

Wrong About Vaccine Safety: A Review of Andrew Wakefield's "Callous Disregard"

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Andrew J. Wakefield

Callous Disregard: Autism and Vaccines – The Truth Behind a Tragedy

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Abstract: On February 28, 1998, Dr. Andrew Wakefield published an article in the *Lancet* on 12 children “with a history of pervasive developmental disorder and intestinal symptoms. Onset of behavioral symptoms was associated, by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children.” Though not claiming the MMR vaccine caused the symptoms, adding what parents thought certainly raised the possibility. Statements and articles by Wakefield suggested he believed such a link probable. Vaccination rates plummeted in the UK and outbreaks of vaccine preventable diseases followed. Investigative journalist Brian Deer uncovered dishonest and unethical medical practices by Wakefield, resulting in Wakefield losing his medical license. Rather than appeal the decision, Wakefield wrote a book, “*Callous Disregard: Autism and Vaccines – The Truth Behind a Tragedy*,” wherein he claims loss of his license was a political attempt to silence his criticism of vaccine safety. This paper examines the validity of Wakefield’s claims. A careful review of publicly available information makes it clear that Wakefield’s claims regarding vaccine safety are wrong. It is hoped that this review will be used by doctors and public health personnel to encourage parents hesitating to have their children vaccinated to question anti-vaccination claims in general, given that many proponents often refer to Wakefield as an authority and display in their own writings and pronouncements similar erroneous claims.

Keywords: Anti-vaccination, aseptic meningitis, anaphylaxis, cerebellar ataxia, gait disturbance, MMR vaccine, mumps meningitis, vaccine approval.

INTRODUCTION

Andrew Wakefield is a prominent figure among those who fear that vaccines cause more harm than good. When the UK’s General Medical Council (the Council) revoked his license, his supporters saw a political move to silence his criticism of vaccine safety and his claims that vaccines, the MMR in particular, played a causal role in the rise of autism and other childhood disabilities. The Council’s hearings and action [1,2], along with articles by investigative journalist Brian Deer [3], presented Wakefield with the opportunity to become a martyr. As of November 14, 2013, a petition supporting Wakefield has been signed by over 4,000 people [4].

The following provides an account of Wakefield’s controversial article, reactions to that article, and the publishing of “*Callous Disregard*.”

On February 28, 1998, Wakefield published an article in the *Lancet* describing 12 children “with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms. . . . Onset of behavioral symptoms was associated, by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children” [5]. The paper itself did not claim that the MMR vaccine caused the symptoms, but the inclusion of the parent’s attributions raised such a

possibility. Previous and subsequent statements and articles by Wakefield indicated he believed a causal link was highly probable [6-11]. Vaccination rates plummeted in the UK from 92% in 1996/97 to 80% in 2003/2004 [12,13], and outbreaks of vaccine preventable diseases followed [14-16].

On February 22, 2004, the first report in a series by investigative journalist Brian Deer was published in *The London Sunday Times*, revealing numerous acts of dishonest and unethical medical practices by Wakefield related to the published article [17]. Mr. Deer’s articles led 10 of the 13 co-authors to publicly retract the part of the *Lancet* article associating the MMR vaccine with autism [18]. Wakefield’s original article was retracted by the *Lancet* in February 2010 [19].

As a result of the above and other actions by Wakefield, a UK General Medical Council Fitness to Practise Panel (the Panel) held hearings that lasted over 2.5 years (July 2007 – May 2010). On January 28, 2010, the Panel found that Dr. Wakefield’s behavior involved “serious professional misconduct” [2]. On May 24, 2010, the Panel reported,

On behalf of Dr. Wakefield, no evidence has been adduced and no arguments or pleas in mitigation have been addressed to the Panel. In fact Mr. Coonan [Dr. Wakefield’s lawyer] specifically submitted: “we call no evidence and we make no substantive submissions on behalf of Dr. Wakefield at this stage.” “I am instructed to make no further observations in this case [1].”

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Accordingly, the Panel has determined that Dr. Wakefield's name should be erased from the medical register. The effect of the foregoing direction is that, unless Dr. Wakefield exercises his right of appeal, his name will be erased from the Medical Register [1].

Dr. Wakefield, instead of submitting additional evidence or appealing, wrote the book "Callous Disregard," which contains much of what one would assume would have been used in an appeal.

The main theme of Wakefield's book is that the Fitness to Practise Medicine hearings and decisions were politically motivated to silence his whistleblowing about the lax safety standards used for approval of vaccines and his fight to improve them. The book's two main topics are: 1) vaccine safety studies and the vaccine-approval process; and 2) an attempt to discredit both Brian Deer and the Panel hearings. The book refers to medical records, memos, and other documents, some that cannot be publicly verified. What can be verified and questioned is Wakefield's presentation and interpretation of vaccine safety studies and the vaccine approval process. This paper reviews the verifiable, publicly available, evidence that Wakefield's presentation employed to question vaccine safety. The findings of the UK Panel are online, and the reader is encouraged to review the document [2].

This paper systematically examines the claims in Wakefield's book as an example of similar erroneous claims being made within the anti-vaccination movement, contrasting these approaches to scientific foundations of vaccine risk and benefit. It is hoped that this review will be used by doctors and public health personnel to encourage parents hesitating to have their children vaccinated to question anti-vaccination claims in general, given that many proponents often refer to Wakefield as an authority and display in their writings and pronouncements similar examples of erroneous claims. The public health risks from decreased vaccination are significant. Based on the old adage "trust but verify," readers should examine the references and, where possible (URLs to many documents are included), obtain and read the original papers rather than rely on the "interpretations" of others.

ARE DR. WAKEFIELD'S CLAIMS ABOUT VACCINE SAFETY STUDIES CREDIBLE?

The following presentation follows the order of Wakefield's claims regarding vaccine safety, the first of which refers to his communications with a Swedish vaccine researcher.

According to Dr. Wakefield, when the UK adopted a policy to include a second dose of measles-containing vaccine (MCV) in the National Health Service (NHS) pediatric vaccination schedule:

[I] sought evidence that any MCV revaccination policy had ever been studied for safety but could find none. As part of this quest, I contacted Dr. Christenson on the basis of her being one of the architects of the Swedish vaccine program. Systematic revaccination with MMR started in Sweden in 1982. I asked her about her expert knowledge of safety studies of 2-dose MMR schedules . . . She replied:

We have followed the 12-year old children with blood specimens drawn before vaccination and 2 months after vaccination.

[According to Dr. Wakefield], "measurement of serum antibodies . . . is *no* kind of a safety study at all. . . Christenson later confirmed to me in a telephone call that there had been no safety studies of 2-dose schedules in Sweden, nor was she aware of any having been performed elsewhere, reinforcing the experimental nature of this policy in the UK." [20].

In his endnotes [21] Wakefield refers to an article co-authored by Dr. Christenson in the *British Medical Journal* [22]. This article reports the findings of a 1987 Swedish study of a 2-dose schedule. Under "Reports on Measles, Mumps, and Rubella, and on Adverse Events," the article states: "In Sweden it is obligatory to report severe and unexpected side effects of drugs and vaccinations to the adverse reactions advisory committee of the National Board of Health and Welfare. . . Most of the reported reactions were not serious, and in all but a few cases no symptoms remained after a follow-up period of at least one year. Case follow-up continued up to two years [my emphasis]" [22]. Thus, in the very publication Wakefield cites to bolster his claim that no safety studies were performed, it is clear that case follow-up for safety not only was carried out; but up to two years.

Another 1983 article that refers to the Swedish two-dose MMR vaccine program as well as the Swedish general approach to vaccine safety with Dr. Christenson as first author, also in the *British Medical Journal* [23] states:

As in other countries, public opinion in Sweden is extremely sensitive to reports of major side effects of drugs and vaccines. Hence to secure a vaccine acceptance rate high enough to ensure the eventual elimination of measles, mumps, and rubella it was considered necessary to supply a valid estimate of the average incidence and severity of the adverse reactions expected with the combined immunization programme, especially among the youngest target group.

Wakefield refers to another scientific paper, giving only the Swedish title [24], a safety study of the Swedish 2-dose schedule [25]. PubMed (The U.S. National Library of Medicine online database) gives the following translated title: "The low number of reported adverse effects after vaccination against measles, mumps, rubella [Article in Swedish]." According to the article, the authors obtained the actual case files for all reported cases of adverse events, noting a follow-up period of at least one year. In the Discussion section, the authors write:

In relation to the large number of doses administered of the combination MMR vaccine during this three-year period, the number of reported adverse events was incredibly low. Similar to experiences from the introduction of other pharmaceuticals, the number of reports decreased over time. In almost every case, even the more serious ones, the symptoms resolved rapidly [my translation] [25].

According to Wakefield, after the Swedish introduction of a 2-dose MMR vaccination program, only a short-term study was performed that measured virus-specific antibodies

with no evaluation of adverse events; however, Wakefield's book refers to two Swedish studies stating that reporting of serious events is mandatory and that follow-ups were for at least one year and up to two years. Furthermore, the two articles in the *British Medical Journal* studying a 2-dose schedule, and authored or co-authored by Dr. Christenson, discuss adverse events. Finally, Wakefield gave the Swedish title of an article instead of the translated title, which specifies not only "adverse events", but also a "low number" of them.

DID THE UK APPROVE USE OF COMBINED MEASLES, MUMPS, AND RUBELLA (MMR) VACCINE BASED ON INADEQUATE SAFETY STUDIES?

Wakefield writes that he sent a letter to Dr. John Walker-Smith in 1997 which stated: "In addition to our own work and that of others, my opinion is also based upon a comprehensive review of all safety studies performed on measles, MR and MMR vaccines and re-vaccination policies. This now runs into a report compiled by me of some 250 pages." [26].

Since Wakefield's ca. 250 page review has never been made public, the following is based on claims made in his book and an earlier paper. Wakefield published an article in 2000, referred to in his book [21] where he states: "the principal focus of this paper is pre-licensing studies of MMR . . . The first thing to note is that these were short-term safety studies." [10]. Wakefield mentions seven "peer-reviewed studies bearing on safety of polyvalent measles containing vaccines . . ." [10]. Note that two of the studies were after 1988, the year the UK first approved combined trivalent MMR vaccines. Yet, Wakefield's article also refers to a report by the U.S. Institute of Medicine which included an extensive reference list of approximately 200 published studies, including 18 studies of trivalent MMR vaccines, along with studies of monovalent or bivalent combinations of measles, mumps, and rubella vaccines [27]. Furthermore, three months after publication of Dr. Wakefield's article, researchers from the UK Medicines Control Agency published a detailed rebuttal in the same journal where they not only referred to the Swedish studies but also wrote:

There were about 30 studies of combined measles, mumps [and] rubella vaccines carried out prior to the decision to introduce it into the UK national immunization programme in 1988. [28].

They point out that the first combined vaccine was "licensed in the US in 1971 and in the UK in 1972" [28]. One study vaccinated 30 children with an MMR vaccine in 1968 and obtained serum titers for virus-specific antibodies from 14 of the children 10 1/2 years later [29,30]. Finally, a 1988 article by Karin Fahlgren states: "About 200 studies on measles, mumps, and rubella vaccines against these diseases have been published during the last few years. Some 30 reports deal with combined, trivalent vaccines" [31]. Wakefield's 250 page review of safety studies seems to have missed ALL of the above. His book even leaves out these seven studies from his own published article.

Table 1 provides information about published studies of MMR vaccines that included information on adverse events and were available prior to the UK approval of the vaccine.

The table includes year published, study sample size, follow-up time and strain of mumps vaccine used. The studies include those from Wakefield's 2000 article [10], those culled from Fahlgren's 1988 review article [31], and the 1994 Institute of Medicine report [27]. This suggests poor scholarship and science by Wakefield resulting in under representing the empirical research showing safety of vaccines.

Wakefield's claim that Dr. Christenson told him she did not look at adverse events was first stated in his 2000 article [10]. I think it important to show flaws in the presentation of the studies he did discuss, given that this paper predated both Brian Deer's investigative reports and the British Medical Council hearings. The following paragraphs, which refer to studies in Table 1, are based on the British rebuttal to Wakefield's article, published in the same journal a few months later [28].

The report by Stokes referenced in Table 1 [38] summarizes the results of three clinical trials involving testing of a trivalent MMR vaccine: (1) a pilot study in a small number of children in a suburb of Philadelphia; and large scale field trials on children in (2) suburban Philadelphia and (3) Costa Rica/San Salvador. Wakefield writes that "data on adverse events in both groups were gathered for 28 days post vaccination and combined for the purpose of statistical analysis" [10]. The British rebuttal wrote: "the results for both geographical groups are given separately and they were not combined for the statistical analysis, of which there is little mention. Thus, there appears to be no basis for the statement by Wakefield that the data from both groups were combined for the statistical analysis" [28].

The only statistical analysis carried out in the Stokes paper was a comparison of virus-specific antibody levels. Separate tables of adverse events were given for the Philadelphia cohort and Costa Rica-San Salvador cohort. Though the tables provided by Stokes indicate a maximum follow-up time of 28 days, the actual follow-up time was 6 – 9 weeks. "The parents of the children were given a report card for each child for recording temperatures once daily for 28 days, plus any other illness, and they were asked to notify one of us (R.E.W.) immediately when any illness occurred. Finally, the parents were queried by the physician (R.E.W.) at the time of the second bleeding six to nine weeks after vaccination and asked whether any problems had developed" [38]. In addition, the British rebuttal to Wakefield's article states:

The original authors presented the number of children with GI symptoms in days 1-4, 5-12, 13-18 and 19-28. Wakefield and Montgomery have added up all the occurrences of GI symptoms across the entire 28-day period, regardless of whether the same child or episode is being counted more than once. When analyzing such trial data, it is essential to compare the numbers with symptoms in a specified period, each child only being counted once. It is misleading to add across all intervals as Wakefield and Montgomery have done since many children will be counted twice or more [28].

So Wakefield carried out an incorrect statistical analysis, claimed the authors combined the data when they did not, and incorrectly gave a shorter follow-up time. All of these inaccuracies move evidence from showing safety to showing possible harm.

Table 1. Published Combined MMR Vaccine Studies Prior to 1988

Author	Year	Two-Dose	Sample Size (including controls)	Follow-Up Time	Mumps Strain*
Articles Mentioned by Dr. Wakefield					
Buynak <i>et al.</i> [32]	1969		273	12 days	JL
Böttiger <i>et al.</i> [22]	1987	Yes	588,300	1–2 yrs	JL
Crawford and Gremillion [33]	1981		1347	19 days	JL
Edees <i>et al.</i> [34]	1991		420	3 wks	U
Miller <i>et al.</i> [35]	1989		10,090	21 days	U
Minekawa <i>et al.</i> [36]	1974		174	4 wks	
Schwarz <i>et al.</i> [37]	1975		1,481	21 days	JL
Stokes <i>et al.</i> [38]	1971		715	28-63 days	JL
Taranger and Wiholm	1987	Yes	700,000 doses	1-2 yrs	JL
Additional Articles Found Published Prior to UK's Approval of Trivalent MMR Vaccine					
Böttiger <i>et al.</i> [39]	1985	Yes	247	8 wks	JL
Borgono <i>et al.</i> [40]	1973		188	28 days	JL
Christenson <i>et al.</i> [23]	1983a	Yes	150	28 days	JL
Evers <i>et al.</i> [41]	1983		208	21 days	
Isozaki <i>et al.</i> [42]	1982		82	6 wks	U
Just <i>et al.</i> [43]	1985		120	2 months	JL
Karchmer <i>et al.</i> [44]	1971		235	60 days	JL
Khanjanasthiti <i>et al.</i> [45]	1978		243	6 months	
Lerman <i>et al.</i> [46]	1981		502	42 days	
JLNorrby <i>et al.</i> [47]	1984		30 million		
Sedvall <i>et al.</i> [48]	1984		1,726	30 days	
Peltola <i>et al.</i> [49]	1986a	Yes	430,000	2.5 yrs	JL
Peltola and Heinonen [50]	1986b	Yes	1162	42 days	JL
Sugiura <i>et al.</i> [51]	1982		470	15 days	U
Vesikari <i>et al.</i> [52]	1984		58 JL, 116 U	21 days	JL, U
Weibel <i>et al.</i> [29]	1980a		586	42 days	JL

* U – Urabe, JL – Jeryl Lynn

Finally, as pointed out in the British rebuttal, Wakefield's article failed to mention a 1995 comprehensive report of adverse reactions based on eight million recipients following adoption of the UK two-dose policy which stated: "serious adverse reactions are very rare" [53]. The reader is encouraged to read the additional criticisms in the rebuttal [28].

Urabe Strain of Mumps Vaccine

A main focus of Wakefield's critique of vaccine safety is on aseptic meningitis associated with the Urabe strain of mumps vaccine used in the combined MMR vaccines. If Wakefield's allegations were actually true, the revelations in his book would paint quite a dismal picture of the vaccine-approval process in the UK.

Wakefield writes: "[Canada's] own Urabe-containing MMR vaccine, sold under the name of *Triverix*, was withdrawn in Canada for safety reasons in July 1998 [typo, Wakefield probably intends date to be 1988 when one province, Ontario, recalled lots of the vaccine], in the *same* month the *same* vaccine under a different name (*Pluserix*) was granted a license in the UK" [54]. "In light of its known dangers, one would have expected that vigilant surveillance of adverse events would have been put in place" [55].

In Addition, Wakefield Writes:

According to the minutes of the working party to discuss the introduction of MMR vaccine (January 23, 1987), data from other countries (the US and Finland) that used

Merck's MMR II that contained the Jeryl-Lynn mumps strain and not the Urabe-containing MMR, were accepted as a proxy for the safety of the Urabe-containing vaccine. Secondly, the UK 'trial' of MMR lasted only 3 weeks. Meningitis following the Urabe-containing MMR is rarely seen before 21 days post-vaccination and can occur up to 35 days later. The UK 'trial' would have missed it" [56].

DID THE UK GRANT A LICENSE FOR A URABE-CONTAINING MMR VACCINE AFTER CANADA WITHDREW THE URABE MMR VACCINE?

Canada licensed Trivirix in May 1986 [57]. The starting date for the UK for MMR vaccinations was **October 1, 1988** [58,59]. The license for Trivirix was withdrawn in Canada in **May 1990** stating: "Recent laboratory findings from the United Kingdom, Canada and Japan have provided sound evidence. . . In addition, the report states: "The infection follows the course of benign aseptic meningitis" [60]. The UK withdrew the Urabe-containing vaccine on September 14, 1992 [61].

Based on reports of aseptic meningitis, the Canadians estimated its occurrence in association with the vaccine as 1 case per 100,000, compared with 1 in 400 following natural mumps. A prospective epidemiological and laboratory study was planned to run from 1987 through 1989 [57]. Minutes of a UK meeting read: "Members read a report of cases of mumps encephalitis which had been associated with MMR vaccine containing the Urabe strain of the mumps virus. . . It was agreed that North Hertfordshire would use the Jeryl-Lynn vaccine, if it was available from MSD [Merck, Sharp and Dohme], to obtain comparative data" [62]. From the following meeting's minutes "It appeared that only certain batches of the Canadian vaccine had been suspended and that they had not banned all vaccine containing the Urabe strain of mumps. Dr. Begg would check with the Canadians" [63]. "The Canadians, "in a July 18th memo to all physicians in Ontario receiving vaccines from the Ontario Government Distribution Centre requested the return of any remaining stock of TRIVIRIX vaccine from doctors' offices" [64]. Note that not all vaccines in Ontario were distributed by the Ontario government; thus, even in Ontario, not all batches of Urabe-containing MMR vaccines were recalled.

The Canadians did not withdraw the licensure of the vaccine prior to the UK's program beginning; they recalled only certain lots. Licensure was withdrawn 20 months after the UK program began. The UK received reports of aseptic meningitis, investigated, and found that, at the time, only Ontario had withdrawn some lots of the vaccine. The Canadian report indicated that the risk for vaccine-associated aseptic meningitis was approximately 1/250th of the risk arising from natural mumps and that the vaccine-associated meningitis was benign, that is, with "no sequelae," and "it is important to note that these cases had short hospital stays and complete recoveries" [64]. Note that the Canadian decision to withdraw the vaccine was based partly on laboratory data from the UK.

WHAT WAS THE UK DECISION TO LICENSE THE URABE MMR VACCINE BASED ON?

From Table 1 above, there were at least three reported studies using the Urabe strain that found no serious problems [42,51,52]. The Japanese study included a six-week follow-up [42]. A German study of 197 children found no major adverse reactions based on parents keeping a 30-day written record. In addition, the children were seen at a clinic six weeks after the vaccination [65].

Several studies compared vaccines containing the Urabe with those containing the Jeryl Lynn strains. A Swedish study randomized 454 children to receiving the Urabe or Jeryl Lynn-containing MMR vaccines. Parents filled out a daily record for 28 days. In addition, the children were seen at a clinic eight weeks after vaccination. "The miscellaneous post-vaccination side-effects were mild and inconsequential" [66]. Popow *et al.* found the two vaccines equally well-tolerated, with no serious adverse events in 400 Austrian children, based on a 28-day follow-up. Post-vaccination serum samples for virus-specific antibodies were taken between days 29 and 230 (median 91 days for both groups) at which time one can assume that either health care personnel would inquire about any problems and/or parents would report them [67]. Vesikari *et al.* gave one or the other of the two vaccines to 146 Finish children. Only mild adverse events were found in a 20-day follow-up [68].

Before the beginning of the program, vaccine trials were conducted in the UK, starting in early 1987 [69]. By the beginning of October 1987, data had been collected for five months from three districts: Somerset, Fife and North Hertfordshire. The data included health diaries kept by the parents covering the three weeks before vaccination and three weeks after [58]. Approximately 5,000 children were included in these studies [70]. However, the diaries were not the only means used for reporting adverse events (see below)

WHAT TYPES OF SURVEILLANCE DID THE UK USE?

Wakefield writes: "In light of its known dangers, one would have expected that vigilant surveillance of adverse events would have been put in place" [55]. "From the 1 October [the start of the MMR vaccination program] rubella, mumps and meningococcal septicaemia had become notifiable" [71]. "Adverse Reactions Surveillance – Dr. Bowie advised that active surveillance of MMR vaccine in Somerset had just started" [72]. As of 1988, there were "four avenues for adverse reaction reporting following MMR vaccine; via the Yellow Cards, British Paediatric Surveillance Unit (BPSU) scheme, directly to Communicable Disease Surveillance Centre (CDSC) and through Laboratory reports" [73] and hospital discharge reports provided a fifth source.

Yellow Card Scheme: The Yellow Card Scheme, established 1964, is the UK system for collecting information on suspected Adverse Drug Reactions (ADRs) to medicines. ADRs can be reported by anyone; this is usually done by healthcare professionals -- including doctors, pharmacists and nurses -- but patients and caregivers also made reports [74].

British Paediatric Surveillance Unit (BPSU), established 1986: “(BPSU) is a unit which enables doctors and researchers to find out how many children in the UK and Republic of Ireland are affected by particular rare diseases or conditions each year” [75]. “An Orange Card with a list of disorders is sent monthly to more than 3,200 consultant paediatricians and other specialists [76].

Communicable Disease Surveillance Centre (CDSC) [currently Notifications of Infectious Diseases, Public Health England]: “Since 1968 clinical suspicion of a notifiable infection is all that is required” [77,78].

Laboratory reports: “The linking of laboratory records of CSF samples with district computer databases on immunization had been very effective” [79]. In addition, hospital discharge data were collected [80].

The UK decision to withdraw Urabe containing MMR vaccines was based on the Canadian reports, surveillance data from five sources, and a study that asked all pediatricians where both Urabe and Jeryl Lynn strains were used to “report all confirmed and suspected cases diagnosed during 1990-91 . . . cases were actively sought in thirteen other districts by obtaining vaccination histories for children with laboratory evidence or a hospital discharge diagnosis of aseptic meningitis. National reports of virus positive mumps meningitis cases before and after the introduction of the combined MMR vaccine were compared . . . Aseptic meningitis 15 – 35 days after vaccine was defined as vaccine-associated” [80].

The UK devoted considerable attention and resources to surveillance, both active and passive, of MMR vaccinations as exemplified in the following: “On adverse reactions to the vaccine, the most worrying reports had been studies which showed problems with Urabe vaccine, particularly mumps meningitis. Reports had also come from overseas countries, Canada being the most helpful. Surveillance had been introduced through BPSU. As sources of information were collated, the Oxford-based Research Fellow was investigating all reports, then reviewing the children’s development 12 months later” [81].

Canada was not the only country to base its decision partly on data from the UK; but “the [JCVI] committee was told that all the countries which had had a choice had switched from Urabe to Jeryl Lynn; the UK data had been accepted by all these countries” [79]. In other words, it was the quality of the UK surveillance data that prompted its worldwide use for vaccination decisions; and although the “UK’s quality of surveillance was unsurpassed . . . Many lessons had been learnt from MMR. It was agreed that better surveillance was needed as well as a consideration of how adverse events were followed up [79].”

Wakefield writes: “I have confined this chapter to my state of knowledge in 1996-7.” His “state of knowledge” regarding vaccine safety surveillance was, to say the least, deficient.

Additional information on UK vaccine approval and safety can be found in an article by David M. Salisbury [82].

ONSET OF ASEPTIC MENINGITIS FOLLOWING VACCINATION

According to Wakefield: “Meningitis following the Urabe-containing MMR is rarely seen before 21 days post-vaccination and can occur up to 35 days later. The UK ‘trial’ would have missed it.” [56]. The three-week’s of health diary collections was only part of the picture. Five other surveillance sources supplemented it. It is highly unlikely that many, if any, cases of aseptic meningitis would have been missed. Based on a recent review “postvaccinal aseptic meningitis, if it occurs, usually does so between 2 and 3 weeks after vaccine administration” [83]. The Japanese found “the interval between vaccination and the onset of meningitis was from 11 to 32 days but the majority became ill between Days 15 and 21.” [84]. According to the World Health Organization (WHO), “The onset of aseptic meningitis usually occurs 2-3 weeks after vaccine administration; the median interval is 23 days (range, 18-34 days)” [85]. So even the three week diaries would have found most cases. Any missed would have been picked up by the other five surveillance sources, and the decision to withdraw the vaccine was based on “aseptic meningitis 15-35 days after vaccine was defined as vaccine-associated” [80]. In other words, Wakefield’s claim was incorrect when he wrote that “meningitis following the Urabe-containing MMR is rarely seen before 21 days post-vaccination and can occur up to 35 days later. The UK ‘trial’ would have missed it” [56].

WAS THE URABE STRAIN-CONTAINING MMR VACCINE A DANGEROUS VACCINE?

According to Wakefield: “Against expert advice, a dangerous vaccine was given preferred status” [86]. The Canadians noted “It is important to note that these 8 cases had short hospital stays and complete recoveries” [64]. For the UK, 12-month follow-ups of cases of aseptic meningitis found vaccine-associated cases to be neuro-developmentally normal [81]. The WHO Global Advisory Committee on Vaccine Safety stated that “all reported cases of vaccine-derived mumps meningitis have recovered” [87]. In addition, the U.S. Institute of Medicine found no cases of long-term disabilities associated with aseptic meningitis [27]. And, from Japan “meningitis was generally mild and there were no sequelae from the illness” [84].

All of this information was available to Wakefield prior to writing his book. The comprehensive surveillance system being used by the UK was in place long before Wakefield’s claimed interest in vaccine safety began. The reports of the benign nature and lower frequency of Urabe vaccine-associated aseptic meningitis as compared with natural mumps were known as well.

Possible “Overreporting” of Aseptic Meningitis

Wakefield’s claim that the Urabe strain-containing vaccine was a “dangerous” vaccine is questionable. If one compares the unpleasant, but relatively rare experience of having a child hospitalized for a short period of time with no long term sequelae with risks from the natural disease (see below) then, if the only available vaccine included the Urabe strain, it would be prudent to use it. Keep in mind that initial studies

found no increased risk from the Urabe strain compared with the Jeryl Lynn strain. There is even evidence that the incidence of aseptic meningitis, a benign condition, was "over-reported" because more spinals were given to vaccine recipients following news reports of aseptic meningitis. Referring to Japan, a UK report states: "It was noted that the incidence of meningoencephalitis in Japan had been 1 in 100,000 before the increased publicity, where afterwards the incidence had risen to 1 in 8000. It was suggested that lumbar punctures might have been carried out on all admitted patients including those who were asymptomatic, which would not have been done in the UK" [88].

According to Schmitt *et al.*

None of the eight [UK] patients with CSF pleocytosis following MMR vaccination had clinically overt meningitis. All patients had mild disease and recovered uneventfully. This again raises the question of why lumbar punctures were done and how the laboratory data should be interpreted. Since other causes of CSF pleocytosis were not sought, the causal relationship between CSF pleocytosis and mumps vaccination is unproven.

In order to be meaningful, laboratory data need to be interpreted in the light of clinical findings. Naturally acquired mumps infection leads to a CSF pleocytosis in 50% of all patients, to clinically overt meningitis in 1%-10%, and to encephalitis in 0.1% [89].

WHY DID THE UK TAKE LONGER TO WITHDRAW THE URABE-CONTAINING VACCINE THAN CANADA?

As is evident from the above, compared with the naturally occurring disease, the Urabe-containing MMR vaccine had far fewer and less serious adverse events. The UK did decide early on to replace it with the Jeryl Lynn strain. The decision to continue using the vaccines containing the Urabe strain while working on obtaining supplies of the MMR vaccine containing the Jeryl Lynn strain was a prudent one given the far greater risks arising from the natural disease. Minutes from a 1993 JCVI meeting state, as follows:

The Health Departments had had a difficult time with regard to MMR supply, problems caused in the main by the manufacturers. Other vaccine manufacturers producing MMR which contained the Jeryl Lynn strain of the mumps virus included RIVM (under a very prescriptive license from MSD making sale in the UK impossible) and Rubini in Switzerland (a vaccine which lacked sufficient study in the field to be certain that there would not be a Urabe-like problem). Merck and Merieux were collaborating to produce a Jeryl Lynn strain vaccine [90].

In the UK, "despite the benign nature of vaccine-induced meningitis, a decision was made to replace the brands containing Urabe (Immravax by Merieux, and Pluserix MMR by SmithKline Beecham) with that containing Jeryl Lynn" [91].

As Summarized in a 2008 Lancet Article:

First, aseptic meningitis after mumps vaccination is generally benign and short term with no sequelae. Second,

postvaccinal aseptic meningitis is rare compared with natural mumps meningitis. In Japan, where routine mumps vaccination was discontinued in 1993, Nagai and colleagues compared the rate of aseptic meningitis after natural mumps infection and after vaccination with three different Japanese mumps vaccine strains and reported a rate of one per 2700 virologically confirmed cases of aseptic meningitis after vaccination; however, aseptic meningitis was 17 times more likely with natural mumps infection in the same setting. Third, Urabe seems to be more immunogenic than, for example, Jeryl Lynn. Fourth and final, Urabe is cheaper—the cost of MMR vaccine containing that strain is about 50–60% of the cost of MMR vaccine containing the Jeryl Lynn strain." [92].

With limited resources, Third World nations can either risk aseptic meningitis from the vaccine or the greater risks from the natural disease.

JAPAN'S EXPERIENCES WITH THE MMR VACCINE

Japan stopped using the MMR vaccine after three deaths; however, vaccines were reportedly given to tens of thousands of children even after the vaccines expiry [expiration date] [93]. "Following introduction of MMR vaccine in Japan, a close study had been made of adverse events. . . . Differences in the measles (this is of higher potency) and rubella strains exist between the products used in Japan and the UK, although the same Urabe mumps strain is used, but at a higher dose" [88]. "No deaths or sequelae directly attributed to aseptic meningitis were reported in any of these aseptic meningitis cases" [94].

Following withdrawal of the MMR vaccine, "the Ministry for Health, Labour, and Welfare of Japan estimated the number of mumps cases in Japan to be 2.26 million in 2001; only 226 cases were reported in the USA in the same year" [95]. In addition,

The incidence of measles in Japan increased following withdrawal of the combined MMR vaccine in 1993 and continues to be a public health problem. In 1980, before the combined MMR was available, over 13,000 cases of measles were reported. This number decreased to below 3300 in 1990 shortly after introduction of the combined MMR vaccine in 1989. In 2002, more than 30,000 cases of measles were reported in Japan compared with <100 cases in the US. The death rate associated with measles has ranged from 15 to 90 deaths annually. The true mortality rate of measles disease in Japan is believed to be higher due to inaccurate reporting of cause of death, which is often listed as multi-organ failure or pneumonia instead of measles [96].

In 2003, an Osaka District Court found that, of three cases of death, two were caused by the vaccine [97]. However, the Japanese MMR vaccines contained higher doses, possibly poor manufacturing controls, and some may have been expired. In addition, a court finding does not necessarily reflect or substitute for scientific evidence.

As another example of comparing vaccine-associated adverse events with those associated with the natural diseases,

from 1970 to 1993 in the United States, approximately 75,000,000 children received measles vaccine by age 4 (an immunization rate of about 90%). Only 48 cases of encephalopathy were reported. Even though this might reflect a slight underreporting, most cases are believed to be captured due to the high financial compensation available and these 48 cases may include some nonvaccine-related cases representing background rates. However, for approximately 75,000,000 vaccinees over 23 years, the incidence of acute encephalopathy caused by measles vaccine can be described as very low [98].

It must be emphasized that Wakefield neglects comparing the risks from vaccines with the exponentially higher risks associated with the actual natural disease.

Finally, **Wakefield's writes:** "The JCVI members had reasonable fears that they may be liable, and SKB, for their part, appear to have been given a "Get Out of Jail Free" card by Her Majesty's Government. Confirmation of this was later to appear in the JCVI minutes of May 7, 1993, where it states: '*...SKB continue to sell the Urabe MMR without liability*'" [86].

The actual minutes read: "The Health Department *had had* [my emphasis] a difficult time with regard to MMR supply, problems caused in the main by the manufacturers. . . producing MMR which contained the Jeryl Lynn strain of the mumps virus. Merck and Merieux *were* [my emphasis] collaborating to produce a Jeryl Lynn strain vaccine whilst SKB *continued* [my emphasis] to sell the Urabe strain vaccine without liability. Merieux's Urabe strain vaccine was still in use in Sao Paulo in Brazil where independent studies had given similar results to the UK studies confirming the *wisdom of the UK's discontinuation of the two Urabe strain vaccines*" [my emphasis] [90]. An earlier document states: "At the end of August [1992] SKB decided to stop producing vaccine and advise licensing authorities worldwide accordingly"[79]. And "one strain of mumps virus (Urabe) in an MMR vaccine previously used in the UK . . . was replaced in 1992 and is no longer licensed in the UK" [99].

Wakefield changed the tense of "continued" to "continue." Note the entire paragraph is in the past tense. The phrase "Get Out of Jail Free" implies a criminal, or, at least, some serious act. Any illness in ones children is a cause for distress; but given that aseptic meningitis is a benign condition leading to, at most, a short-term hospital stay for a few children with complete recoveries, especially compared with estimates of aseptic meningitis from naturally acquired mumps (see above "**Was the Urabe strain-containing MMR vaccine a dangerous vaccine?**" and "**Possible "Overreporting" of Aseptic Meningitis**"), the phrase reflects hyperbole rather than reality. Finally, as childhood vaccinations are mandatory as a public health program, the U.S. government, through the Vaccine Court [100], takes responsibility for compensating vaccine-associated adverse events and the UK does the same [101]. What Wakefield writes does not accurately reflect what was stated in the JCVI minutes.

Though the research results have clearly indicated that the Urabe strain has higher rates of adverse events than the

Jeryl Lynn, this research has also found that the risks from permanent sequelae are infinitesimal compared with the risks arising from the actual diseases. Since the MMR vaccine with the Urabe strain currently is significantly cheaper than the vaccines containing the Jeryl Lynn and has been found to confer higher levels of immunity, it is still being used in much of the Third World where costs and the ability to revaccinate are limiting factors [83].

In Summary

Wakefield's report that the UK introduced the Urabe-containing MMR vaccine following Canada's withdrawal is wrong. His claim that the UK based the introduction on a few international studies and a UK study with only three weeks of follow-up data is incorrect. His claim that most cases of vaccine-associated aseptic meningitis develop after three weeks is incorrect. His assertion that the UK's surveillance system was inadequate and was not increased following introduction of the MMR vaccine is incorrect. His claim that the UK continued with the Urabe strain-containing vaccine and indemnified its manufacturers is not only incorrect, but also an inaccurate rendering of a partial quote from the JCVI minutes. And, most importantly, his claim that the Urabe strain-containing vaccines are "dangerous" vaccines is misleading and is contradicted by both the UK and international data. By all accounts, the UK's decision was based on extensive surveillance and the decision to switch vaccines perhaps overly cautious.

ANAPHYLAXIS -- FEAR-MONGERING --IGNORING THE DATA -- COMPARED TO WHAT?

Wakefield writes: "There are well-established side effects from measles-containing vaccine (MCV); anaphylaxis is one of these [102]. Based on a 1992 letter to Pediatrics from one clinic in New York [103], Wakefield goes on to write: "Without prompt treatment, this reaction, which occurred in 1 in 558 recipients of an MCV, might well have been fatal" [102]. Finally, Wakefield writes: "Trying to persuade parents of the merits of an MR campaign on the basis of up to 50 possible measles deaths while ethically warning them of the possibility of up to 14,337 anaphylaxis deaths from the MR vaccine would have doomed the campaign to failure" [104].

Once more, Wakefield misses the large Swedish and Finnish two-dose studies published in the British Medical Journal and the Lancet respectively, among the approximately 30 studies mentioned in the British rebuttal to his 2000 article. The Swedish study found seven cases of anaphylaxis in two years out of 588,300 [22] with no deaths and the Finnish study of 430,000 stated: "without a single permanent sequela observed" [49]. The other Swedish publication studying a two-dose regimen, based on 700,000 doses, given in Dr. Wakefield's endnotes states: "No full-blown case of anaphylactic shock was reported." [my translation, [25]]. The 1994 Institute of Medicine report, based on a comprehensive review of the literature, found: "estimates from the studies described . . . range from 1 per 20,000 to 1 per million doses distributed . . . the evidence favors acceptance for a causal relation between measles vaccine and death from anaphy-

laxis. *There is no direct evidence for this; the conclusion is based on the potential of anaphylaxis to be fatal. The risk would seem to be extraordinarily low* [my emphasis]" [27]. Finally, two more examples of large scale research looking at adverse reactions within a two-dose MMR regimen, available to Wakefield long before publication of his book:

1. An Australian study of 1.7 million children found one case of anaphylaxis which was promptly treated with adrenaline [105],
2. A 14-year Finnish prospective follow-up of MMR vaccinations of 1.8 million individuals was launched in 1982 [106]. "Thirty suspected cases of anaphylaxis were reported . . . in 15 of the 30 cases the physician ultimately diagnosed fainting. Full recovery within 1 h, and usually within a few minutes, was the rule" [106].

Since Wakefield Refers to the UK Joint Committee on Vaccine Minutes, What They Said Follows

There had been no reports of harm following anaphylactic reactions; it was agreed that this information should be made more widely available [107].

This paper was based on spontaneous reports of anaphylaxis . . . received from the MR campaign between November 1994 and April 1995. The reports had used a wide range of terminology but few cases had been severe or life-threatening. . . . 81 (1 in every 100,000) were anaphylactic. . . . Half the cases did not receive adrenaline and cases were rarely serious. . . . All children with anaphylaxis had recovered completely [108].

In summary, there had been no new or unrecognized adverse reactions during the campaign, there had been *no deaths* [my emphasis] and most of the 8 million children immunized did not have any adverse reaction whatsoever [109].

It would be difficult to characterize the discrepancy between Wakefield's estimate of "up to 14,337 anaphylaxis deaths from the MR vaccine" and the real-world's figure of zero as anything less than gross fear-mongering, especially given that all this data was available to Wakefield long before he wrote his book. Wakefield refers to the two-dose campaign as "experimental," when in fact it was based on large Swedish and Finnish studies as well as several other smaller studies (see Table 1 above). It was anything but "experimental;" and it applied well-researched science. Missing the studies indicating the safety of the MMR in a two-dose regimen, Wakefield found only one letter discussing anaphylaxis in the journal *Pediatrics*, missing what this letter actually stated: "All patients responded to treatment with aqueous adrenaline and/or diphenhydramine. There were no reported serious reactions in 406 children between 1 and 2 years old who received the vaccine. We cannot be certain that all five allergic reactions were secondary to the MMR vaccine . . ." [103]. Based on the mere mention of anaphylaxis, Wakefield proceeded to make a completely unjustified claim.

DOES THE MMR VACCINE CAUSE GAIT DISTURBANCES AND/OR CEREBELLAR ATAXIA?

According to Wakefield

Dwelling briefly upon the clinical features of ataxia in combination with developmental regression, potentially novel adverse events associated with the combined MMR vaccine, rather than the monovalent component vaccines, have emerged from Plesner's Danish study of ataxia. Earlier studies had indicated that ataxia with gait disturbance might occur in up to 1 in 1000-4000 recipients of MMR. In Denmark this association had not been detected with any other vaccine administered to children of the same age prior to the introduction of MMR in 1987. In a follow-up of the mandatory passive reporting system for vaccine adverse events operated in Denmark, Plesner not only confirmed this association but also indicated that the more severe ataxias following MMR may be associated with residual cognitive deficits in some children, a finding of specific relevance to the MMR-autism debate [110].

According to the First Plesner *et al.* Paper

In Denmark we have received 24 notifications of temporary gait disturbances after measles, mumps, and rubella vaccination in 15-month-old children. . . . The mandatory notification system in Denmark is of a high standard and this adverse reaction has been registered only after M-M-R-II vaccination. Since 1987 . . . 362,000 doses were given to 15-month-old children . . . *Health authorities might not take note of this adverse reaction to measles, mumps, and rubella vaccine because it seems to be a slight and temporary condition* [my emphasis], which is difficult to describe. Symptoms usually disappear within a few days, but in some children they can last several months. . . *It is yet to be established what causes the disorder* [my emphasis] [111].

Plesner *et al.*'s follow-up paper states: "During the following 10-y period . . . a total of 41 notifications [to the mandatory notification system] have included 'gait disturbance'. This corresponds to a frequency of 8 per 100 000 doses of MMR vaccine used for 15-mo-old children [from 1987 to 1996 a total of 533,000 vaccinations were given]." Additionally, "two other large parental questionnaire studies regarding the Danish vaccination programme, but not specifically including this adverse event, were searched for possible descriptions of gait disturbance . . . According to these two studies, a frequency could be estimated to be 1 per 1000-4000 vaccinees. . . In all cases [from the parental questionnaires], the GPs were contacted and according to their files no residual symptoms or sequelae were observed during subsequent examinations of the children" [112].

The Paper Goes on to State

Six of the 41 children (14%) had some kind of lasting neuropsychological complaint. Neuropsychological problems have been described as occurring in 5-10% of Danish and Swedish children, and *it is not possible in the present study to evaluate further the cause of the children's complaints* [my emphasis]. . . A prospective fol-

low-up study or a case-control study would be the design of choice for further descriptions of this reaction . . . In Denmark, including all 50 000 vaccinated children per year, might only disclose a few, short-lasting reactions. Since introduction of the MMR vaccine, the lives of many children have been saved and severe developmental disorders due to measles encephalitis have been avoided [112].

Besides the two Danish studies, Wakefield also refers to a Swedish study, the Taranger study mentioned earlier where he only gives the Swedish title. Taranger reports out of 700,000 doses five cases of “Acute symptom with motor difficulty. Gait disturbances disappeared after one to three days [my translation]” [25].

Miller *et al.* in the UK, based on the two Danish reports, conducted a study on a population of 3.4 million patients using computerized hospital admission records and the General Practice Research Database of circa 500 general practitioners. All MMR vaccinations were followed up for 60 days which allowed comparing vaccinated with non-vaccinated children. According to Miller *et al.*: “this study provides no evidence that MMR vaccine causes acute ataxia or other gait disturbance and suggests that the cases originally described by Plesner were chance occurrences, reflecting background incidence” [113].

Finally, a review by the Cochrane Collaboration which “included five randomised controlled trials (RCTs), one controlled clinical trial (CCT), 27 cohort studies, 17 case-control studies, five time-series trials, one case cross-over trial, two ecological studies, six self controlled case series studies involving in all about 14,700,000 children and assessing effectiveness and safety of MMR vaccine . . . [found] “exposure to the MMR vaccine was unlikely to be associated with . . . gait disturbance” [114].

Wakefield claims that “Plesner . . . confirmed this association” when both Plesner papers stated that the cause of the gait disturbance could not be evaluated based on their data. The Taranger study cited by Wakefield reports only a few short-duration cases of ataxia without claiming vaccine causation and Wakefield omits Miller’s paper, published five years prior to his book. The Cochrane Collaboration’s comprehensive review, published subsequent to Wakefield’s book, found an association unlikely. Most of the studies reviewed by the Cochrane Collaboration which were designed to test a hypothesized association between the MMR vaccine and ataxia/gait disturbances were published prior to Wakefield’s book and available to Wakefield. Instead, he only

includes two papers, both of which state they were not designed for such a test and could not determine any causation.

As for Wakefield’s claim “that the more severe ataxias following MMR may be associated with residual cognitive deficits in some children,” he misses the following from Plesner:

Cerebellar ataxia has been described previously after some of the first measles vaccines and is also a well-known symptom in connection with encephalitis after natural infections with measles (10%), mumps (36%) and rubella virus (13%). Encephalitis or meningoencephalitis after natural measles, mumps and rubella infections is found to occur in 1 per 1000-2500, 1 per 100-250 and 1 per 5000 cases, respectively. In children with cerebellar ataxia due to a natural infection the condition might be prolonged. There is no estimate of the total number of small children in Denmark who develop cerebellar ataxia due to infections” [112].

Table 2 gives the estimated rates of ataxia from natural measles, mumps, and rubella reported in association with MMR vaccination, as given by Plesner *et al.*

Though scientific studies have found no evidence of causal association between MMR vaccination and ataxia (see Miller study and Cochrane review above), it is evident from this data that if one were to assume an association, the risk for ataxia from the natural disease would be several fold higher than any possible risk of ataxia due to MMR vaccination. In the study by Plesner *et al.*, “Six of the 41 children (14%) had some kind of lasting neuropsychological complaint.” Since, according to Plesner: “Neuropsychological problems have been described as occurring in 5-10% of Danish and Swedish children,” six of 50,000 having lasting neurological complaints, approximately 1%, would not be unexpected, within expected background rates. Wakefield’s claim “that the more severe ataxias following MMR may be associated with residual cognitive deficits in some children” does not represent Plesner’s findings.

Summary

1. Wakefield’s claim that the Danish papers’ “confirmed” an association between the MMR vaccine and ataxia is incorrect.
2. Wakefield’s hypothesizing residual cognitive deficits following severe ataxias following MMR vaccinations does not reflect the best evidence.
3. Wakefield omits the numerous studies designed to test the hypothesis, and omits the background rates of ataxia

Table 2. Estimated Frequency of Ataxia and Encephalitis

	Natural Infection			Frequency of ataxia reported in association with MMR vaccination
	Frequency of ataxia following encephalitis upon natural infection	Frequency of encephalitis upon natural infection	Combined frequency of ataxia	
Measles	10%	0.04% - 0.1%	0.15% - 0.37%	0.008% - 0.025%
Mumps	36%	0.4% - 1.0%		
Rubella	13%	0.02%		

and encephalitis, both higher and more severe even if an association had been found.

VACCINE-ASSOCIATED RISKS COMPARED TO WHAT?

When discussing the risks associated with vaccines, it is necessary to include and compare with the risks involved in not being vaccinated – the risk of contracting naturally occurring infections and their sequelae – which is something Wakefield does not discuss. No one in public health would claim that vaccines are without risk, but when compared with the actual natural diseases, these risks are exponentially fewer and usually less severe. However, autism is not one of these risks. Numerous studies done on different populations, different children, by different researchers, in different health care systems, with varying methodologies, in different countries have found no association between vaccines and autism [115-119]. Few, if any, scientific studies are perfect. One can always find “weaknesses”; but when numerous studies from so many different sources and methodologies all result in the same findings, the odds favor the results being valid (*ibid*).

Mumps: “In contrast to natural mumps disease with a known risk of encephalitis, leading in some cases to permanent disability or death, complications of post-vaccine aseptic meningitis are generally of mild to moderate intensity and resolve spontaneously within 1 week with no reported sequelae” [83]. In addition to cases of aseptic meningitis, all reported adverse events possibly associated with vaccines were investigated. For instance, in the UK, one death was reported; but was found to be caused by an echovirus [72] and “one case of bilateral deafness had been reported, and coded as ‘possible’. This was an atypical reaction, and there was no proof as to the presence of meningoencephalitis. The wild mumps disease may cause unilateral deafness, and 2 reports have been received of unilateral deafness following the MSD vaccine. There have been no reports in the medical literature of bilateral deafness following MMR” [88].

According to the WHO

With a case-fatality rate of only 1/10,000 cases, mumps is generally a mild self-limiting disease, although complications may occur. Asymptomatic pleocytosis of cerebrospinal fluid is found in 50-60% of mumps patients; symptomatic meningitis is reported in as many as 15%. Mumps encephalitis is reported in 0.02-0.3% of cases. Although the case-fatality rate of mumps encephalitis is low, permanent sequelae, including paralysis, seizures, cranial nerve palsies, aqueductal stenosis and hydrocephalus, may occur. Acquired sensorineural deafness caused by mumps is one of the leading causes of deafness in childhood, affecting approximately 5/100,000 mumps patients (half the rate of fatalities).

Orchitis occurs in 20% of post pubertal males who develop mumps. . . Acquisition of mumps during the first 12 weeks of pregnancy is associated with a 25% incidence of spontaneous abortions [85].

In the U.S. between 1963 and 1968, there were an estimated annual average of 162,344 cases and 39 deaths, with a peak number of 50 deaths in 1964. Following mass vaccina-

tion, less than three deaths have been reported annually, and as of 2006, no deaths attributable to mumps have been reported [120]. That is, mumps incidence declined from > 100 cases per 100,000 population in most years in the prevaccine era (pre-1967) to 10 cases per 100,000 population in 1977 [121,122]. Following the 1989 institution of a two-dose MMR vaccine schedule, the number of reported cases further declined to one case per 100,000 by 1992 and to 0.1 cases per 100,000 population by 2001 [123]. Prior to vaccinations, the UK had 20,713 cases with only 174 cases following the introduction of vaccinations [124].

The Centers for Disease Control (CDC) *Pink Book* [125] gives the following natural mumps complications: CNS involvement – 15% of clinical cases; Orchitis -- 20%-50% in post-pubertal males; Pancreatitis – 2%-5%; Deafness – 1/20,000; and Death – Average 1 per year (1980-1999).

Measles: Measles is a potentially serious disease, much more serious than most people realize. The British launched a campaign to get parents to vaccinate their children. “Initial trials of a vaccine for measles took place in the UK in 1961 [126], comparing three live attenuated vaccines. . . Three years later, the MRC [Medical Research Council] set up four trials of an improved, safer, vaccine” [127]. The measles vaccine was introduced in the US in 1963 and the UK in 1968. As the proportion of children vaccinated increased, notifications of measles gradually fell in the UK from half a million cases and 100 deaths each year to fewer than 100,000 cases and 13 deaths a year by the mid-1980s. Between 1985 and 1988, many measles cases occurred in children who had been vaccinated. The children who received only one dose were not always protected – this triggered a recommendation that a second dose was necessary” [12,128].

In the U.S. One Article From 1985 States

During the prevaccine period 1950 to 1962, there was an average of 475 deaths per year. The lowest official total for reported measles deaths is two in 1981 – a 99.6% reduction from the prevaccine era. . . . In the prevaccine era, the average incidence rate of encephalitis after measles was slightly less than one in 1,000 Of those who survived acute encephalitis, 35% had neurologic sequelae. . . The most common sequelae were mental retardation (10% to 25% of discharged patients) . . . visual impairment (3%), ataxia (2%), and major behavioral disorder (2%). Less frequent complications included . . . deafness. Follow-up of patients 2 to 10 years after acute measles encephalitis indicated that 57% had sequelae, principally mental retardation or behavior disorders. This included patients who appeared normal at discharge who subsequently showed evidence of mental retardation or behavior disorders. . . . During the prevaccine period of 1960 to 1962, there was an . . . estimated 4,000 cases annually. In 1982, the most recent year for which data are available, there was a record-low total of one reported case of encephalitis . . . Thus, measles has been essentially eliminated as a cause of encephalitis in the United States [129].

The above paper gave an incidence of 0.34 cases of encephalitis per million doses of vaccine administered within 30 days of vaccination compared with 586.80 cases per million measles cases. In other words, the odds for encephalitis

Table 3. Measles, Mumps and Rubella in the United States: Before and After Vaccines (Roush, 2007 [120])

Measles			
	Estimated Annual Average	Peak	Recent Post-vaccine Reported No.
Cases	530,217 (1953-1962)	763,094 (1958)	55 (2006)
Deaths	440	552 (1958)	0 (2004)
Mumps			
Cases	162,344 (1963-1968)	212,932 (1964)	6,584 (2006) ^a
Deaths	39 (1963-1968)	50 (1964)	0 (2004)
Rubella			
Cases	47,745 (1966-1968)	488,796 (1964)	11 (2006)
Deaths	17 (1966-1968)	24 (1968)	0 (2004)
Congenital Rubella Syndrome			
Cases	152	20,000 (1964-1965) Above the 20,000 cases there were 11,250 miscarriages	1 (2006)
Disabilities		11,600 deaf 3,580 blind 1,800 mentally retarded (1964- 1965)	
Deaths	Not available	2,160 (1964-1965)	0 (2004)

^a Note. 2006 was an exceptionally high year for mumps, though still much lower than pre-vaccine years. Since 2000 fewer than 1,000 cases per year have occurred (see below).

from the natural diseases was 1,725 times greater than from the vaccine! The paper then estimates that from 1963 to 1982 approximately 5,210 lives were saved, 17,470 cases of mental retardation averted, and 2,972,000 hospital days were saved. It is important to keep in mind that the U.S. population has increased by over 50 percent since these data were obtained and no specific treatment other than supportive therapy is currently available [130]. Despite this, for example, in 2006, only 55 cases of measles were reported and no deaths [120]. In the Third World measles is a killer of children with an estimated death total in 1999 of 873,000 (90 per 1000 live births). A WHO program to increase coverage led to a 60% reduction in deaths; the estimated total for 2005 was 345,000 (62 per 1000 live births) [131].

Table 3 gives statistics for measles, mumps, rubella, and congenital rubella before and after vaccinations. The U.S. population has almost doubled since vaccinations began. Because measles, mumps, and rubella remain highly contagious and “treatments” have not changed [130], one can speculate that the pre-vaccination number of cases, deaths, and disabilities would be much higher today. No one denies that vaccines incur some risk, but serious adverse events arising from vaccines are quite rare. Wakefield not only misses the substantial data on vaccine safety; but estimates risks not reflected by the data and he does not put risks in perspective by comparing them with the real and substantial risks incurred in the absence of vaccination as suggested in Table 3.

Numerous papers and books give similar statistics to those in Table 3 [121,125,129,132-137].

SUMMARY AND CONCLUSIONS

Wakefield has a following who trust what he says. They believe that the British Medical Council’s hearings were politically motivated to silence his crusade to put vaccine safety first, and they ignore what journalist Brian Deer wrote. To summarize:

1. Wakefield claims that a leading Swedish vaccine researcher, Dr. Christenson, told him that vaccine safety studies had not been carried out in Sweden; yet, gives references to two Swedish papers that extensively report on vaccine safety studies in Sweden, one of them co-authored by Dr. Christenson.
2. Wakefield claims that the adoption of MMR vaccinations in the UK was based on inadequate research; yet, at least 23 studies, including ones in Sweden and Finland involving ca. 1/2 million children each followed-up for up to 2 years had been published by that time. A 1994 Institute of Medicine report [27] listed over 200 studies and Fahlgren’s 1988 paper [31] a similar number. Wakefield claims: *In addition to our own work and that of others, my opinion is also based upon a comprehensive review of all safety studies performed on measles, MR and MMR vaccines and re-vaccination policies. This now runs into a report compiled by me of some 250 pages.*” This alleged report remains unpublished. How comprehensive could it be given the studies presented here? In addition, Wakefield’s book omits seven studies he discussed in a previous article [10]. And, finally, his presentation and critique of the seven studies was wrong.

3. Wakefield claims that the Urabe mumps strain contained in the MMR vaccine used in the UK starting in 1988 had been approved after the Canadians withdrew it. Not true. That the vaccine had been approved based on inadequate safety studies. Not true. That the UK's surveillance system for adverse vaccine events was inadequate and not heightened for the introduction of the mass vaccination campaign. Not true. Wakefield claims the Urabe strain was a "dangerous vaccine"; yet, reports from Canada, UK, and elsewhere found slightly higher short term adverse events compared with the Jeryl Lynn strain with no long term sequelae. Compared with the risks from the natural diseases, something Wakefield does not discuss, while the UK was working on increasing availability of the Jeryl Lynn strain containing MMR vaccine, continuation of vaccinations with the Urabe strain was a prudent policy. Finally, Wakefield quotes only part of a paragraph, implying the UK had continued vaccinations using the Urabe containing vaccine when they had clearly discontinued its use.
4. Based on a letter to the journal *Pediatrics* from one small clinic, Wakefield estimates "up to 14,337 anaphylaxis deaths from the MR vaccine," missing the fact that the letter reported mild cases not necessarily associated with the vaccine, that studies, including a 1994 evaluation of the MMR program by the British Medical Council, and numerous international studies of literally millions of vaccinated children did not report a single death.
5. Wakefield describes an association between gait disturbances and/or cerebellar ataxia and the MMR vaccine based on two Danish papers; however, both papers stated they could not draw any conclusions regarding causation while he ignores numerous studies, including a 2005 study by Miller *et al.* that were designed to test the hypothesized association and found none. In addition he claims that MMR vaccine-related neurological problems were more severe, missing what the two papers actually stated.
6. Wakefield does not deal with the critical question, "compared to what?" No discussion of the ravages of the vaccine-preventable diseases is included in his book.
7. As discussed in this paper, the same poor scholarship and science regarding vaccine safety studies found in his book "Callous Disregard" can be found in his 2000 article [10], an article written long before Brian Deer's investigation and the BMC hearings.

The foundation of Wakefield's claims to political persecution is his reading/evaluation of vaccine safety. For Wakefield, he and the general public are the victims of a vast conspiracy involving governments, public health departments, medical researchers and assorted others, all to downplay the risks from vaccines, a conspiracy so immense that these very same people are willing to sacrifice their own loved ones, their own children, by vaccinating them. Wakefield's presentation of vaccine safety is wrong!

I have shown that every major claim Wakefield makes in his book concerning vaccine safety is wrong. I have given accurate quotes from both Wakefield's book and sources that contradict his claims, including those he misquotes. Based

on the old adage, "trust but verify," where possible I have given the URLs to many of the documents and articles referred to in this paper. My hope is that those who take the time to check will realize that Wakefield's claims regarding vaccine safety are not only wrong but also harmful, and that once this is realized, people will read Deer's articles [3] and the British Medical Council's findings [1,2] with an open mind.

In addition, given that many within the anti-vaccination movement refer to Wakefield as a trusted expert and themselves display similarly erroneous claims, it is hoped that readers of the paper will refer to other sources of vaccine information such as the CDC [138,139], Institute of Medicine reports [140,141], and a comprehensive up-to-date book by Plotkin *et al.* [142]. The only conclusion that can be reached from this review is that the title of Wakefield's book is incomplete. It should read: "Andrew Wakefield's Callous Disregard for the Facts."

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

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