

Looking at events at the time of the earlier trials of pertussis vaccine when given alone (i.e. not as part of triple vaccine) in the USA and UK, it becomes clear that the inclusion of pertussis vaccine makes triple vaccine much more likely to be followed by adverse reactions involving the heart and nervous system. Such reactions include shock, collapse, convulsions and screaming fits, all of which had been recorded in some of the children who received pertussis vaccine alone in the earlier trials. Such signs were extremely infrequent or altogether absent in the earlier usage of the other two components of triple vaccine.⁵

[The foregoing is from a restricted list of publications pre-1990. Fuller details can be located in Howson et al.⁶]

From the many papers and books written on the subject over the last 70 years, it is obvious that many of the descriptions of events and terminology are not consistent or rationalised. It is not always possible to determine the exact nature of the events from the terms and descriptions used. Also, in some cases, because there is a probability that even where the eventual outcome was severe, the triggering event was restricted to a comparatively short period of time, and there then seemed to be a recovery to normality. The reason for this is that the damage caused was to areas of the brain that were in the course of development, and which were not fully functional at the age of vaccination.

This would explain why the sequelae were only obvious at a later time.⁷

Advent of adverse reactions following vaccination

The claim for damages in Loveday v Renton and The Wellcome Foundation, heard in the High Court of Justice in London, from early October 1987 until late February 1988, dealt with the general issue of whether, on the balance of probabilities, pertussis vaccine could cause permanent brain damage.

The cornerstone of the claim that pertussis vaccine can cause permanent brain damage has always been the apparent clustering of onset of neurological disorders within the first 24–48 h after vaccination. One of the main finds of the NCES, however, which was not divulged in any published report but emerged in

5

Stewart, G. Danger. Here's Health. March 1980

6

Howson, Christopher P.; Howe, Cynthia J. and Harvey V. Fineberg, (Editors). Adverse Effects of Pertussis and Rubella Vaccines. A Report of the Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines. Division of Health Promotion and Disease Prevention. Institute of Medicine. National Academy Press, Washington, D.C. 1991. Can be read online at: <http://books.nap.edu/books/0309044995/html/R1.html>

7

Challoner, A. Towards a Better Understanding of Early Atraumatic Brain Injury and its treatment: With specific associations to LJC. (oakwoodbank.ac@virgin.net)

the course of the hearing, was that in those cases considered and included in the NCES Report, all referred to those where adverse reports occurred after 48 h of the DTP vaccination being given to the children. The report covered children in England, Scotland and Wales from mid-1976 to mid-1979 when 2 million doses of vaccine were used.⁸ [See also page 10]

Many of the research papers, that have been used in attempting to define causation in cases of possible brain damage following vaccination with DPT, have involved subjects whose initial reaction was beyond 48-hours after the vaccination.

The Green Book published by HMSO is a reference text about vaccinations. At Chapter 24.6.1b, it states, "Immunisation should not be carried out in children who have a history of a general reaction to a preceding dose." Although this advice was available as early as 1958, many children were given a second and even a third dose after a serious adverse reaction to the first dose.

Causation.

On the question of causation, doubters suggest that, it is not whether the vaccine can cause seizures, or febrile reactions, but permanent brain damage."

How can this 'permanent brain damage' occur?

The brain consists of about 100 billion interconnected neurones. There is a huge variation in the number of neurones that different people have. Each neurone has a cell body out of which axons extend. Axons are like wires along which electronic information flows. At the end of each axon, chemicals are released that excite or inhibit the next neurone. In this way, all the neurons are interconnected.

The two main chemicals released are glutamate, which excites neurones, and GABA, which inhibits them. A substantial amount of inhibition is required; otherwise the brain would be a mass of excitation all the time. Seizures are like an electrical storm, with a lot of neurones firing and releasing substantial amounts of glutamate.

As far back as 1957 it was shown that at high enough concentrations, glutamate is toxic to neurones. There is evidence that prolonged seizures in convulsive status epilepticus may lead to damage of nerve cells for this reason.

Blood pressure drops during a seizure. If the seizure is prolonged and blood pressure remains low for longer, insufficient blood will reach the brain. Blood transports oxygen and also glucose, which is the food for cells. If seizures are prolonged, the brain will eventually be deprived of oxygen and the nerve cells will start to die. In addition, a convulsion uses up glucose; therefore if insufficient blood reaches the brain to provide enough glucose, this too can cause damage to nerve cells.

When a nerve cell dies it cannot be resuscitated. In the long-term other neurones may take over some or all of the work of the dead neurones, but that will not guarantee that the loss of the damaged neurones will be mitigated.

The realisation that prolonged seizures can damage the brain is not new. It was noted as far back as 1825 that long seizures seemed to cause damage to the hippocampus, the part of the brain important for the formation of memory.

The fever-induced convulsions that some young children suffer, appear to have no long-term impact on their brain functioning. However, there is a risk of

8

Griffith, A. H. Permanent brain damage and pertussis vaccination: is the end of the saga in sight? *Vaccine*; Volume 7, Issue 3, June 1989, Pages 199-210.

Page 4 of 17

developmental problems when infants suffer the seizures. Recent research shows that children with a history of fever-induced seizures actually outperformed others in tests of memory and learning capacity. The exception was for children who suffered febrile convulsions before the age of 1 year.

These children were at increased risk for deficits in mental abilities. However, it also reinforces the concern that during infancy, these seizures may injure certain brain cells and lead to more profound dysfunction.^{9, 10} Ling has drawn attention in his study to the fact that the risk of the development of neurological deficits following febrile convulsions was related directly to increasing duration of seizure.¹¹

Serious reactions that might imply the existence of brain damage from the vaccine were tabulated by Greco et al and quantified as indirect evidence that pertussis vaccines may result in a post-vaccine encephalopathy.¹²

The US federal government continues to maintain that, on rare occasions, permanent brain damage does occur. The report of a single case-control study in support of this position prompted the establishment of a special committee under the sponsorship of the United States Public Health Service, the Institute of Medicine, and the National Research Council to determine the validity of the report. The special committee concurred that pertussis vaccine does produce permanent brain damage in rare instances. Physicians are required to warn all responsible parties of vaccine recipients that pertussis vaccine may cause "lasting brain

damage.” This requirement has been authorised by Congress and the National Childhood Injury Act of 1986.¹³

Another patient study indicates that seizure activity originating in a specific location of the brain (hippocampus) causes the region to become irreversibly damaged.¹⁴

Earlier reports had presupposed that infantile convulsions following DPT vaccinations were only triggered and not caused by the vaccine. This was one of the pillars of the Loveday v Renton case. Cherry et al have refuted this.

“Pertussis immunisation is a precipitating factor of the first febrile convulsion in children prone to have febrile convulsions...” [People should not generalise by concluding that only children who are 'genetically predisposed' have vaccination-induced febrile seizures (FS).]

In a similar study, with more focused data, only 6 of 60 and 15 of 60 children with severe DPT reactions had personal or familial history of prior seizures,

9

Baram, Tallie Z. and Shinnar, Shlomo. Do febrile seizures improve memory ? Neurology 2001 57: 7-8

10

Chang, Y. C.; Guo, N. W.; Wang, S. T; Huang, C.C.; and Tsai J.J. Working memory of school-aged children with a history of febrile convulsions: A population study. Neurology 2001 57: 37-42.

11

Ling, S.G. Clinical Characteristics and Risk Factors for a Complex First Febrile Convulsion. Singapore Med J 2001 Vol 42(6) : 264-267.

12

Greco D, Salmaso S, Mastrantonio P, et al. A controlled trial of two acellular vaccines and one whole-cell vaccine against pertussis. N Engl J Med. 1996;334:341-348.

13

Sepkowitz S. Perverse reactions to pertussis vaccine by government medical agencies. J Okla State Med Assoc. 1996 Apr; 89(4):135-8 (ISSN: 0030-1876)

14

Theodore, W. H.; Bhatia, S.; Hatta, J.; Fazilat, S.; DeCarli, C.; Bookheimer, S. Y. and Gaillard, W. D. Hippocampal atrophy, epilepsy duration, and febrile seizures in patients with partial seizures. Neurology 1999 52: 132.

Page 5 of 17

indicating that the majority of children with severe reactions had no prior personal or familial FS as indicators of 'genetic predisposition'.¹⁵

Cytokines and vaccine-induced brain damage

Following vaccination, cytokines¹⁶ are released in response to:

- (i) as part of the processes by which vaccinations induce antibody formation, and
- (ii) as indicated by the occurrence of fever and, in many children, lethargic behaviour.

The cytokines so released are causally associated with two other processes:

- (i) oedema within the central nervous system, and
- (ii) clonal expansions of T-cell and B-cell subsets already activated by specific antigens from recent processes within the central nervous system (central nervous system).

Of significance to autism, is that some T-cells and B-cells in peripheral circulation may be encoded with neuron-derived epitopes¹⁷ (Nde) subsequent to various infections and/or various treatments with antibiotics. In children having such NdE-encoded T-cells, B-cells, and antibodies, vaccination-induced clonal expansions of those T-cells and B-cells may, in some cases, initiate further neuronal damage. In other words, brain regions whose pre-vaccination neuronal damage had been relatively insignificant may, via vaccination-induced clonal expansions, suffer additional damage.

The sequence is as follows: individuals primed with NdE-encoded immunological cells may, given cytokines-release induced by one or more vaccinations, experience clonal expansions of those T-cells and B-cells, which can re-cross the blood brain barrier into the brain and then induce additional damage, i.e., resulting in vaccination-enhanced neuropathy presenting clinically as autism.

In his book, Harris Coulter makes an important observation: in many children, post-vaccination traits appear to be similar to those described as sequelae to various central nervous system infections.¹⁸

This paper's hypothesis shows molecular mechanisms that may account for the similarities in sequelae to various central nervous system infections and, in some children, to vaccinations.¹⁹

15

Cherry JD, Holtzman AE, Shields WD, et al. Pertussis immunization and characteristics related to first seizures in infants and children. Journal of Pediatrics 1993 ;122 : 900 -903.

16

"Cytokine" is a word that comes from cyto- a combining form meaning "cell" - and -kinin - a combining form used in naming hormones, especially peptide hormones (e.g., bradykinin). Nomenclature has always been a problem because these factors were originally named for the activity that they described. This resulted in a large number of three or four or occasionally five letter acronyms.

The idea that the "interleukin" - between leukocytes - designation would simplify nomenclature has not proved to be the case. A review in 1979 by Byron Waksman listed almost 100 apparently distinct activities. At the time no one knew whether these represented distinct cytokines or a few cytokines with multiple activities.

The answer is: some of both.

17

Epitopes: A part of an antigen to which an antibody binds

18

Coulter, H.L. (1990), Vaccination, social violence, and criminality: The medical assault on the American brain. Berkeley, North Atlantic Books; Washington, Center for Empirical Medicine.

19

Allen, A.J., Leonard, H.L., & Swedo, S.E. (1995), Case study: a new infection-triggered, autoimmune subtype of pediatric OCD and Tourette's

Page 6 of 17

Based upon the facts,

(i) that fever is a vaccination reaction experienced by many individuals 20, and

(ii) that fever and oedema are stimulated by similar cytokines^{21, 22, 23}.

A subset of vaccinated children — as a direct result of vaccination-induced cytokines release — may be likely to experience both encephalitis and subsequent encephalopathy.²⁴

For instance, recent research findings are instructive regarding autistic children for whom — as neonates, infants or toddlers — medical records show a history of infections, antibiotic treatments, vaccinations, and temporally associated onset of autistic traits (e.g., Baker et al (idem), & Coulter (idem)).

As suggested by Coulter (idem), a range of mild but significant post-vaccination neuropathies may occur.

- Fever is strongly associated with interleukin-1, interleukin-6, and tumour necrosis factor alpha (IL-1, IL-2, TNF-alpha; (Luheshi et al, idem)).

- Brain inflammation is strongly associated with those same cytokines^{25, 26}.

- IL-1 and IL-6 are among primary components in inflammatory expansions of B-cells and T-cells, which can migrate to tissues from which, for instance, the anti-neural epitopes are derived. Furthermore, because the very mechanism of vaccination-induced immunity derives from clonal expansions of B-cells²⁷, cytokines needed for B-cell clonal expansions are induced and present as a causally related response to vaccination. If, prior to or immediately subsequent to vaccination, any neuronal damage, however slight, has occurred in response to the child's infections and/or syndrome. Journal of the American Academy of Child and Adolescent Psychiatry, 34, 307-311.

20

Bellanti, J.A., Fishman, H.D., & Wientzen, R.L. (1987), Adverse reactions to vaccines. Immunology and Allergy Clinics of North America, 7, 3, 423-445.

21

Luheshi, G., & Rothwell, N. (1996), Cytokines and fever. International Archives of Allergy and Immunology, 109, 301-307 [listing IL-1, IL-6, and TNF-alpha as the primary cytokine pyrogens].

22

Quagliarello, V.J., Wispelwey, B., Long, Jr., W.J., & Scheld W.M. (1991), Recombinant human interleukin-1 induces meningitis and blood-brain barrier injury in the rat: characterization and comparison with tumor necrosis factor. Journal of Clinical Investigation, 87, 1360-1366.

23

Yamasaki, Y., Matsuura, N., Shozuhara, H., Onodera, H., Itoyama, Y., & Kogure, K. (1995), Interleukin-1 as a pathogenetic mediator of ischemic brain damage in rats. Stroke, 26, 676-81.

24

Baker, S.M., & Pangborn, J. (1996), Clinical assessment options for children with autism and related disorders: a consensus report of the Defeat Autism Now! (DAN!) conference, Dallas, Texas, January 1995. San Diego, Autism Research Institute.

25

Banks, W.A., Kastin, A.J., & Gutierrez, E.G. (1993), Interleukin-1-alpha in blood has direct access to cortical brain cells. Neuroscience Letters, 163, 41-44.

26

Ceriani, G., Macaluso, A., Catania, A., & Lipton, J.M. (1994), Central neurogenic antiinflammatory action of alpha-MSH: modulation of peripheral inflammation induced by cytokines and other mediators of inflammation.

Neuroendocrinology, 59, 138-143.

27

Ada, G.L. (1993), Vaccines. In: Fundamental Immunology, 3rd edition, Paul, E.P., editor, New York: Raven Press, Ltd.

Page 7 of 17

antibiotic treatments, then the child probably has some activated microglia²⁸ and some anti-neuronal antibodies, as well as activated T-cells and B-cells whose epitopic focus is derived from neurons that were injured either,

(i) during the prior infections and treatment, or

(ii) as a result of vaccination-induced oedema²⁹.

Not only do inflammatory cytokines modulate blood-brain barrier permeability³⁰, but perivascular microglial cells of the blood brain barrier can become antigen-presenting cells encoded with epitopes from the injured tissue within the brain, and these perivascular cells allow activated T-cells to pass from peripheral circulation, across the blood brain barrier, into cerebro spinal fluid wherein additional autoimmune-like damage can ensue.

A similar crossing of the blood brain barrier occurs with activated B-cells.

If, from the child's prior infection(s) and/or from vaccination-induced oedema, activated T-cells and B-cells exist with neuronally derived epitopes, at least in some individuals during their response to vaccination, the following sequence may ensue:

(i) clonal expansions of existing T-cells and B-cells having neuronally derived epitopes,

(ii) further activation of microglia in brain regions already damaged,

(iii) increases in blood brain barrier permeability, thereby allowing activated T-cells, etc, to enter the brain.

(iv) Furthermore, as the clonally expanding T-cells, etc, travel toward brain cells having sequences similar to the neuronally derived epitopes, encephalitis would be one result of these events and, more importantly, additional sequelae would include increased autoimmune-like damage to neurons that, prior to the vaccination, had been only mildly, perhaps even unnoticeably damaged by the prior infections.

In extreme cases of individuals having vaccination-induced clonal expansions of immunological cells with neuron-based epitopes, autism might be a result.

Nearly any vaccine may have the potential for inducing neuronal damage in persons with neuronally derived epitopes. In other words, any vaccination that induces strong antibody responses,

(i) would appear to be capable of inducing fever-generating cytokines and, therefore at least hypothetically,

(ii) could simultaneously induce clonal expansions of pre-existing T- and B-cells encoded with neuronally derived epitopes, thereby leading to increased neuronal damage in varying degrees across individuals.

28

Microglia are the smallest of the glial cells. Some act as phagocytes cleaning up CNS debris. Most serve as representatives of the immune system in the brain. Microglia protect the brain from invading micro-organisms and are thought to be similar in nature to macrophages in the blood system.

29

Fukuyama, Y., Seki, T., Ohtsuka, C., Miura, H., & Hara, M. (1996), Practical guidelines for physicians in the management of febrile seizures. Brain & Development, 18, 479-84.

30

Banks, W.A., & Kastin, A.J. (1991), Blood to brain transport of interleukin links the immune and central nervous systems. Life Sciences, 48, PL117- PL121.

Page 8 of 17

Three additional concepts are helpful for understanding inflammation-related pathologies of the central nervous system:

(i) molecular mimicry— whereby epitope sequences are virtually identical between an immunogenic pathogen and a naturally occurring molecular sequence³¹,

(ii) cross-reactivity— e.g., when a lipo-polysaccharide amidst a cellular bilipid layer induces a wider range of immunological responses involving self-membrane sequences³², and

(iii) epitope-spreading or "determinant spreading", i.e., a process that also describes spontaneously occurring widening ranges of immunogenicity.

Each of these three processes illustrates ways that autoimmune neuronal damage may be induced and the range of neuronal targets expanded in response to fever-related levels of cytokines release that occur in response to vaccinations. These processes would be more likely in some children if, due to infections and/or antibiotics, the child has T- and/or B-cell subsets encoded with neuronally derived epitopes.

In extreme cases, sufficient interleukin-2 levels in damaged areas of the central nervous system could mobilise lymphokine-activated killer cells (LAKs), which then might induce a more general damage, thereby yielding increasingly severe neurological deficits.

Additional factors may augment the mechanisms of neuronal damage outlined here above:

- Targeting the cerebellum and temporal lobe: Swartz³³ mentions that the temporal lobe and cerebellum are likely targets for oedema-induced neuronal damage. Furthermore, certain hippocampal regions as well as Purkinje cells of the cerebellum have a relative deficit of apoptosis-related protein Bcl-2, thereby inclining cells in those regions toward apoptosis if and as oedema-induced injury occurs³⁴.

- Cerebellum: Discrete lesions of the cerebellum are associated with mania, depression, bipolar disorders, and OCD; and more than thirty bacterial, fungal, and viral infectious agents are known to be able to affect the cerebellum³⁵.

- Other inflammatories: In addition to IL-1, IL-6, and TNF-alpha, the following are additional factors influencing brain inflammation: Platelet-activating factor, prostaglandins E2 and I2, leukotriene B4, and polymorpho-nuclear neutrophil leukocytes³⁶.

31

Baum H, Davies H, & Peakman M. (1996), Molecular mimicry in the MHC: hidden clues to autoimmunity? Immunology Today, 17, 64-70.

32

van Rooijen, N. (1989), Are bacterial endotoxins involved in autoimmunity by CD5+ (Ly-1+) B cells? Immunology Today, 10, 334-336.

33

Swartz, M.N. (1984), Bacterial meningitis: more than just the meninges. New England Journal of Medicine, 311, 912-913.

34

Hara, A., Hirose, Y., Wang, A., Yoshimi, N., Tanaka, T., & Mori, H. (1996), Localization of Bax and Bcl-2 proteins, regulators of programmed cell death, in the human central nervous system. Virchows Archives. 429, 249-53.

35

Cohen, B.A., & Lipton, H.L. (1990), The cerebellum and CNS infections. In: Infections of the central nervous system. D Schlossberg, editor; New York: Springer-Verlag.

36

Saez-Llorens, X., Ramilo, O., Mustafa, M.M., Mertsola, J., & McCracken, G.H. (1990), Molecular pathophysiology of bacterial meningitis: Current

Page 9 of 17

As stated in the 1996 guideline for physicians, vaccination-induced inflammation ought to be treated aggressively (Fukuyama et al, 1996; de m), and better understanding of pathogenic processes, of risk factors, and of preventive or corrective measures are worthwhile goals.

Other vaccines have also been investigated as causes of brain damage. These include MMR (The U.S. Department of Health & Human Services, Centers for Disease Control and Prevention, National Immunization Program, promulgates that the risks from MMR vaccine can be permanent brain damage.)³⁷

It should also be noted that there have been suggestions of problems with the influenza vaccine. (The US Institute of Medicine's immunisation safety review committee has been investigating whether the influenza vaccine might carry a risk of the demyelinating disorder Guillain-Barré syndrome.)³⁸

The National Childhood Encephalopathy Study 1976

In response to the controversy surrounding whole-cell pertussis vaccination, in the United Kingdom, The National Childhood Encephalopathy Study [NCES] was established in 1976 to determine if whole-cell pertussis vaccine caused brain damage in children and, if so, to establish how often such damage occurs. This was a prospective case controlled study and the results of the first one thousand cases for the three years ending June 30, 1979, was reported. A case was defined as acute neurological illness in a 2- to a 36-month-old child that required hospitalisation. Permanent brain damage was defined as a case with residual effects after one year.

There are those who dismiss the 1976 NCES Study as being unhelpful in supporting causation. However the Opinion of Simeon Maskrey QC, in July 2000, had this to say:

At Page 11, para. 13;

"It is one thing to say that Loveday is not an impediment to further litigation. It is another to say that the further litigation will be successful. As I understand Dr Kinsbourne, he considers that the NCES study is

crucial in proving a causal link. He emphasises that the NCES study does not of itself establish a causal link. What it does is to exclude coincidence as an explanation for damage occurring in close temporal proximity with the administration of vaccine. However the exclusion of coincidence, together with proof that there is no scientific reason to deny possibility of a causal link between the vaccine and damage, is sufficient (in the absence of any other identified cause for the damage) to establish that the causal link is probable.”

Also at Page 15, para 18.1;

“Given that it is proved that the vaccine does cause permanent damage in some cases, it seems to me to be arguable that if a given claimant meets the criteria established and used by the NCES, and if the chance of coincidence is then proved to be (say) one in four or one in five, he will have proved that on balance of probabilities, his injury was caused by the vaccine.”

This study will of course have missed the many children who had serious reactions and who were not admitted to hospital.

For previously normal children, the estimated risk of permanent neurological illness attributed to immunisation with DTP vaccine was one in 310,000 immunisations. In addition to this rare rate of major brain damage there is the very real possibility that the highly neurotoxic whole-cell pertussis vaccine may cause minor brain damage in a much higher percentage of vaccine recipients.

This damage might manifest itself in loss of intelligence quotient points, concepts and therapeutic implications. The Journal of Pediatrics, 116, 671-684.

37

<http://www.cdc.gov/nip/publications/VIS/vis-mmr.pdf>

38

BMJ 2003;326:620 (22 March 2003)

Page 10 of 17

reading problems, language difficulties and autism. Since these types of brain damage show up years after vaccination, we may never know who was truly damaged by whole-cell pertussis vaccination.

In 1985 The Institute of Medicine, (IOM), of the U.S. National Academy of Sciences after an extensive review of the problem of adverse reactions to pertussis vaccine gave the highest possible priority to switching from whole-cell pertussis vaccine to acellular vaccine to prevent monetary loss and personal suffering. In 1990, after extensive hearings another IOM committee concluded that the evidence was sufficient for them to conclude that whole-cell pertussis vaccine caused acute encephalopathy.

They were unable to conclude satisfactorily whether whole-cell pertussis vaccine caused permanent brain damage. (See Causation, Page 3) They never said what level of proof they required to come to their conclusion. This was important because scientists generally require a 95 percent or better certainty for such a conclusion, but U.S. Courts only require a more likely than not standard. In 1993 a ten-year follow-up of the NCES was published, to help address this legitimate criticism. This study again concluded that whole-cell pertussis vaccine most likely caused permanent brain damage, in otherwise apparently normal children, if they developed significant neurological symptoms within seven days of the pertussis vaccination.

Vaccine-induced Autism

This type of autism is characteristic of post-natal brain damage. Thus it will be seen from the foregoing reports that subjects who are affected in this way do not suffer from classical autism. The symptoms are consistent with damage to certain areas of the brain. However, some of these areas are those which are known to be affected in classical autism.³⁹

Levels of development are consistent with the outcome of early, sporadic brain damage. Many will have capabilities that are not normally possessed by those with autism of a genetic aetiology. An examination of their DNA could establish if there are any genetic markers. Several researchers have located what they believe to be genes associated with autism. These include chromosomes, 2, 7, 15, 16 & 17.⁴⁰

The Association between Autism and Mental Retardation

There may sometimes be confusion in diagnosis where both of these conditions are thought to co-exist in a subject. Mental retardation is attributed to those with an IQ of less than 70. Some of these subjects will also have social impairments; this is especially so in those with an IQ of less than 50. Even in those who are diagnosed with the full, typical picture of autism, over 90% will have IQs of between 20 and 69. Whether one adopts a broad or narrow perspective on this issue, one needs to consider the source and significance of the association between mental retardation and autism-like impairments in interpersonal relatedness.⁴¹

It is important in the vaccine damage cases for there to be cognisance of the possibility that brain damage, having caused developmental abnormalities to a degree that is accepted as mental retardation, may also mimic autism-like impairment. There is frequently no evidence that this brain damage has been

39

Challoner, A. (2008) Autism and Abnormalities in the Brain.

<http://www.scribd.com/oakwoodbank>

40

Am. J. Hum. Genet., 69:570-581, 2001.

brought about by any other cause than vaccination with DPT during the first six months of life.

Social Behaviour and the Amygdala

Dr. David Amaral,⁴² of the University of California, Davis Department of Psychiatry, Center for Neuroscience, California Regional Primate Center, and MIND Institute has presented animal data on the neuroanatomy of the amygdala and its connections with the orbitofrontal and temporal cortices. This was done with a view toward developing a larger picture of how the amygdala affects social behaviour — through which one could investigate how disruptions of amygdaloid connections might affect social impairments of functioning such as autism.

He suggested that early works by Brothers⁴³ and Rosvald and colleagues^{44,45} were important in understanding these connections. Rhesus dominance hierarchies were disrupted when a subject had progressive amygdaloid lesions and was then reintroduced to a troupe. This permitted the inference that the amygdala was related to the emitting of socially appropriate behaviours, and that its lesions disrupted that functioning. Connections of the amygdala with the neocortex, basal forebrain, hippocampus, thalamus, and hypothalamus supported this.

Amygdala and Vaccine-induced Autism

For more than a decade, the amygdala has been identified as a substrate whose dysregulation is likely to contribute to some aspects of autism. Via artificially induced status epilepticus (SE), Tuunanen et al,⁴⁶ identified a number of amygdaloid regions experiencing SE-induced neuronal damage, most sensitive to damage were neurons within the accessory basal, lateral, basal, medial, and anterior cortical nuclei. Based upon neuro-anatomical studies of the amygdala in higher primates including humans, the sub-areas identified by Tuunanen et al are linked with certain traits in autism.

The specific amygdaloid areas identified by Tuunanen et al include:

- (i) within deep nuclei: accessory basal, lateral, and basal nuclei;
- (ii) within superficial nuclei: anterior cortical, medial, and posterior cortical nuclei, as well as lesions in the lateral olfactory tract, the bed nucleus of the accessory olfactory tract, and the peri-amygdaloid cortex; and
- (iii) within additional nuclei such as anterior amygdaloid area, central nucleus, amygdalo-hippocampal area, as well as the intercalated, lateral, and basal nuclei.

The Tuunanen et al paper may be important for understanding aetiology and patho-physiology in a large subgroup of autistics and other individuals along the pervasive development disorder spectrum.

42

Amaral D. Amygdala, social behavior and autism. Program and abstracts of the American Academy of Child and Adolescent Psychiatry 49th Annual Meeting; October 22-27, 2002; San Francisco, California. Institute IIIB.

43

Brothers L. The social brain: a project for integrating primate behavior and neurophysiology in a new domain. *Concepts Neurosci.* 1990;1:27-51.

44

Rosvald HE, Mirsky AF, Sarason I. Amygdectomy and social behavior. *J Comp Physiol Psychol.* 1954; 11:10-93.

45

Rosvald HE, Mirsky AF, Sarason I, Bransome ED, Beck LM. A continuous performance test of brain damage. *J Consult Psychol.* 1956;90:343-350.

46

Tuunanen J, Halonen T, Pitkanen A. Status epilepticus causes selective regional damage and loss of GABAergic neurons in the rat amygdaloid complex. *Eur J Neurosci* 1996; 8: 2711-2725.

Page 12 of 17

Tuunanen et al (idem) suggest that their findings about SE-induced neuronal damage also may apply to effects induced by febrile seizures, which is reinforced by the febrile seizures / status epilepticus relationships cited above.

In some individuals, if by these processes certain amygdala neurons die, then numerous autonomic, emotional, motivational, behavioural, and social processes will become atypical. For these reasons, the Tuunanen et al findings may,

- (i) delineate the neuro-pathological substrate and
- (ii) provide the "acceptable animal model" that Golden and O'Donohue did not feel existed in 1990 and 1994.^{47, 48}

The additive-effects principle may account for some cases of inter-individual variation, even among siblings including twins. Consider the subset of children whose autism may have come via the "FS to SE to amygdaloid-damage" route.

The medical history of each sibling, while very similar in regard to vaccination timings, nonetheless may have been different with regard to one or more early, severe infections. As a result, when a subsequent fever and related cytokines- release occurred (Luheshi et al, idem), the sibling with one or more extra FS in his or her medical history would, in contrast with other siblings, have been more inclined to have had a FS- and SE-induced neuropathy within the amygdala⁴⁹. Another source of inter-individual variations is presented in Tuunanen et al (idem), wherein status epilepticus stimulation led to variations in degrees of damage within primary and secondary amygdaloid locales having neuronal death.

The possibility remains that, in some individuals, reactions to a single infection or a vaccination may be sufficient for inducing the sequence from febrile seizures to status epilepticus to amygdaloid-damage.⁵⁰ Pitkänen et al have shown that research data using rodents and nonhuman primates suggests that structural and functional alterations caused by seizure activity originating in the amygdala are not limited to the amygdala itself, but may also affect other temporal lobe structures. The information gathered so far on damage to the amygdala in epilepsy or after status epilepticus suggests that local alterations in inhibitory circuitries may contribute to a lowered seizure threshold and greater excitability within the amygdala. Furthermore, damage to select nuclei in the amygdala may predict impairment of performance in behavioural tasks that depend on the integrity of the amygdaloid circuits.⁵¹

47

Golden GS. Pertussis vaccine and injury to the brain. J Pediatr., 1990;116;854-861.

48

O'Donohoe NV. Epilepsies of Childhood. 3rd ed. Oxford: Butterworth- Heinemann Ltd, 1994.

49

Verity CM, Ross EM, Golding J. Infantile febrile status epilepticus: risk factors and outcome. Brit Med J 1993;307;225-228.

50

Binstock, T. Febrile Seizures and the Amygdala in autism-spectrum disorders.

Researcher in Developmental and Behavioral Neuroanatomy, University of Colorado Health Sciences Center, Denver. {Direct communication, 31 Jan 1997 }

51

Pitkänen A, Tuunanen J, Kälviäinen R, Partanen K, Salmenperä T.

Amygdala damage in experimental and human temporal lobe epilepsy. Epilepsy Res 1998; 32 :233-253
Page 13 of 17

Thiomersal

The Green Book published by HMSO is a reference text about vaccinations. It suggests that thiomersal is added at a concentration of 0.01%. The National Network for Immunisation Information (see below this page) suggests that in some instances the concentration may be as high as 3 micrograms for each 1cc dose. Pichichero et al tell us that, concentrations of mercury in infants exposed to thiomersal following vaccination were very variable, and assessment depended upon the time lapse between vaccination and testing. Although mercury concentrations were uniformly low, the highest levels were recorded soon after vaccination.⁵²

Most of the toxic effects of organic mercury compounds take place in the central nervous system, although the kidneys and immune system can also be affected. Organic mercury readily crosses the blood-brain barrier, and fetuses are more sensitive to mercury exposure than are children or adults. The researchers estimated that the half-life of mercury in blood after vaccination to be seven days.

The US Food & Drug Administration has produced a safety review⁵³ of the use of mercury in plasma-derived products. The latest version is dated 29th January

2003. The committee involved with the review reports that it, "... believed that the effort to remove thiomersal from vaccines was 'a prudent measure in support of the public health goal to reduce mercury exposure of infants and children as much as possible.' Furthermore, in this regard, the Committee urged that, 'full consideration be given to removing thiomersal from any biological product to which infants, children, and pregnant women are exposed.' "

Ball et al⁵⁴ have reported that, delayed-type hypersensitivity reactions from thiomersal exposure are well recognised. They have identified acute toxicity from inadvertent high-dose exposure to thiomersal including neurotoxicity and nephrotoxicity. Chronic, low-dose methyl mercury exposure may cause subtle neurologic

abnormalities. Depending on the immunisation schedule, vaccine formulation, and infant weight, cumulative exposure of infants to mercury from thiomersal during the first 6 months of life may exceed EPA guidelines. Their review revealed that some infants might be exposed to cumulative levels of mercury during the first 6 months of life that exceed EPA recommendations.

Mercury was eventually removed from the DPT vaccines given to British babies in 2004.[See 'Certiva' below page 16]

The National Network for Immunisation Information

(<http://www.immunizationinfo.org/>) suggests that the safe levels of thiomersal for a six-month-old child have been calculated as 0.8 micrograms. Some vaccines have at least 3 micrograms for each 1cc dose.

Another valuable reference on this subject is the Immunisation Safety Review: Thiomersal - Containing Vaccines and Neuro-developmental Disorders (2001) Institute of Medicine (IOM). It can be read online at:

<http://books.nap.edu/books/0309076366/html/R1.html>

52

Pichichero ME, Cernichiari E, Lopreiato J, Treanor J. Mercury

Concentrations and Metabolism in Infants Receiving Vaccines Containing Thimerosal: A Descriptive Study.

Source: The Lancet, November 30, 2002, Vol. 360:1737-1741.

53

Thimerosal in Vaccines.<http://www.fda.gov/cber/vaccine/thimerosal.htm>.

54

Ball, Leslie K.; Ball, Robert; and Pratt, R. Douglas. An Assessment of Thimerosal Use in Childhood Vaccines. Pediatrics Vol. 107 No. 5 May 2001, pp. 1147-1154.

Page 14 of 17

Brain Damage caused by Vaccination Alan Challoner MA (Phil) MChS That vaccinations are helpful to society is without question; however,

The Injection Site⁵⁵

Most vaccines should be given via the intramuscular route into the deltoid (upper arm) or the antero-lateral aspect of the thigh. This optimises the immunogenicity of the vaccine and minimises adverse reactions at the injection site. Recent studies have highlighted the importance of administering vaccines correctly.

In the case of vaccines in which the antigen is adsorbed to an aluminium salt adjuvant such as diphtheria, tetanus, and pertussis vaccines, the intramuscular route is strongly preferred because superficial administration leads to an increased incidence of local reactions such as irritation, inflammation, granuloma formation, and necrosis.

The injection technique and needle size both determine how deep a substance is injected. Injection technique involves stretching the skin flat before inserting the needle or pinching a fold of skin before injection, which may necessitate the use of longer needles. To make sure the needle reaches the muscle and that vaccine does not seep into subcutaneous tissue the decision on the size of the needle and injection site should be made individually for each person. It should also be based on the person's age, the volume of material to be administered, and the size of the muscle.

Consideration should be given to needle gauge. A wider bore needle ensures

that the vaccine is dissipated over a wider area, thus reducing the risk of localised redness and swelling. A standard size of needle will not guarantee successful intramuscular injection in all people.

It is therefore relevant to consider that incorrect procedure may contribute to an adverse reaction. This ought to give rise to a view that although individual factors may not of themselves contribute entirely to an adverse response, a series of militating factors might.

Non-specific effects of vaccines⁵⁶

This report shows that the increase in mortality from the DPT and polio vaccines is worrying, but they are preliminary findings. There is a clear message from this study: in areas of high mortality, vaccines may have substantial effects on mortality from all causes through non-specific effects on deaths from diseases other than those targeted by the vaccines.

The Guinea-Bissau investigators speculate that DPT vaccine may have adverse non-specific effects because the aluminium adjuvant stimulates Th2 immunity.

(See section on cytokines – page 6 above) It has been suggested that reduced exposure to BCG and other microbes combined with increased exposure to aluminium, DPT vaccine, and other Th2 adjuvants may have contributed to the apparent increase in allergic disease in developed countries

Some will argue that the Guinea-Bissau data should not have been published, because publication might damage immunisation programmes. However, it would be inappropriate to suppress this evidence just as it would be inappropriate to withhold DPT vaccine on the basis of these preliminary results.

Certiva™

55BMJ 2000; 321:1237-1238 (18 November 2000) Editorials

56

BMJ 2000;321:1423-1424 (9 December) pp 1435 Editorials

Page 15 of 17

As recently as 1998, North American Vaccine, Inc., manufacturers of Certiva™

(Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed), has stated:

“Routine vaccination with whole-cell DTP vaccine has significantly reduced pertussis-related morbidity and mortality. However, concerns regarding reactogenicity of whole-cell DTP vaccine have spurred development of safer pertussis vaccines. The role of different components produced by *B. pertussis* in either the pathogenesis of, or the immunity to, pertussis is not well understood.”

This admission seems not to have been seen by Lord Brennan. With reference to page 11, para. 28 in his September 2001 Advice to the Legal Services Commission, it should be noted that whilst it may not be negligent to use the whole cell vaccine, despite its “reactogenicity” (Certiva™), the precautions brought forward by Berg (1958) [See pages 2 & 16] and Feldman (2002) [See page 2 above], need to be emphasised. Lord Brennan does not pay attention here to the possibility that batches of vaccine vary and that a particular specimen may have been faulty by dint of time lapse rather than manufacture, nor that the vaccination procedure and the quantity of vaccine used may vary in individual cases.

Tripedia®

The manufacturer’s leaflet from Aventis for Tripedia includes the following under Contraindications.

“Encephalopathy not due to an identifiable cause, occurring within 7 days of a prior whole-cell pertussis DTP or DTaP immunization and consisting of major alterations of consciousness, unresponsiveness, generalized or focal seizures that persist for more than a few hours and failure to recover within 24 hours should be considered a contraindication to further use; this includes severe alterations in consciousness with generalized or focal neurologic signs. Even though causation cannot be established, no subsequent doses of pertussis vaccine should be given and immunization with DT should be continued to complete the series.”⁵⁷

Additional REFERENCES

Aicardi J, Chevrie JJ. 1975. Accidents neurologiques consecutifs a la vaccination contre la coqueluche.

[Neurological complications following immunization against pertussis.] Archives Francaises de Pediatrie 32:309- 317.

Berg JM. 1958. Neurological complications of pertussis immunization. British Medical Journal 2:24-27.

Byers RK, Moll FC. 1948. Encephalopathies following prophylactic pertussis vaccination.

Pediatrics 1(4):43 7- 457.

Cavanagh NPC, Brett EM, Marshall WC, Wilson J. 1981. The possible adjuvant role of Bordetella pertussis and pertussis vaccine in causing severe encephalopathic illness: a presentation of three case histories. Neuropediatrics 12:374-381.

Coulter HL, Fisher BL. 1985. DPT: A Shot in the Dark. New York: Harcourt Brace Jovanovich.

Ehregut W. 1977. Neurale Komplikationen nach Pertussis-Schutzimpfung. [Neurological complications following whooping-cough vaccination.] Monatsschrift für Kinderheilkunde 125:908- 911.

57

http://www.vaccineshoppe.com/US_PDF/298-10_4043_4058.pdf

Page 16 of 17

Ehregut W. 1980. Laesst sich die Reserve gegenueber der Pertussis-Schutzimpfung begruenden? [Is the reserve in respect of protection against pertussis by immunization well-founded?] Paediatrische Praxis 23:3-13.

Globus JH, Kohn JL. 1949. Encephalopathy following pertussis vaccine prophylaxis. Journal of the American Medical Association 141:507 - 509.

Kulenkampff, M, Schwartzman, JS, Wilson, J. Neurological Complications of Pertussis Inoculation; Archives of Disease in Childhood; 1974, 49, 46.

Madsen T. 1925. Whooping cough: its bacteriology, diagnosis, prevention, and treatment.

Boston Medical Surgical Journal 192(2):50 - 60.

Madsen T. 1933. Vaccination against whooping cough. Journal of the American Medical Association 101:18 7- 188

Malmgren B, Vahlquist B, Zetterstrom R. 1960. Complications of immunisation. British Medical Journal 2:1800 - 1801.

Stewart GT. 1977. Toxicity of pertussis vaccine (letter). Lancet 1:1130.

Stewart GT. 1979. Toxicity of pertussis vaccine: frequency and probability of reactions. Journal of Epidemiology and Community Health 33:150 - 156.

Ström J. 1960. Is universal vaccination against pertussis always justified? British Medical Journal 2:1184-1186.

Sutherland JA. 1953. Encephalopathy following diphtheria-pertussis inoculation. Archives of Disease in Childhood 28:149- 150.

Toomey JA. 1949. Reactions to pertussis vaccine. Journal of the American Medical Association 139:448-450.

September 2004 — Revised 3.1.10

Page 17 of 17

Tratto da: <http://www.scribd.com/doc/19408267/Brain-Damage-Caused-by-Vaccination>

Prosegue in: <http://www.shirleys-wellness-cafe.com/vaccines.htm>