Vaccine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Short communication

Subacute sclerosing panencephalitis mortality, United States, 1979–2016: Vaccine-induced declines in SSPE deaths

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ARTICLE INFO

Article history:
Received 1 May 2018
Received in revised form 26 June 2018
Accepted 15 July 2018
Available online xxxx

Keywords:
Subacute sclerosing panencephalitis
SSPE
Measles
Mortality

ABSTRACT

Subacute sclerosing panencephalitis (SSPE) is a neurodegenerative disease caused by measles virus. We estimate SSPE age-specific mortality in the United States, 1979–2016. The general decline in SSPE mortality reflects that of measles. Shifts, over time, in SSPE mortality by age echo changes in the age distribution of measles in the 1970s and in the 1989–91 outbreak. The current epidemiological situation is that autochthonous SSPE will disappear in the United States, assuming measles vaccination rates remain high.

1. Introduction

Subacute sclerosing panencephalitis (SSPE) is a rare, always-fatal, neurodegenerative disease caused by measles virus infection of the central nervous system, as a sequela of measles. The syndrome was long-recognized [1], although differentiation from symptomatically-similar conditions came later [2], and proof of measles etiology was shown in the late 1960s and early 1970s [3–11]. By the late 1970s and early 1980s [12–14], the virological basis of SSPE pathology was better understood: "an abnormality in the synthesis of the M protein of measles virus is involved in the pathogenesis of subacute sclerosing panencephalitis" [15].

Subacute sclerosing panencephalitis is caused by persistent measles infection, and thus is rare, since measles typically elicits a sterilizing immune response among survivors. The brain offers a refuge for measles virus in SSPE cases, who have otherwise recovered fully. Cases skew young, as measles is typically a childhood infection, and the SSPE incubation period is about 7 years (±2 years SD) [16–19]. Risk is highest among measles cases in the first two years of life [20]. Typically, virus replication in the brain cannot go on for decades without showing symptoms, although adult-onset cases are documented [21]. We present SSPE age-specific mortality estimates in the United States in the last 38 years. The data show this to be the twilight period of SSPE, as measles was eliminated from the United States in 2000 [22].

2. Methods

We extracted data on recorded SSPE mortality, from publicly available data files on every death in the United States, 1979–2016 (87,925,884 total deaths from all causes) [23]. There are no data before 1979 because the International Classification of Diseases (ICD), revision 8 (and prior) does not include SSPE. For ICD-9 (1979–1998), the code for SSPE is 046.2 [24], and for ICD-10 (1999–2016) the code is A81.1 [25]. Any mention of SSPE on the death certificate (i.e., as underlying or contributory cause) counted as an SSPE death. We emphasize that our data comprise recorded SSPE mortality on death certificates (net of errors of inclusion and omission). We do not have clinical data. On the other hand, the data we present is a census, not a sample, of all recorded SSPE deaths in the United States.

As a comparison, we extracted the same information for Batten disease (ICD-9 330.1, ICD-10 E75.4), an unrelated neurological disorder [26,27]. The logic of including Batten disease is as a control for monitoring of deaths due to neurodegenrative disorders. Batten disease is similar to SSPE in that it is rare, fatal, and kills mostly children, adolescents, and young adults. We do not believe SSPE deaths are misclassified as Batten disease, or vice versa, but we use it as a check on the ability of the vital statistics system to pick up rare neurodegenrative deaths. Since Batten disease is genetic and therefore should not decline in the way infectious diseases

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https://doi.org/10.1016/j.vaccine.2018.07.030
0264-410X/

have, it would possibly indicate reporting problems if Batten disease deaths fall in-step with those of SSPE. We used the ICD 9/10 comparison dataset [28,29] to estimate the effect of changes due to the switch to ICD-10. We also present data on measles cases in the period 1964 to 2000 [30], to compare to our SSPE results.

3. Results

Fig. 1 shows our results. This is a bar chart of SSPE deaths over time, with the top panel being all ages; the panels below break out age categories, as labeled. The vertical white lines denote four time periods which will frame our discussion, below. There were 334 recorded SSPE deaths in the United States in this time period, of which one (in 1979) had no reported age. There were no recorded SSPE deaths in the United States in 2010 or 2014–2016 in our data set. However, there is a case report of an SSPE death in 2015 [31], indicating that it is possible that the database we used missed some deaths, presumably from incorrect ICD assignment. Fig. 2 shows measles cases, 1964–2000; this will be discussed below as an aid to interpretation of Fig. 1. The winter of 1963–64 was the first measles season in which the vaccine was available, and measles was eliminated from the United States in 2000 [22].

Fig. 3 gives a time series plot of SSPE and Batten disease deaths. While SSPE mortality has declined in the last 35 years, deaths due to Batten disease have been steady (with noise), modulo a decline due to the transition to ICD-10 coding, discussed immediately below. From the use of Batten disease as a control, we conclude that it is unlikely that the decline in SSPE is due to a systematic change in detection of central nervous system disorders.

It appears that the transition to ICD-10 death coding (in 1999) results in fewer recorded SSPE deaths at older ages (Fig. 1). This makes sense in terms of refinement of classification criteria, because in theory SSPE cases at older ages ought to be extremely rare. We believe that most (indeed, potentially, all) SSPE deaths at older ages are false positives. This can occur if the ICD code for SSPE appears erroneously on the death certificate. The evidence

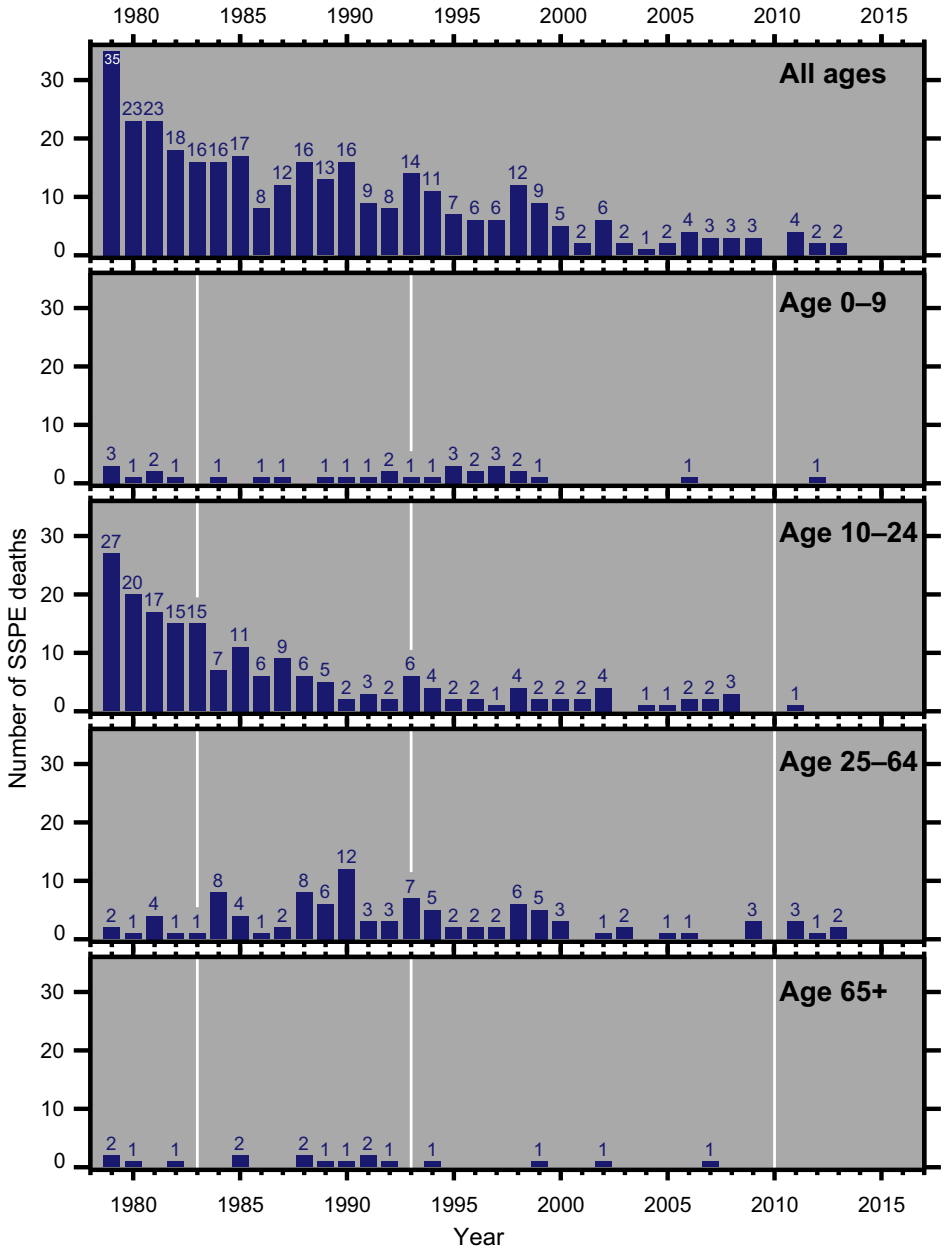

Fig. 1. SSPE deaths by age categories, United States, 1979–2016. White vertical rules mark time periods discussed in the text.

Please cite this article in press as: Pallivathucal LB, Noymer A. Subacute sclerosing panencephalitis mortality, United States, 1979–2016: Vaccine-induced declines in SSPE deaths. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.07.030