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To Dr. Ellen D. Burgess
Professor, Department of Medicine
Foothills Medical Centre, Calgary, Alberta

Nov.10, 2016 by mail & email
ellen.burgess@ahs.ca

Re: Oct. 31, 2016 Global News Okanagan story with video Interview:
Calgary doctor calls for mandatory measles vaccinations in wake of new study

Dear Dr. Burgess,
We are writing to you regarding the October 31, 2016 Global News story and the live interview you gave about a new study that purports a risk rate of 1 in 600 children for SSPE, a devastating and fatal complication of measles.

The study you reference, *Subacute Sclerosing Panencephalitis: The Devastating Measles Complication Is More Common Than We Think*, was presented as an oral abstract on Friday October 28 at an annual medical conference–IDWeek–held in New Orleans, Louisiana from Oct. 26-30.

To our knowledge the full paper has not been published, but the Abstract specifically states that the **1:600 incidence of SSPE in children under 1 year of age is based on data from the 1988–1991 measles epidemic in California**. This risk assessment means 1 case of SSPE per 600 reported measles cases in infants in that region during that time period. See Appendix 1 for detailed quotes/data and Appendix 2 for references with hyperlinks on this and all of the following points. (Hyperlinks are undelined on all pages of this letter.)

Your Global News interview raises some questions to which we request your response:

1. **Does it concern you that only 8 of the 17 SSPE cases in this study were living in the US when they contracted measles?**
   On reading the published abstract (Results section), we note it states that only 8 of the 17 cases had measles when they were living in the United States. This means it is unlikely that 11 of SSPE cases actually relate to the SSPE risk estimates for California given in the study, **Risk estimates are based on the number of cases of measles occurring in a location and the number of SSPE cases occurring after exposure to those measles cases.** See Appendix 1.1 for details on the Abstract and especially see Appendix 1.3.1 for good practice when associating SSPE cases with risk estimates for a given location. [Appendix 1.1]

2. **Why is this being reported as *current risk* when It is not?**
   It is SSPE risk for children less than 1 year of age (age specifics not mentioned by you or the reporter) from an epidemic that occurred over 25 years ago with a 9-fold increase in volume of measles cases and a **very particular demographic** for those cases. According to the 2015 edition of the CDC *Pink Book*: "In addition to the increased number of cases, a change occurred in their age distribution. Prior to the resurgence, school-aged children had accounted for the largest proportion of reported cases. During the resurgence, 45% of all reported cases were in children younger than 5 years of age. In 1990, 48% of patients were in this age group, the first time that the proportion of cases in children younger than 5 years of age exceeded the proportion of cases in 5–19-year-olds (35%)." [Appendix 1.2.1] Further, children infected with measles under the age of 1 year carry a risk of 16 times greater incidence of SSPE than those infected at age 5 years or later (2013 Sardana et al). So this demographic change resulted in a much higher rate of SSPE during the epidemic then seen before or since. That is why this cannot be considered a current risk assessment.

3. **Do you expect the demographics during the epidemic discussed above and the vaccine failures discussed below would ever occur again in either the USA of Canada? If so, please explain how this might happen.**
   The CDC further explains it was the **waning vaccine efficacy** in young mothers who had received only one

dose of MMR vaccine in their childhood that resulted in so many infants contracting measles coupled with the low vaccination coverage of low-income, inner city, pre-school children that resulted in the large numbers of under-five year old children getting and spreading measles. [Appendix 1.2.1] In 2004, Orenstein et al stated: "Two major causes of this epidemic were **vaccine failure** among a small percentage of school-aged children who had received 1 dose of measles vaccine and low measles vaccine coverage among preschool-aged children." The **primary and secondary vaccine failure** resulting in this epidemic is why the change was made to a two-dose regime of MMR vaccine and why vaccination campaigns for pre-school children were instigated. As a result of these changes, today we see a completely different demographic for measles cases than occurred in the 1989-1991 epidemic with a concomitant lower risk of SSPE cases today. In fact, a 2016 CDC *MMW*R report says: "SSPE is a rare, long-term complication of measles. Widespread use of measles vaccines has been associated with the **near disappearance of SSPE in the United State**s."

4. **Why did you choose to use an SSPE risk assessment from one state in the United States, which is based on completely different data and circumstances than what happened in Canada?**
   The Canadian Pediatric Society undertook a study (2005 Campbell et al) to access Canadian risk of SSPE that arose from the measles resurgence that occurred in Canada in 1990–1991 with 7178 cases of measles reported. They assessed SSPE risk as follows: **1 case every 2 years in Canadian children** or 2 cases of SSPE for children < 2 years of age for every 7,178 cases of measles (which translates to 1:3589). The study does not give a risk assessment for children under 5.

   If you wanted to use another country's assessment of SSPE risk, the 2013 German study (Schönberger et al) is a beautifully designed and comprehensive study. Its conclusion states: "...this study provides data on the SSPE epidemiology in Germany for the period 2003 to 2009. Our data suggest the risk of developing SSPE after acute measles infection below 5 years of age is in **the range of 1:1700 to 1:3300**.

5. **Do you believe that parents should be made aware of the low incidence rates of both measles and SSPE (or other rare measles complications for that matter) when discussing risks of complications for their various aged children?**
   Alberta Public Health has excellent documents on both SSPE and Measles incidence in Canada and Alberta. They are easy to understand and would give parents a much better idea of the true SSPE Risk than the California study. **In over 20 years there have been no reported cases of SSPE in Alberta children** (1993–2015). The Public Health Agency of Canada has an on-line database of reportable diseases current to 2014 from which measles incidence and age of infection can be accessed as well. We have included documents and data from both sources in the Appendix 1.2.2 and 1.2.3.

6. **Did you use the 1:600 SSPE risk to infants in the interview as though it were current risk for all children in Canada in order to justify (even if only in your own mind) mandating vaccines?**
   If so, we can only caution you that it is this kind of "slight of hand" with the facts that results in the public mistrust of the medical establishment's recommendations regarding vaccines.

7. **When you call for mandating vaccines, do you recognize the constitutional right of every Canadian citizen to informed consent or refusal of vaccinations and other medical procedures?**
   We have an excellent article on our web site regarding the legal ramifications of mandating vaccinations. It begins: **Health Canada States That Immunization is NOT Mandatory in Canada**

   > "Unlike some countries, immunization is not mandatory in Canada; it cannot be made mandatory because of the Canadian Constitution. Only three provinces have legislation or regulations under their health-protection acts to require proof of immunization for school entrance. Ontario and New Brunswick require proof for diphtheria, tetanus, polio, measles, mumps, and rubella immunization. In Manitoba, only measles vaccination is covered [since Redacted]. It must be emphasized that, in these three provinces, exceptions are permitted on medical or religious grounds and reasons of conscience; **legislation and regulations must not be interpreted to imply compulsory immunization**."

8. **Will you consider either making a correction to your Global News interview or doing another interview to clarify that the SSPE Risk you quoted in your first interview does not actually apply to Canadian children at this point in time?**

Quoting the easy to understand Canadian study findings of 1 case of SSPE every 2 years in Canada would do a lot to alleviate any fear you may have generated in Canadian parents with your use of the 1:600 California risk assessment figure.

Considering the data presented here and in the Appendix, beating the fear drums of SSPE misery and death to justify mandatory vaccination of school children seems not only inappropriate, but also highly unethical.

We will be posting this letter on our web site so the public has access to our analysis of this new study, to Public Health data and to peer-reviewed articles on the risk of SSPE in children following measles infection.

Sincerely,

Nelle Maxey, VCC Director on behalf of the Board of Directors of Vaccine Choice Canada

CC: Alberta Minister of Health Sarah Hoffman, Dr. Craig Jenne & Global News Reporter, Carolyn Kury de Castillio

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Appendix 1: Data supporting comments in Dr. Burgess letter

1.1 Information on the California Study (All links in Appendix 2)

As the full study has not yet been published, we have no access to the full data and researchers' discussion. Perhaps the anomalies listed below will be cleared up once the study is published.

• **Dates of Cases and Epidemic:**

The measles resurgence (the epidemic) in the USA is always stated as occurring between 1989-1991. However the California researchers added 1998 to their data (perhaps to pick up an SSPE case from the California Encephalitis Project (2003 Glaser et al) data which began in 1998). Also the news stories (quoting Dr. Cherry, one of the authors) say the epidemic dates in California were 1988–1990, not 1989-1991. All very confusing. Perhaps the epidemic began in California a year earlier than the rest of the US and spread from there. We don't know.

• **Number of Cases related to the California epidemic**:

According to the Abstract, the investigators searched records in California from 1998 through 2016 to understand "current" risk of SSPE and found 17 cases of SSPE in that 18 year time period. No details of how many of the 17 cases were related to the 1989–1991 measles resurgence California is given in the Abstract.

The Global News article says "most" of the cases" were "related to the California measles epidemic in 1988 through 1990". Most means more than 50%.

The *MedPage Today* article has more details:

> "The researchers were able to use data from the 1988-1990 outbreak to calculate estimated rates of SSPE:
>
> • Some 9,564 children younger than age five had measles in the outbreak, including seven SSPE cases exposed at the time. The numbers yield a risk ratio of 1 to 1,367.
>
> • And 3,651 children were less than one when they caught measles during the outbreak, including six who later developed SSPE, yielding a risk ratio of 1 to 609.
>
> The researchers cautioned that the analysis is retrospective and the conclusions might vary if some of the underlying numbers are incorrect."

This appears to mean that 13 of the 17 SSPE cases, or 76%, were related to a unique outbreak in 1988-1990. However, if they are adding together the 7 cases (under 5 years of age) and the 6 cases (under 1 year of age) to get 13 cases, which would be "most" of the cases, then the first risk ratio for <age 5 cannot include the 6 cases in the second ratio for <age 1. Perhaps they meant the first ratio to apply to children **between** the ages of 1 and 5 and the less than one-year-olds as a separate category and the reporter got it wrong. Again confusing.

• **Number of cases exposed in California and thus related to the California epidemic:**

The Abstract says (see *Results* below) that only 8 of the 17 cases had measles when they were living in the United States. **This is extraordinary.** It means 11 of the 17 cases did not contract measles in the US, let alone California. Unless a child contracted measles in the California, moved to another country and then returned to California

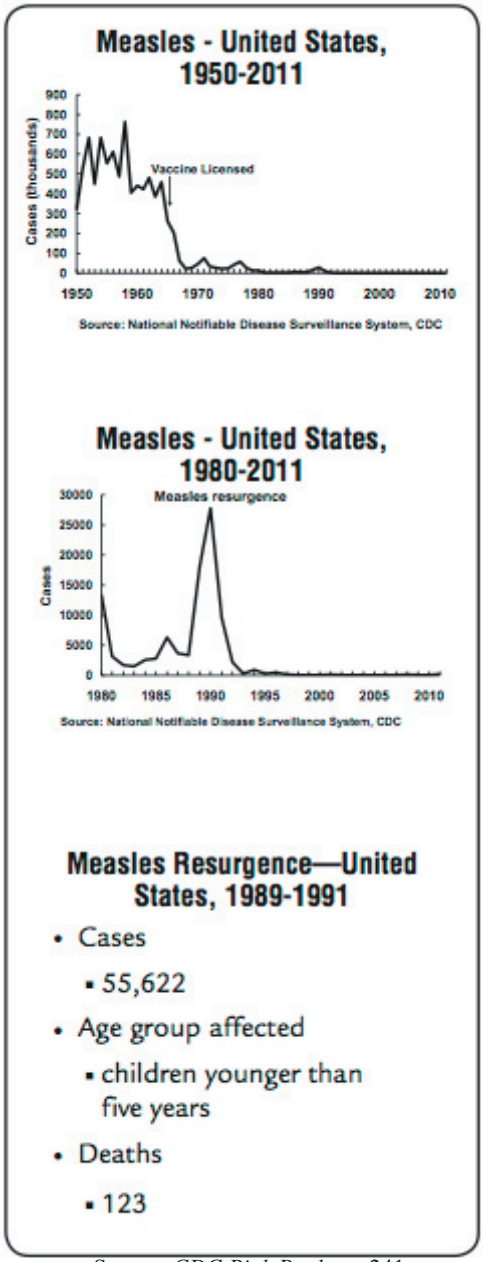
where their SSPE was later diagnosed then their cases should not be used to access risk of SSPE using number of measles cases in California during the epidemic. See Appendix 1.3.1 for how other researchers handle such cases. Below is the *Results* quote from the Abstract:

> "**Results.** Seventeen SSPE cases were identified. Males outnumbered females 2.4:1. Twelve (71%) cases had a clinical history of a febrile rash illness compatible with measles; all 12 had illness prior to 15 months of age and measles vaccination. **Eight (67%) children were living in the United States when they had measles.** SSPE was diagnosed at a median age of 12 years (range 3–35 years), with a latency period of 9.5 years (range 2.5–34 years). Many cases had long-standing cognitive or motor problems prior to diagnosis. Among measles cases reported to CDPH during 1988–1991, incidence of SSPE was 1:1367 for children <5 years, and 1:609 for children <12 months at time of measles disease."

• Please note, we could be wrong about this analysis of what the study actually purports. Until the study is published and we have all the data and discussion, we won't know what the researchers actually did.

1.2 Public Health Data

The general public would have no knowledge that the US measles epidemic of 1989–1991 was a very **unique occurrence** and in no way relates to the present circumstances of either measles or SSPE incidence and risk in the US or in Canada. In Section 1.2.1 we present the CDC Pink Book (2015 edition) information on the **unique** demographics of that outbreak. In Section 1.2.2 we present Alberta Public Health information on the subject. In Section 1.2.3 we present data from The Public Health Agency of Canada. This will assist in an understanding of SSPE risk in Canada today.



Source: *CDC Pink Book*, pg 241

1.2.1 CDC and the USA epidemic 1989–1991

The CDC discusses this unique epidemic in the measles chapter of the *Epidemiology and Prevention of Vaccine Preventable Diseases*, also known as the *Pink Book*. The following points are quotes excerpted from the sections on ***Measles Resurgence in 1989–1991*** and ***Measles After 1993***.

• From 1989 through 1991, a dramatic increase in reported measles cases occurred. During these 3 years a total of 55,622 cases were reported (18,193 in 1989; 27,786 in 1990; 9,643 in 1991). In addition to the increased number of cases, a change occurred in their age distribution. Prior to the resurgence, school-aged children had accounted for the largest proportion of reported cases. During the resurgence, 45% of all reported cases were in children younger than 5 years of age. In 1990, 48% of patients were in this age group, the first time that the proportion of cases in children younger than 5 years of age exceeded the proportion of cases in 5–19-year-olds (35%).

• A total of 123 measles-associated deaths were reported during this period (death-to-case ratio of 2.2 per 1,000 cases). Forty-nine percent of deaths were among children younger than 5 years of age.

• The most important cause of the measles resurgence of 1989–1991 was low vaccination coverage. Measles vaccine coverage was low in many cities, including some that experienced large outbreaks among preschool-aged children throughout the early to mid-1980s. Surveys in areas experiencing outbreaks among preschool-aged children indicated that as few as 50% of children had been vaccinated against measles by their second birthday.

• In addition, measles susceptibility of infants younger than 1 year of age may have increased. During the 1989–1991 measles resurgence, incidence rates for infants were more than twice as high as those in any other age

group. The mothers of many infants who developed measles were young, and their measles immunity was most often due to vaccination rather than infection with wild virus. As a result, a smaller amount of antibody was transferred across the placenta to the fetus, compared with antibody transfer from mothers who had higher antibody titers resulting from wild-virus infection. The lower quantity of antibody resulted in immunity that waned more rapidly, making infants susceptible at a younger age than in the past.

Measles Since 1993

• Reported cases of measles declined rapidly after the 1989–1991 resurgence. This decline was due primarily to intensive efforts to vaccinate preschool-aged children. Measles vaccination levels among 2-year-old children increased from 70% in 1990 to 91% in 1997.

• Since 1993, fewer than 500 cases have been reported annually, and fewer than 200 cases per year have been reported since 1997. A record low annual total of 37 cases was reported in 2004. Available epidemiologic and virologic data indicate that measles transmission in the United States has been interrupted. The majority of cases are now imported from other countries or linked to imported cases.

• Since the mid-1990s, no age group has predominated among reported cases of measles. Relative to earlier decades, an increased proportion of cases now occur among adults. In 1973, persons 20 years of age and older accounted for only about 3% of cases. In 1994, adults accounted for 24% of cases, and in 2001, for 48% of all reported cases.

We connect the SSPE dots in the above CDC quotes.

• "Most" of the cases in the new study relate to an epidemic 25 years ago where the incidence of measles increased 9-fold. Result: more cases of measles equal more cases of SSPE then compared to now.

• Further, during the epidemic **the demographic of measles cases changed** from most measles cases among school-aged children to those **younger than 5 years old**. Result: more cases of measles in younger children equal more cases of SSPE, especially in children under 1 year of age since they are more susceptible to SSPE after measles.

• Three vaccine connections: Low vaccine coverage in toddlers. Waning vaccine efficacy in mothers contributed to the high incidence of measles in infants (those under 1 year old). Infants then became the future victims of the few cases of SSPE. According to the new study there were 6 SSPE cases in infants and 7 cases in toddlers. Another researcher also cites **primary vaccine failure (no immunity**) in a small portion of school age children. This may be where the epidemic started and then spread to younger children who were unprotected due to either low coverage rates or the **secondary vaccine failure** (waning immunity in their mothers).

• This epidemic resulted in two vaccine policy changes: instituting the second dose of MMR vaccine to reduce the serious consequences of waning vaccine immunity and a campaign to increase coverage in the toddler cohort. Two-dose MMR vaccine policy is now standard in both the USA and Canada.

• A moment's reflection and one can see that the new study cannot possibly reflect the risk of SSPE in today's children. Measles incidence in both Canada and the USA is practically nonexistent, in fact measles have been declared eradicated and vaccine coverage rates are higher than those reported during the epidemic. The only constant from the epidemic days is primary vaccine failure which remains in 2–10% of those immunized with 2 doses of MMR vaccine (Poland et al 2012). In the US, the demographic for measles cases has shifted from children under 5 in the epidemic to adults now. It is extremely unlikely under these circumstances that a measles epidemic with the same volume of cases or the unique demographic of children under 5 would break out in either Canada or the United States today.

• While it is interesting that SSPE incidence during the epidemic was greater than originally thought, this has little bearing on the situation today. Nor is it new information. Studies based on the epidemic (2005 Bellini, et al, 2005 Campbell et al) show higher estimates of SSPE incidence than the original CDC 1982 estimate of 1 SSPE case per 100,000 measles cases. This makes perfect sense now that we understand the demographic changes during the epidemic.

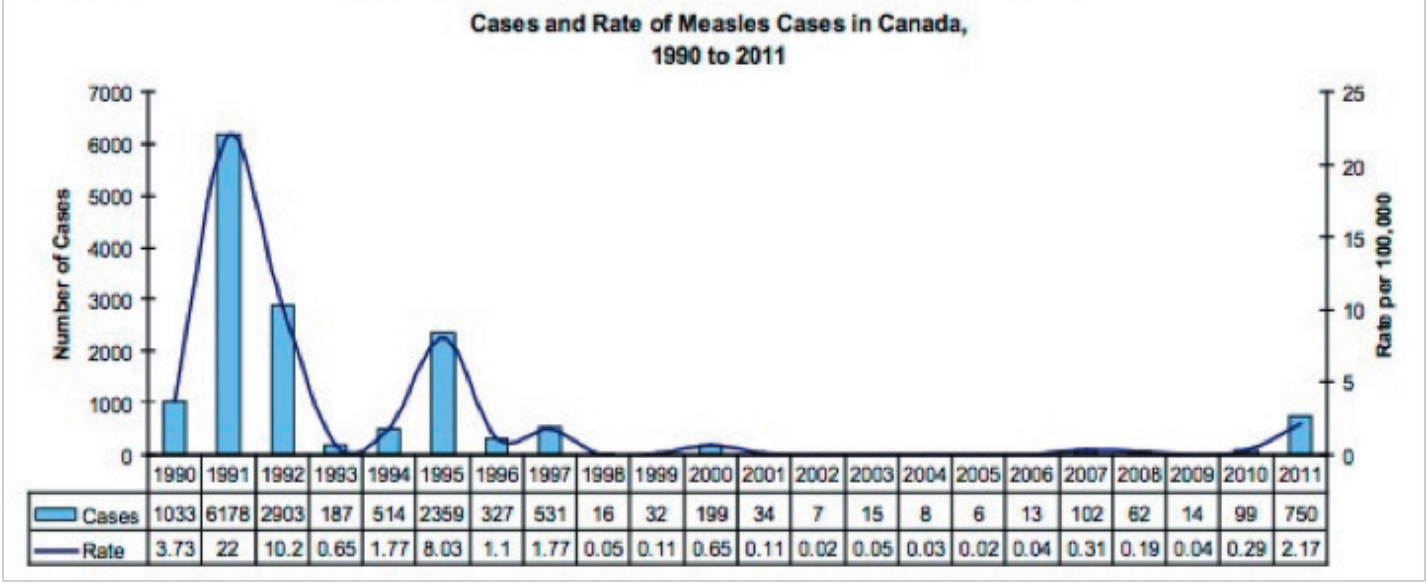
1.2.2 Alberta Public Health

Alberta Public Health has on-line Information sheets on SSPE incidence and measles incidence.

The current (Dec 2015) **Information Sheet on SSPE**, reports the following incidence rates:

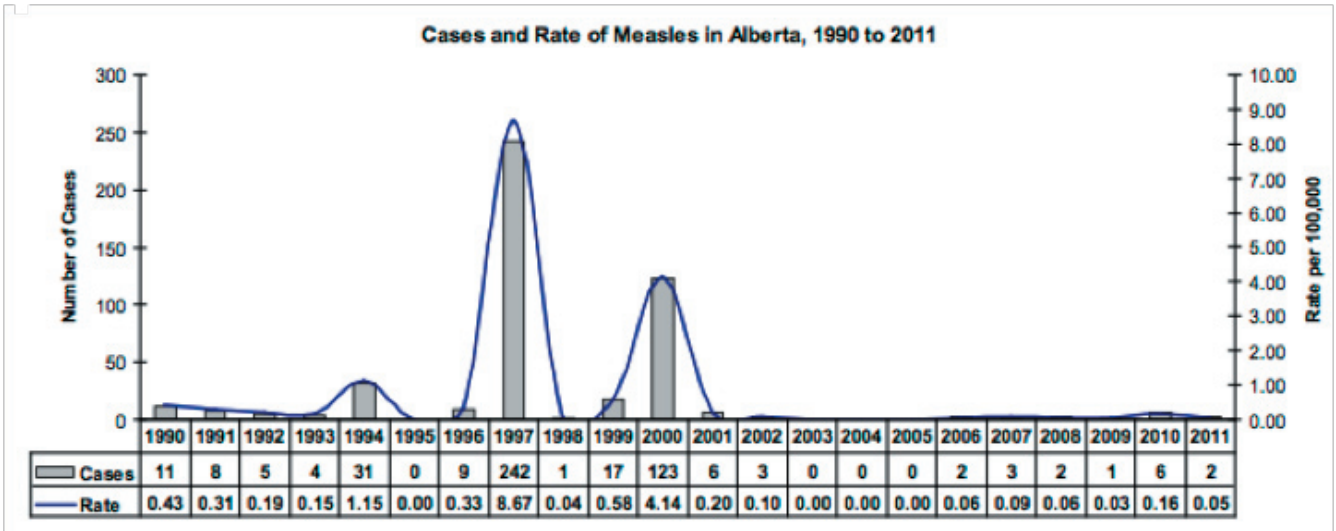
- In the USA, fewer than 10 cases are reported per year.
- In Canada, the Canadian Pediatric Surveillance Program (CPSP) initiated a study in 1997 to determine the national incidence and the epidemiological features of this disorder. The study was concluded in 2000 [2005 Campbell et al]. Altogether, 4 SSPE cases were reported to the CPSP, one case before, two during, and one after the study period. Of these cases, all of whom were diagnosed between ages 4 and 17 years, three children had measles infection in infancy [< 1 year].
- In Alberta, SSPE was first reported in Alberta in 1984, with three cases that year (based on historical data). Subsequently, one case was reported in 1986, one in 1990 and one in 1992. **There were no cases reported from 1993 to 2013.** In 2014 there was a case of SSPE reported in an adult female, foreign born, with an unknown history of measles immunization.

The current (Nov 2013) **Measles Guidelines** report Measles Incidence in two charts. First we see the Canadian epidemic of 1990-1992 with a total of 10,115 reported cases of measles. The 4 SSPE cases in Canada (reported in the 2005 CPSP study above) would be related to this outbreak due to the 7–10 year time lag of SSPE after exposure to measles.



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Cases	1033	6178	2903	187	514	2359	327	531	16	32	199	34	7	15	8	6	13	102	62	14	99	750
Rate	3.73	22	10.2	0.65	1.77	8.03	1.1	1.77	0.05	0.11	0.65	0.11	0.02	0.05	0.03	0.02	0.04	0.31	0.19	0.04	0.29	2.17

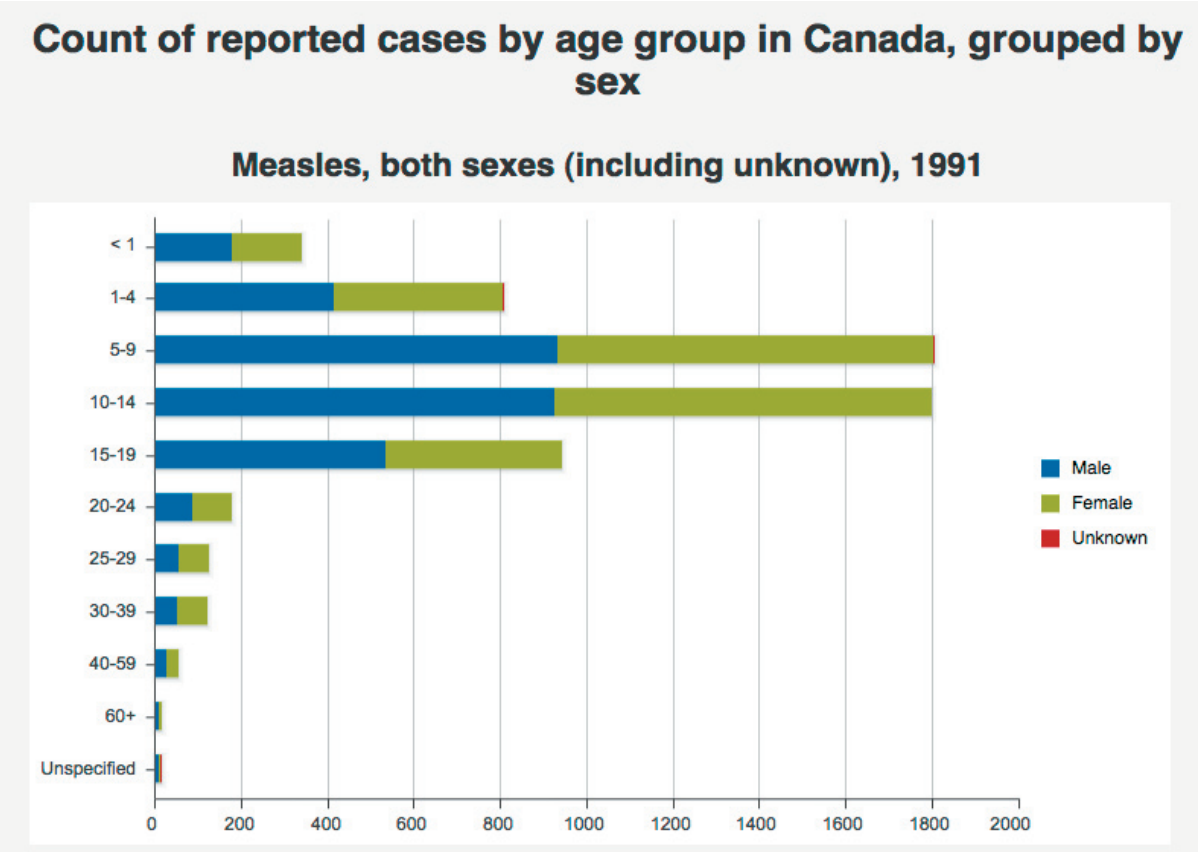
Alberta did not experience the Canadian 1990–1992 epidemic. Despite the two smaller outbreaks in 1997 and 2000 in Alberta, there have been **no reports of SSPE during the subsequent 15 years** per the SSPE Report above. Therefore mandating vaccines for school children in Alberta cannot be based on SSPE occurrence which has been virtually zero for over 20 years (1993-2015).



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Cases	11	8	5	4	31	0	9	242	1	17	123	6	3	0	0	0	2	3	2	1	6	2
Rate	0.43	0.31	0.19	0.15	1.15	0.00	0.33	8.67	0.04	0.58	4.14	0.20	0.10	0.00	0.00	0.00	0.06	0.09	0.06	0.03	0.16	0.05

1.2.3 The Public Health Agency of Canada

The on-line database of **Notifiable Diseases in Canada** can reassure us regarding the Canadian demographic by age for measles cases. We saw above the Canadian epidemic occurred in 1990-1992. Although the charts for disease by age in the database only begin in 1991, we can clearly see a fairly "normal" demographic for measles during 1991, the peak year of the Canadian outbreak. Most cases are in school children between the ages of 5 and 14. We have added a total count column for children and a total for all cases.



Count of reported cases by age group in Canada, grouped by sex, Measles, both sexes (including unknown), 1991

Age Group	Male	Female	Unknown
< 1	173	163	1
1-4	408	392	2
5-9	928	869	4
10-14	919	875	0
15-19	529	410	0
20-24	82	93	0
25-29	48	72	0
30-39	46	70	0
40-59	21	29	0
60+	4	6	0
Unspecified	2	2	3
TOTAL	3,160	2,981	10

Total Count Children

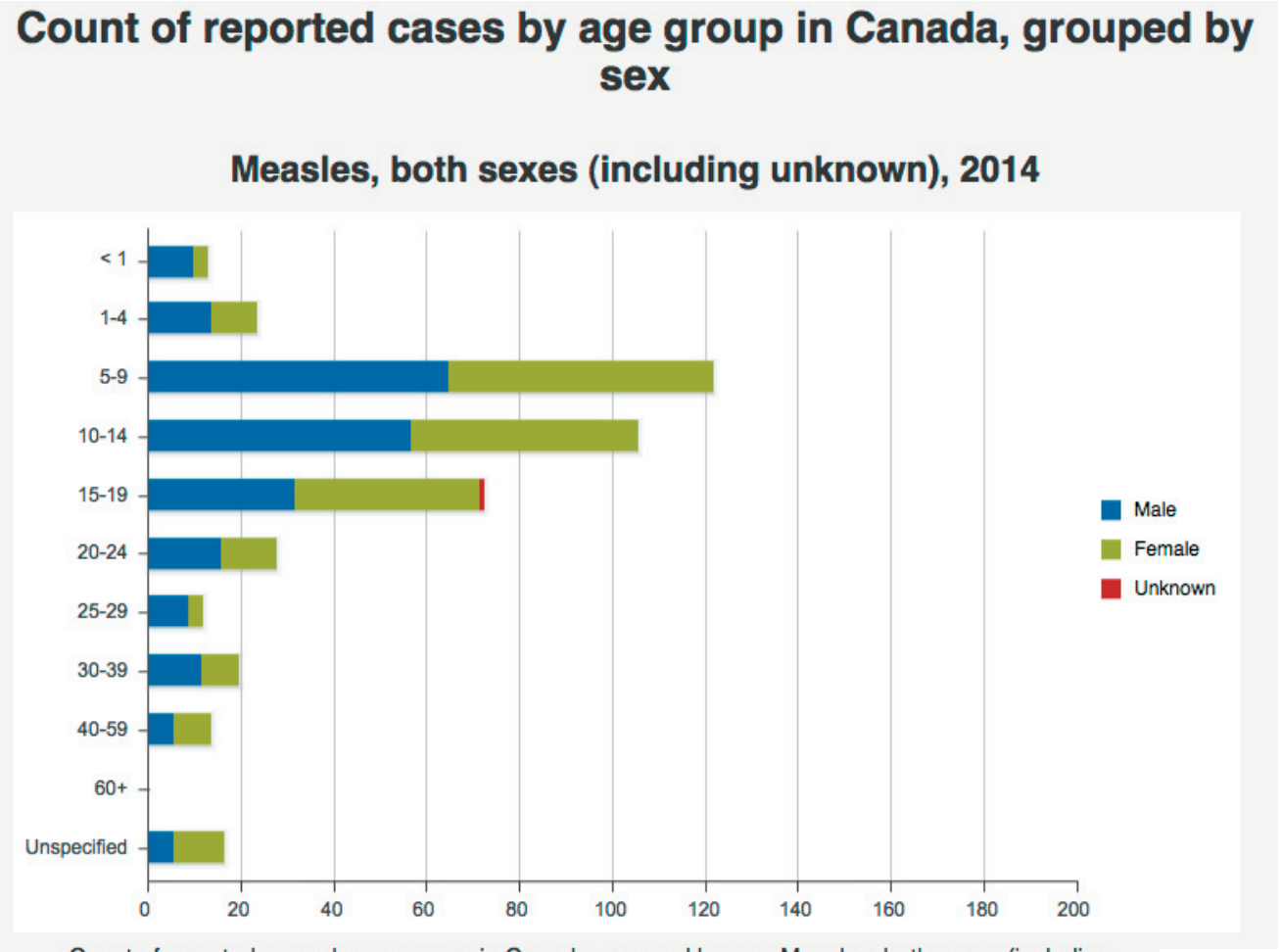
<1	337
1-4	802
5-9	1802
10-14	1794
15-19	939

Total all ages 6151

The Canadian demographic is very different from the American one described in the *Pink Book*. According to the CDC, in the peak epidemic year in the US, almost 50% of measles cases were experienced by children under the age of 5. Whereas in Canada in the peak year, only 18.4% of measles cases occurred in the most susceptible children under the age of 5.

It is obvious caution must be used when applying risk estimates across jurisdictions, especially when data differences like these are not taken into account.

Looking at the most current year on the database, 2014, we see a truly "normal" demographic with most measles experienced by children 5-9 years old. With only 12 cases in <1 year olds and 23 cases in 1-4 year olds we would not expect to see any cases of SSPE resulting from these few measles cases if we applied risk estimates.



Count of reported cases by age group in Canada, grouped by sex, Measles, both sexes (including unknown), 2014

Age Group	Male	Female	Unknown
< 1	9	3	0
1-4	13	10	0
5-9	64	57	0
10-14	56	49	0
15-19	31	40	1
20-24	15	12	0
25-29	8	3	0
30-39	11	8	0
40-59	5	8	0
60+	0	0	0
Unspecified	5	11	0
TOTAL	217	201	1

2014 Count Children

<1	12
1-4	23
5-9	121
10-14	105
15-19	72

Total all Ages 419

1.3. Peer Reviewed Studies

1.3.1 Referencing SSPE cases by location of contracting measles

It is standard good practice to not reference cases in SSPE risk estimates when measles were not contracted in the country from which measles exposure data is collected. Two studies that exemplify good practice are noted below. We question the validity of the SSPE risk assessments in the new California study as they do not appear to have followed this principle. Again, we await publication of the study for verification of methods.

1.3.1 Referencing SSPE cases by location of contracting measles *continued*

The 2013 Schönberger et al study, ***Epidemiology of Subacute Sclerosing Panencephalitis (SSPE) in Germany from 2003 to 2009: A Risk Estimation***, specifically states "Children with SSPE from abroad who were only hospitalized in Germany for diagnostic purposes were excluded from the analysis." Their data table of hospitalized cases has a column titled *country of measles infection* that clarifies excluded cases for the reader.

The 2005 Bellini et al study, ***Subacute Sclerosing Panencephalitis: More Cases of This Fatal Disease Are Prevented by Measles Immunization than Was Previously Recognized***, presents two tables showing how SSPE cases were sorted according to genotype and location using good practice principles.

Patients with subacute sclerosing panencephalitis who were referred to the Centers for Disease Control and Prevention (CDC) and who had measles virus of the wild-type genotype identified in brain tissue samples, although the genotype or patient location ruled out an association with measles acquired in the United States during 1989–1991.

Patient	Year[a] of referral to the CDC (patient age at referral, years)	Patient's year of birth, sex	History of measles or rash, year of occurrence (patient age)	Patient location[b]	History of vaccination (patient age at vaccination, if known)	Genotype of measles virus identified
6	1992 (16)	1976, M	Measles, 1977 (12 months)	Wisconsin	No	C1
7	1993 (28)	1965, M	Measles, 1968 (3 years)	Wisconsin	Yes (12 years)	E
8	1995 (5)	1990, M	Rash, 1991 (15 months)	Ohio[c]	Yes (17 months)	D5
9	1999 (8)	1990, M	Measles, 1991 (7 months)	Puerto Rico	No	D3
10	2001 (16)	1985, M	NR	Nicaragua[d]	Yes (15 years)	D3
11	2003 (36)	1967, M	NR	Illinois	Yes	E

NOTE. NR, not reported.
[a] The year of onset of symptoms of subacute sclerosing panencephalitis was not available for all patients and may not be the same as the year of referral given here.
[b] Location where patient resided during childhood or state of residence at the time of referral.
[c] Patient 8 lived in Okinawa City, Japan, from 5 months of age until ~2 years of age.
[d] Patient 10 lived in Florida after 15 years of age.

Patients with subacute sclerosing panencephalitis (SSPE) who were referred to the Centers for Disease Control and Prevention (CDC) and whose SSPE cases were associated with measles virus infection acquired in the United States during 1989–1991.

Patient	Year[a] of referral to the CDC (patient age at referral, years)	Patient's year of birth, sex	History of measles or rash	Patient location[b]	History of vaccination[c]	Genotype of measles virus identified
1	1996 (5)	1991, F	NR	Georgia	Yes	D3
2	1998 (9)	1989, M	NR	Texas	Yes	D3
3	1998 (7)	1991, F	NR	Texas	Yes	D3
4	2001 (11)	1990, F	NR	Florida	Yes	D3
5	2002 (12)	1990, M	Rash[d]	California	Yes	D3

NOTE. NR, not reported.
[a] The year of onset of SSPE was not available for all patients and may not be the same as the year of referral given here.
[b] Location where patient resided during childhood or state of residence at the time of referral.
[c] Patient age at vaccination was known only for patient 4. Patient 4 was vaccinated at 1 and 5 years of age.
[d] Patient 5 developed rash at 8 months of age.

Source: William J. Bellini et al. J Infec Dis 2005;192:1686-1693

1.3.2 Measles case reporting rates

All of the studies we read that described method of SSPE risk assessment assumed a 10% reporting rate for measles cases. Thus they multiplied the reported number of cases by a factor of 10 to ascertain a more accurate number of exposures that may have occurred. This number was then used as the denominator in their SSPE risk assessment ratios. The only exception was a Japanese report that multiplied their reported measles cases by an even larger factor of 30. Not following this principle would inflate SSPE risk rates.

It is unclear if this principle was applied in the new California study, although it does not appear on the surface to be the case. It is unlikely there were only 956* measles cases reported in children <5 years old (the largest demographic) in the most populous state in the nation in an epidemic in which there were a total of almost 65,000 cases reported.

* 956 reported cases X 10 = 9,564 cases noted in the *Abstract*

1.3.3 Other Reports of interest

According to H. Campbell et al 2007, ***Review of the effect of measles vaccination on the epidemiology of SSPE***, 12 cases of SSPE in the US had been attributed to the 1989-1991 measles epidemic. We find it surprising that the state of California alone would have 13 cases as the new study purports. Although using cases that did not acquire measles in the US could explain the larger number. Again until we see the full study it is difficult to judge.

The Campbell study is also of interest as it references many previous studies and shows the evolution of SSPE risk assessments. The first quote below refers to the 12 cases in the US with both pre-epidemic (historical) and post-epidemic risk estimates. The second quote refers to studies in many different countries and then risk assessments that remain generally accepted today, as seen in the next article from the CDC below.

> "[Historical] Risk of SSPE was estimated as 8.5 per million measles cases and 0.7 per million vaccine doses. Bellini et al. [2005] analysed the 1989–91 measles epidemic. Between 1989 and 1991, there were at least 55, 622 (possibly up to 185,000) measles cases. By 2003, 12 SSPE cases could be linked to this epidemic by year of measles/rash and by virus strain identified in brain tissue in those with no history of infection. Risk estimates of SSPE following natural measles infection were calculated at **6.5–22 per 100 000 cases**."

> "Reported SSPE incidence varied greatly from approximately 0.2 to 40 cases per million population per year. Direct comparison of countries is problematic because methods and quality of ascertainment have been inconsistent. UK and, more recently, USA data analyses have calculated true incidence of SSPE to be approximately **4–11 cases of SSPE per 100 000 cases of measles**. A higher risk is associated with earlier infection: the risk following measles infection **under 1 year of age was 18/100,000** compared with 1.1/100, 000 after 5 years of age in the UK.

The more recent, 2013 (Schönberger et al) German Study (as noted in question 4 in the letter) gives SSPE risk estimates after acute measles infection in those below 5 years of age as **1:1700 to 1:3300**.

2016 CDC MMWR–*Morbidity and Mortality Weekly Report*
Notes from the Field: Subacute Sclerosing Panencephalitis Death — Oregon, 2015
Weekly / January 15, 2016 / 65(1);10–11
Of interest because this recent death is of a child who was vaccinated and then contracted measles in the Philippines. In other words, not a result of measles acquired in the US. Also note the final statements affirming the CDC acceptance of the "4–11 SSPE cases per 100,000 measles cases" and the "near disappearance of SSPE in the United States".

"In 2015, the Oregon Health Authority was notified of the death of a boy with subacute sclerosing panencephalitis (SSPE), a rare and fatal complication of measles. The patient, aged 14 years, had reportedly been vaccinated against measles in the Philippines at age 8 months. However, the patient contracted measles at age 1 year while still in the Philippines. He had been well until 2012, when his neurodegenerative symptoms began.

"Analysis of SSPE among persons who had measles during the 1989–1991 U.S. measles resurgence indicated an incidence of 4–11 SSPE cases per 100,000 measles cases, approximately 10 times higher than earlier estimates [1985 estimates]...SSPE is a rare, long-term complication of measles. Widespread use of measles vaccines has been associated with the near disappearance of SSPE in the United States."

Appendix 2: Further Reading and References with hyperlinks

2.1 The subject of this letter with the two published review articles:

Oct 28, 2016 New Study: Oral Abstract Wendorf et al, *Open Forum Infectious Diseases*
Subacute Sclerosing Panencephalitis: The Devastating Measles Complication Is More Common Than We Think
http://ofid.oxfordjournals.org/content/3/suppl_1/916.full

Oct 29, 2016 *MedPage Today* article on Oral Abstract
Measles Killer: More Common than Believed
http://www.medpagetoday.com/MeetingCoverage/IDWeek/61103?xid=nl_mpt_DHE_2016-10-31&eun=g459917d0r&pos=0

Oct 31, 2016 Global News Okanagan article w/video Interview
Calgary doctor calls for mandatory measles vaccinations in wake of new study
http://globalnews.ca/news/3037014/calgary-doctor-calls-for-mandatory-measles-vaccinations-in-wake-of-new-study/

2.2 Referenced articles on SSPE and measles by year, author and journal or publication

1982 CDC *MMWR*
Subacute Sclerosing Panencephalitis Surveillance—United States
https://www.cdc.gov/mmwr/preview/mmwrhtml/00001185.htm

2002 Garg, *British Medical Journal*
Subacute sclerosing panencephalitis, Review by R K Garg
http://pmj.bmj.com/content/78/916/63.full.pdf

2003 Glaser et al, *Clinical Infectious Diseases*
In Search of Encephalitis Etiologies: Diagnostic Challenges in the California Encephalitis Project, 1998—2000
http://cid.oxfordjournals.org/content/36/6/731.long

2004 Dyken, *Journal of Pediatric Neurology*
Some aspects about the clinical and pathogenetic characteristics of the presumed persistent measles infections: SSPE and MINE
http://www.bioline.org.br/request?pn04025

2004 Orenstein et al, *Journal of Infectious Diseases*
Measles Elimination in the United States
http://jid.oxfordjournals.org/content/189/Supplement_1/S1.long

2005 Bellini, et al, *Journal of Infectious Diseases*
Subacute Sclerosing Panencephalitis: More Cases of This Fatal Disease Are Prevented by Measles Immunization than Was Previously Recognized
http://jid.oxfordjournals.org/content/192/10/1686.full

2005 Campbell et al, *BMC Pediatrics*
Subacute Sclerosing Panencephalitis: Results of the Canadian Paediatric Surveillance Program and review of the literature
http://bmcpediatr.biomedcentral.com/articles/10.1186/1471-2431-5-47

2007 Campbell et al (UK), *International Journal of Epidemiology*
Review of the effect of measles vaccination on the epidemiology of SSPE
http://ije.oxfordjournals.org/content/36/6/1334.long#F3

2012 Poland et al, *Vaccine*
The Re-Emergence of Measles in Developed Countries: Time to Develop the Next-Generation Measles Vaccines?
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3905323/

2013 Schönberger et al (German Study), *PLOS One*
Epidemiology of Subacute Sclerosing Panencephalitis (SSPE) in Germany from 2003 to 2009: A Risk Estimation
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0068909

2013 University of Wurzberg: **Summary of German study** by one of the authors, Dr. Benedikt Weissbrich
https://www.uni-wuerzburg.de/en/sonstiges/meldungen/detail/artikel/masern-ho/

2013 Sardana et al, International Journal of Basic and Applied Sciences
Review Article: Subacute Sclerosing Panencephalitis Revisited
http://www.cibtech.org/J-MEDICAL-SCIENCES/PUBLICATIONS/2013/Vol_3_No_1/37-056...Vijay%20Sardana...Subacute...Revisited...225-241.pdf

3. Public Health Publications/Data, USA & CANADA

Alberta Public Health:

2013 Alberta Public Health
Notifiable Diseases Guidelines: Measles
http://www.health.alberta.ca/documents/Guidelines-Measles-2013.pdf

2015 Alberta Public Health
Subacute Sclerosing Panencephalitis (SSPE)
http://www.health.alberta.ca/documents/Guidelines-Subacute-Sclerosing-Panencephalitis-SSPE-2015.pdf

Center for Disease Control (CDC) USA:

2015 CDC ***Pink Book, Measles Chapter***
Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015.
http://www.cdc.gov/vaccines/pubs/pinkbook/meas.html

2016 CDC MMWR–Morbidity and Mortality Weekly Report
Notes from the Field: Subacute Sclerosing Panencephalitis Death — Oregon, 2015
Weekly / January 15, 2016 / 65(1);10–11
http://www.cdc.gov/mmwr/volumes/65/wr/mm6501a3.htm

The Public Health Agency of Canada (PHAC):

Charts are updated to 2014. The first link takes you to a list of various types of charts available.
Notifiable Diseases in Canada

Single disease, age and sex distribution by year - Stacked Bar Chart