

# Subacute Sclerosing Panencephalitis (SSPE)

## Revision Dates

Case Definition	December 2015
Reporting Requirements	December 2018
Remainder of the Guideline (i.e., Etiology to References sections inclusive)	December 2015

## Case Definition

### Clinical Case

Subacute sclerosing panencephalitis (SSPE) is a persistent, progressive, often fatal degenerative neurological disease, arising from a defective measles virus infection, resulting in a widespread demyelination (pan encephalitis) of the central nervous system. The diagnosis is supported by:<sup>(1-3)</sup>

- Detection of elevated levels of measles antibody in CSF,
- An electroencephalogram (EEG) pattern characteristic of SSPE (i.e., periodic complexes),
- The presence of typical histopathologic changes in neurologic tissues derived at autopsy or from brain biopsy specimens (in particular, intranuclear and cytoplasmic inclusion bodies in neurons and glial cells),
- The identification of measles virus RNA or antigen in brain tissues by means of reverse-transcription polymerase chain reaction (RT-PCR) or immunohistochemical analysis.

The initial diagnosis is based on a typical picture of progressive subacute mental deterioration with generalized myoclonus, and characteristic EEG changes.

## Reporting Requirements

### 1. Physicians, Health Practitioners and Others

Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all clinical cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

### 2. Laboratories

All laboratories shall report all positive laboratory results to support the clinical diagnosis of SSPE by mail, fax or electronic transfer within 48 hours (two business days) to the:

- Chief Medical Officer of Health (CMOH) (or designate), and
- MOH (or designate) of the zone.

### 3. Alberta Health Services and First Nations and Inuit Health Branch

- The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all clinical cases to the CMOH (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical / epidemiological information.

## **Etiology**

The pathophysiology of the disease is not fully understood, however it is a persistent and chronic encephalitis secondary to measles virus infection. The virus is able to infect the neurons and survive in a dormant form for years before becoming clinically evident.<sup>(2)</sup> Eventually the virus triggers an inflammatory response against infected cells resulting in widespread CNS destruction.<sup>(1)</sup>

## **Clinical Presentation**

SSPE has a gradual and harmful onset. Affected individuals typically present initially with intellectual deterioration, personality changes, myoclonus, and seizures, progressing sooner or later, to akinetic mutism and death.<sup>(2)</sup>

Motor regression is seen in 100% of individuals with SSPE, cognitive decline in 86%, myoclonus in 74%, generalized seizures in 16% and focal seizures in 10%.<sup>(2)</sup> Some individuals may present with early visual symptoms that predate cortical signs by a few weeks up to 2 years, with deficits in visuospatial orientation and early macular damage reported.<sup>(2,4)</sup> SSPE has relentless progression; few individuals will have spontaneous remission, the majority die within 1 to 3 years of diagnosis.<sup>(2,4)</sup>

## **Diagnosis**

Diagnosis is primarily based on clinical presentation supported by high titres of serum antibodies against measles virus and the presence of oligoclonal measles virus antibodies in CSF (Serum: CSF measles antibody ratio indicative of intrathecal antibody production)<sup>(5)</sup>, or detection of viral RNA, expressing multiple mutations, from brain biopsy or at autopsy.<sup>(6)</sup>

Ancillary findings such as those obtained by EEG, neuroimaging, and tissue analysis may also be used.<sup>(2)</sup> On EEG, periodic complexes are characteristic features of SSPE.<sup>(2,4)</sup> Neuroimaging (magnetic resonance imaging and computed tomography) have limited roles in the early diagnosis of SSPE but can be used to follow disease progression (may show progressive atrophy and white matter lesions).<sup>(2,7)</sup> Brain biopsy or post-mortem tissue examination show typical histopathological findings.<sup>(2)</sup>

In Canada, brain tissue specimens should be collected posthumously on all suspect cases of SSPE for virus detection. Specimens are forwarded by the ProvLab to the Viral Exanthemata Laboratory at the National Microbiology Laboratory (NML).<sup>(8)</sup>

## **Epidemiology**

### **Reservoir**

Not applicable.

### **Transmission**

SSPE is not transmissible person-to-person

### **Incubation Period**

Approximately 10.8 years. The onset usually occurring 7-11 years after wild-type measles infection.<sup>(2)</sup> Patients with adult onset of SSPE present at a mean age of 24.4 years (range 20-35 years).<sup>(7)</sup>

### **Period of Communicability**

Not communicable.

### **Host Susceptibility**

Most cases have a history of primary measles infection at an early age, usually before 2 years.<sup>(2,4)</sup> When SSPE occurs in vaccinated children, it is thought to result from a subclinical measles infection that occurred before the age of one.<sup>(7)</sup> Children infected with measles under the age of one carry a risk 16 times greater than those infected at age 5 years or later.<sup>(7)</sup> It may also infrequently present in young adults.<sup>(3)</sup> There is a higher incidence of SSPE among males than females, with a ratio of 3 to 1, although primary measles infection shows no such sex disparity.<sup>(7)</sup> Other risk factors associated with SSPE include living in a rural area, poverty and overcrowding in the home.<sup>(2,4)</sup>

## **Occurrence**

### **General**

SSPE has been reported from all parts of the world, but it is considered a rare disease in the West. The prevalence has steadily declined in developed countries that have practiced widespread immunization with measles vaccine.<sup>(2,4)</sup> In the USA, fewer than 10 cases are reported per year.<sup>(9)</sup> The rate of SSPE is still high in developing countries. In India, and other similar countries, >20 per million people are reported each year. For those who have had wild measles infection, 7 – 300 cases per million people become SSPE cases.<sup>(10)</sup> 1 case per million people who receive vaccine become SSPE cases.

### **Canada**

SSPE is not a nationally notifiable disease. Since widespread measles immunization in Canada began in 1963, its associated complications, including SSPE, have become uncommon.<sup>(5)</sup> The Canadian Paediatric 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. Altogether, four 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.<sup>(4)</sup>

### **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.<sup>(7)</sup>

## **Key Investigation**

### **Single Case/Household Cluster**

- Assess measles immunization history.
- Determine measles disease history.
- Obtain a relevant medical history including risk factors.
- Obtain relevant diagnostic test results that support the clinical presentation.

## **Control**

### **Management of a Case**

- Supportive therapy

### **Treatment of a Case**

- There is no cure for SSPE.<sup>(2,4)</sup>
- Antiviral medication and immune modulating agents may help stabilize, but do not make a substantial difference to the clinical outcome.<sup>(2,5,7)</sup>
- Symptomatic therapies such as anticonvulsants may show some benefit.<sup>(5)</sup>

**Management of Contacts**

- No follow up required.

**Preventive Measures**

- Immunization against measles is the only known prevention for SSPE.<sup>(2,4)</sup>
- Provide public education about the risks of measles disease and the importance of immunization.
- See the current *Alberta Immunization Policy* (AIP) for measles vaccine recommendations.

Superseded

## References

1. Bellini WJ, Rota JS, Lowe LE, Katz RS, Dyken PR, Zaki SR, et al. Subacute sclerosing panencephalitis: more cases of this fatal disease are prevented by measles immunization than was previously recognized. *J Infect Dis.* 2005;192(10):1686–93.
2. Gutierrez J, Issacson RS, Koppel BS. Subacute sclerosing panencephalitis: an update. *Dev Med Child Neurol.* 2010;(52):901–7.
3. Fonseca K. Personal Communication. 2015.
4. Garg RK. Subacute sclerosing panencephalitis. *J Neurol.* 2008;(255):1861–71.
5. Campbell C, Levin S, Humphreys P, Walop W, Brannan R. Subacute sclerosing panencephalitis: results of the Canadian paediatric surveillance program and review of the literature. *BMC Pediatr.* 2005;5:47.
6. Cattaneo R, Billeter MA. Mutations and A/I hypermutations in measles virus persistent infections. *Curr Top Microbiol Immunol.* 1992;(176):63–74.
7. Garg RK. Subacute sclerosing panencephalitis review. *Postgrad Med J.* 2002;78:63–70.
8. Public Health Agency of Canada (PHAC). Subacute sclerosing panencephalitis (SSPE) diagnosis [Internet]. 2014. Available from: [www.nml-inm.gc.ca/guide2/pathogen\\_engview.php?refdiagID=226](http://www.nml-inm.gc.ca/guide2/pathogen_engview.php?refdiagID=226)
9. Subacute sclerosing panencephalitis: MedlinePlus Medical Encyclopedia [Internet]. Available from: [www.nlm.nih.gov/medlineplus/ency/article/001419.htm](http://www.nlm.nih.gov/medlineplus/ency/article/001419.htm)
10. Subacute Sclerosing Panencephalitis (SSPE) - Children's Health Issues - Merck Manuals Consumer Version [Internet]. Available from: [www.merckmanuals.com/home/children-s-health-issues/viral-infections-in-infants-and-children/subacute-sclerosing-panencephalitis-sspe](http://www.merckmanuals.com/home/children-s-health-issues/viral-infections-in-infants-and-children/subacute-sclerosing-panencephalitis-sspe)