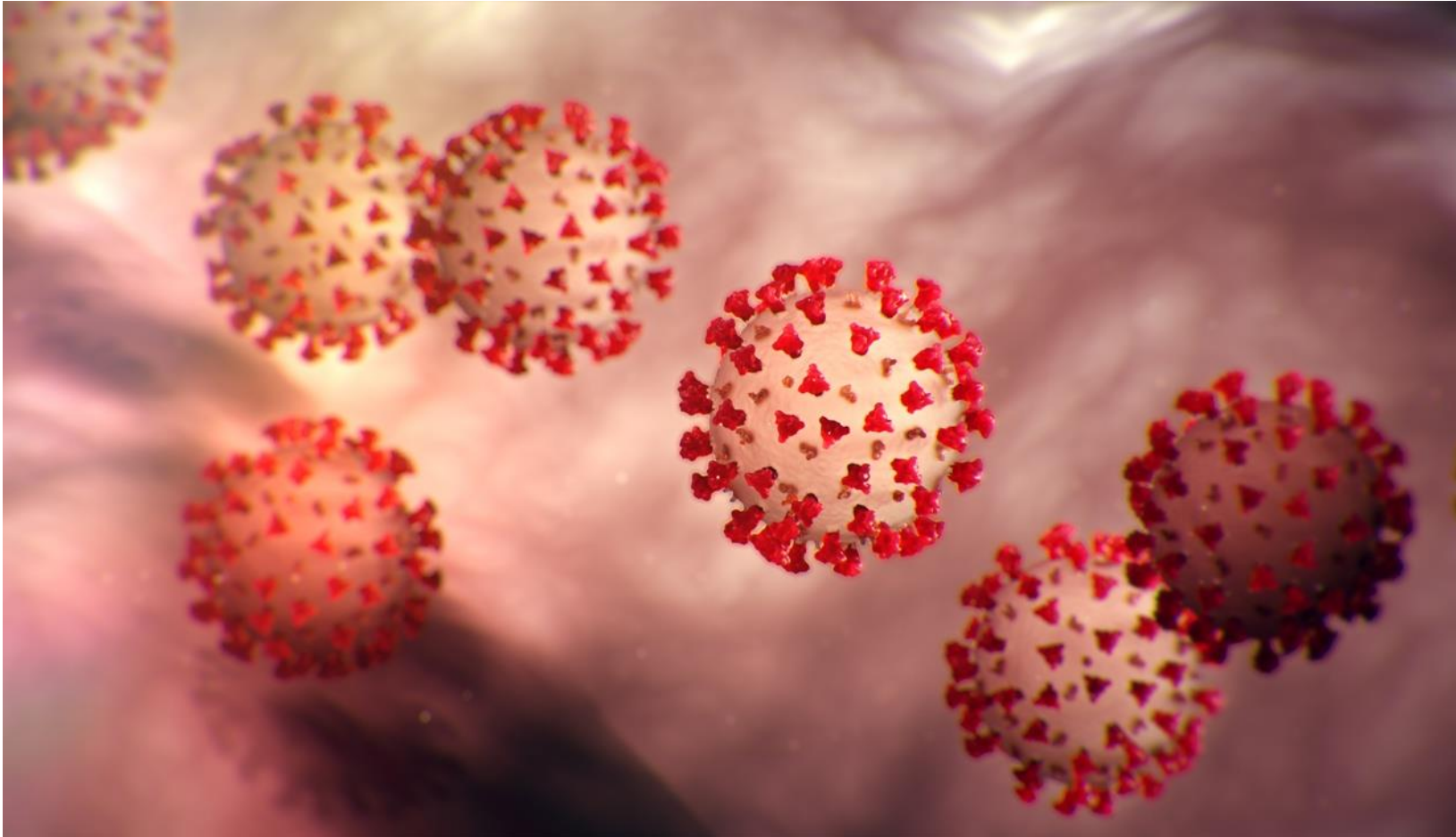
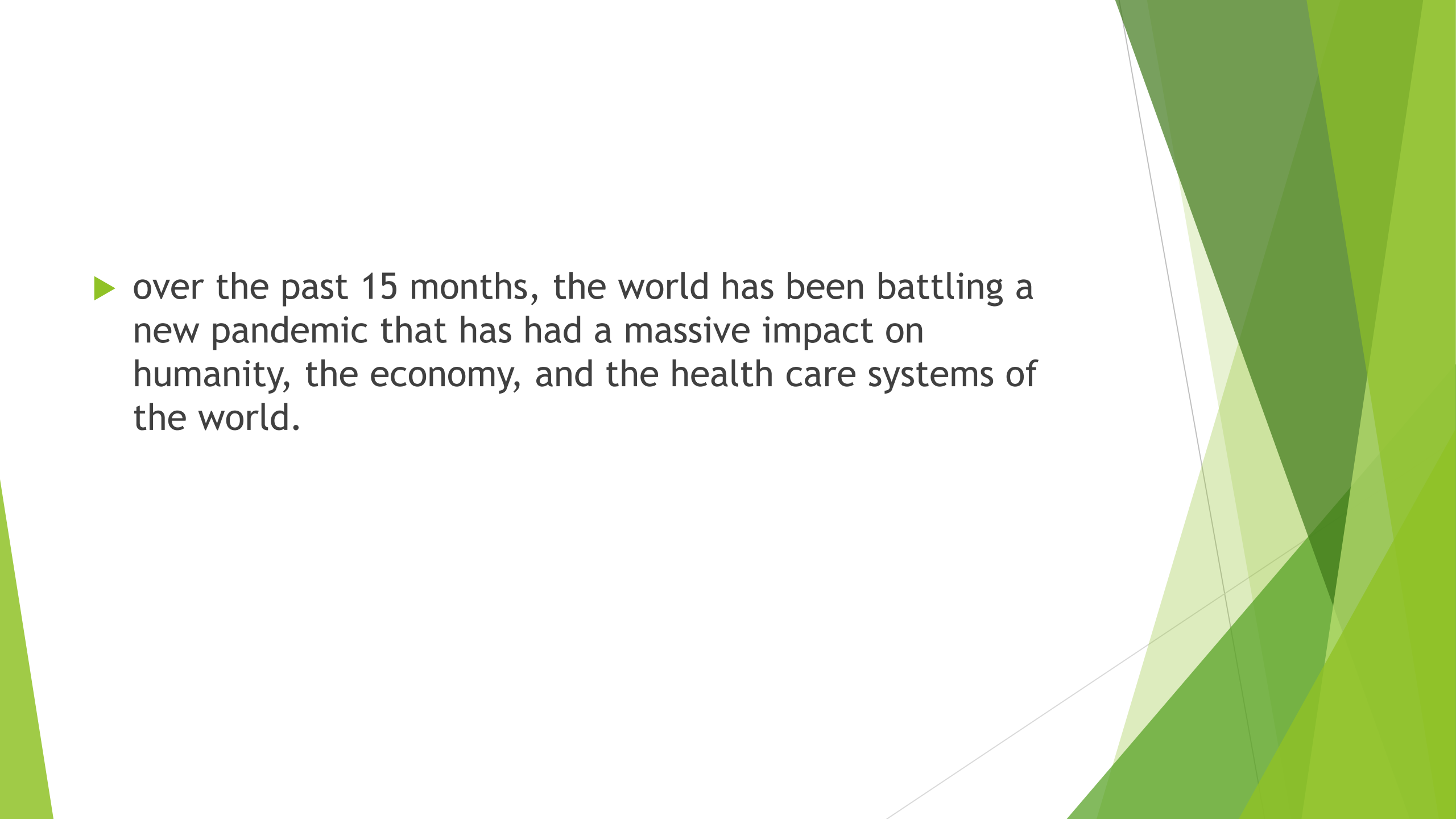
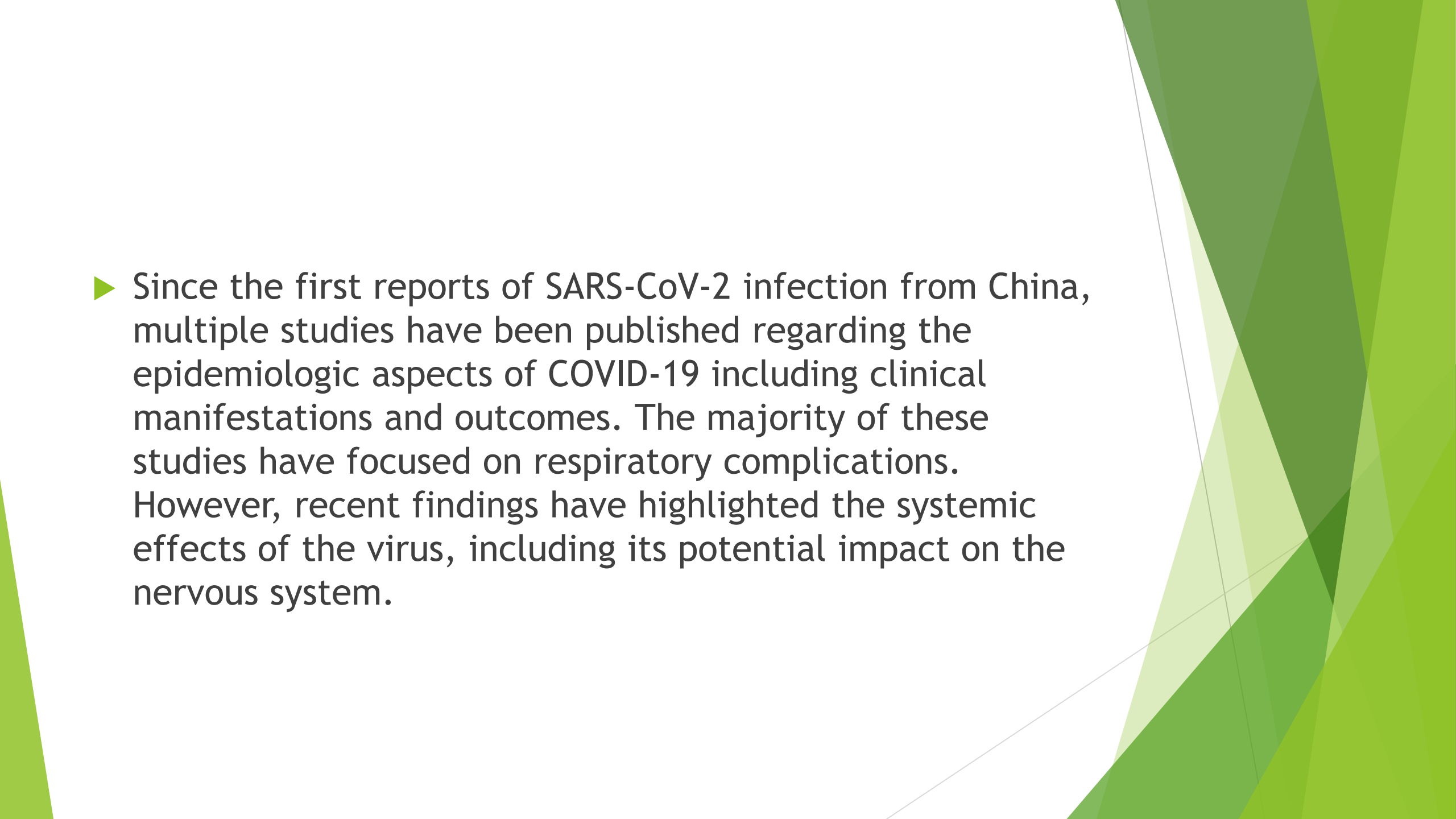


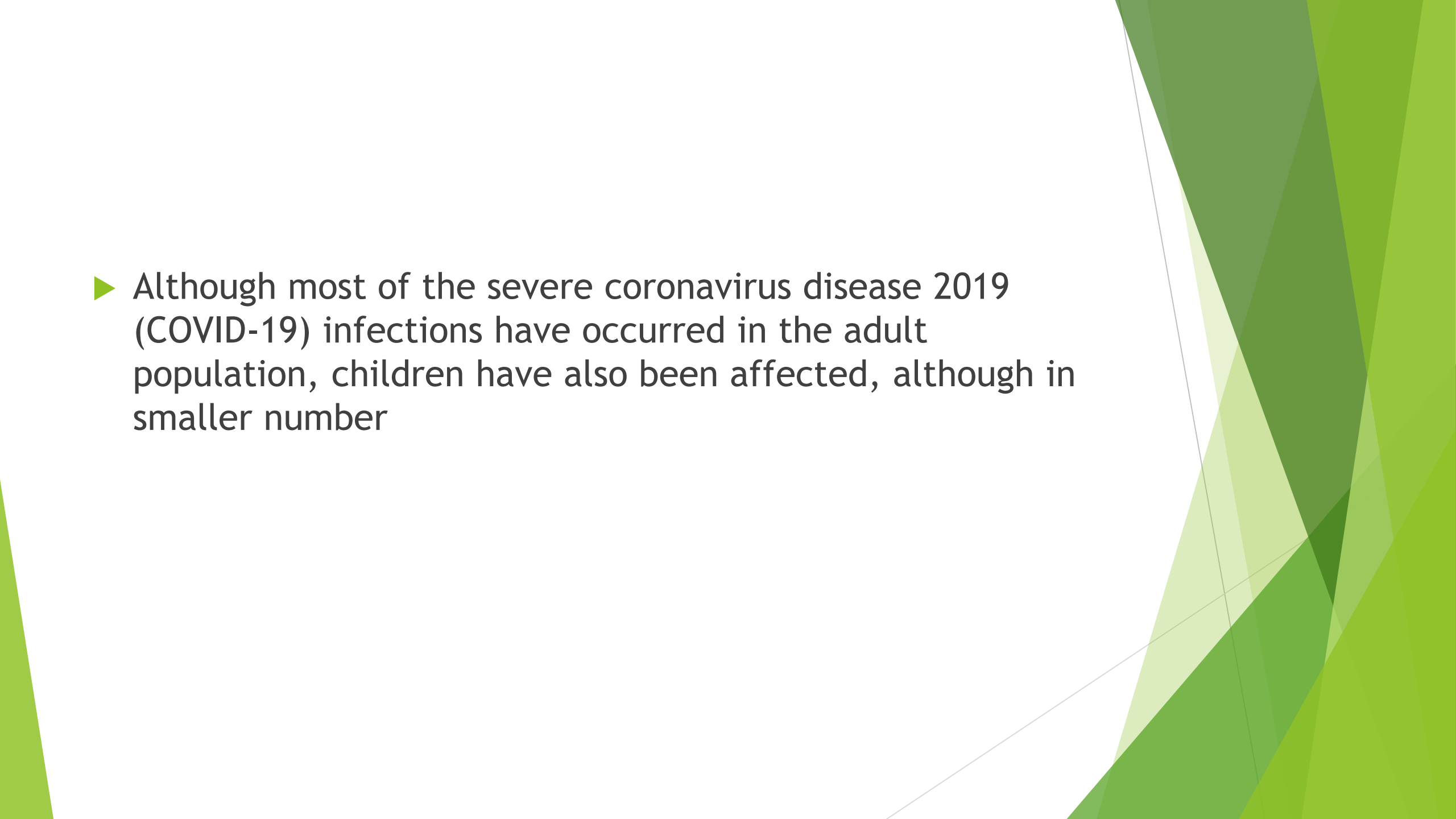
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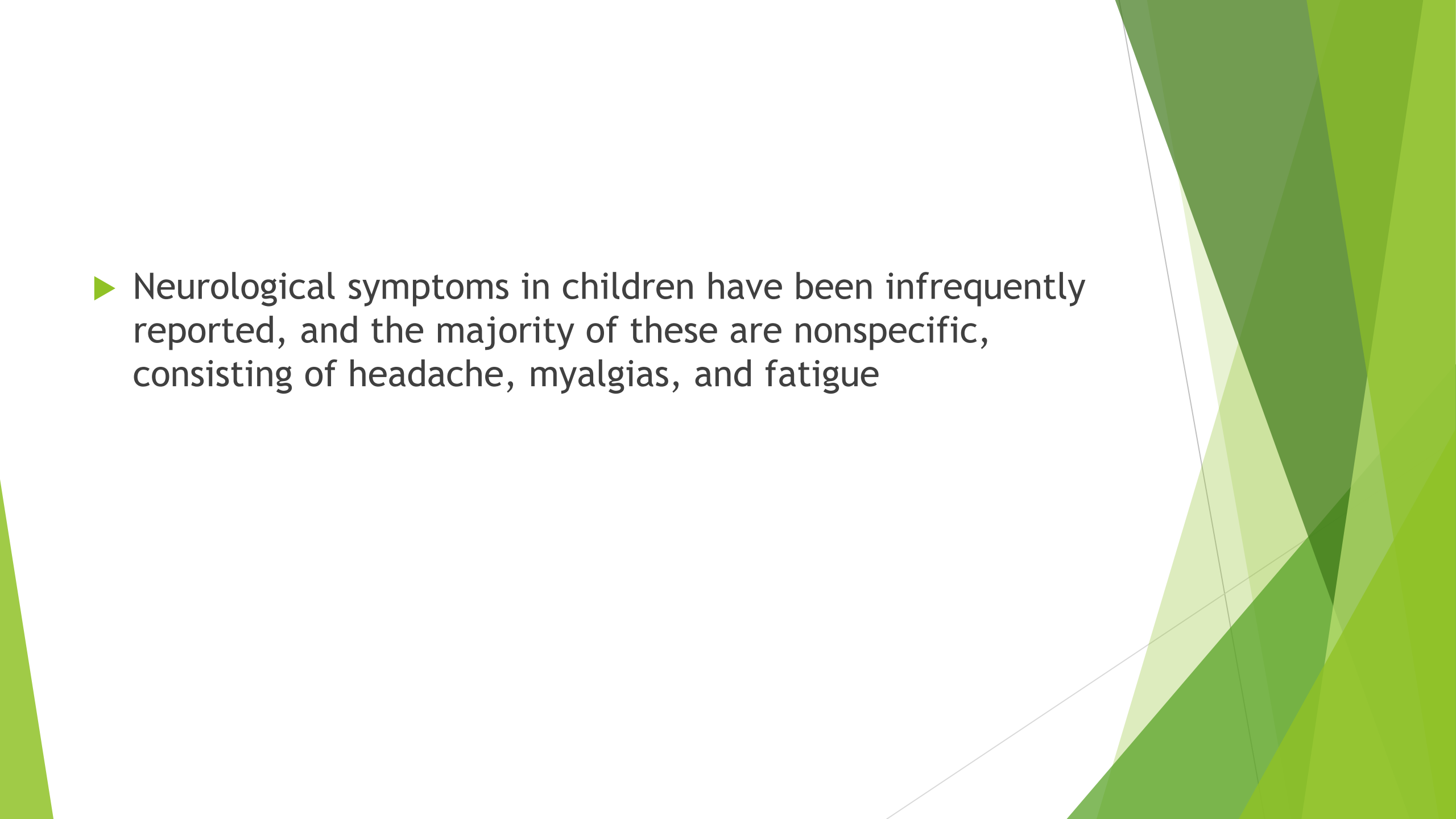




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- The background of the slide features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. These shapes are primarily located on the right side and bottom of the slide, creating a modern, dynamic feel. The main content area on the left is white.
- ▶ over the past 15 months, the world has been battling a new pandemic that has had a massive impact on humanity, the economy, and the health care systems of the world.

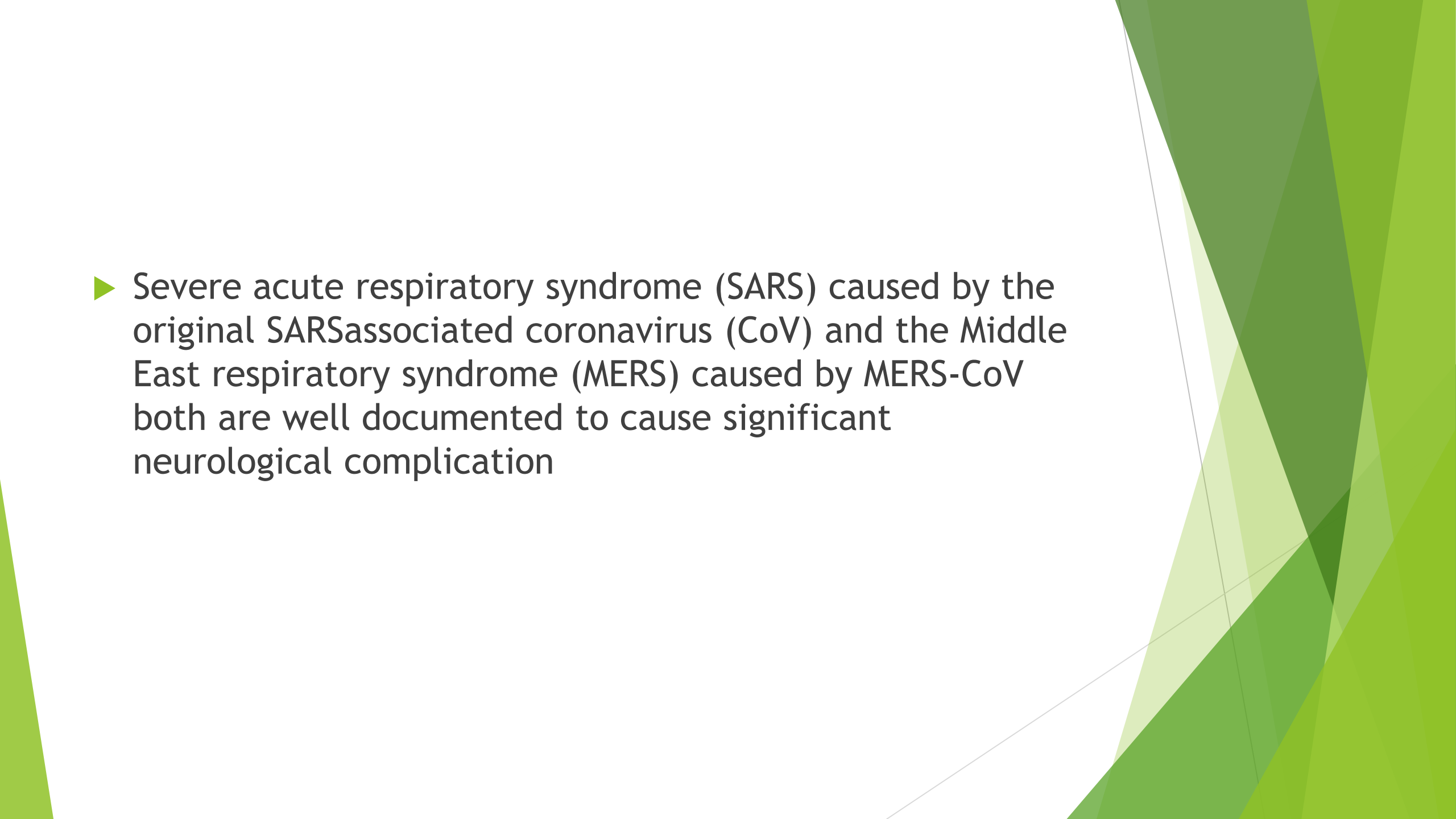
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- The background of the slide features abstract, overlapping green geometric shapes, primarily triangles and polygons, in various shades of green, creating a modern and dynamic visual effect.
- ▶ Since the first reports of SARS-CoV-2 infection from China, multiple studies have been published regarding the epidemiologic aspects of COVID-19 including clinical manifestations and outcomes. The majority of these studies have focused on respiratory complications. However, recent findings have highlighted the systemic effects of the virus, including its potential impact on the nervous system.

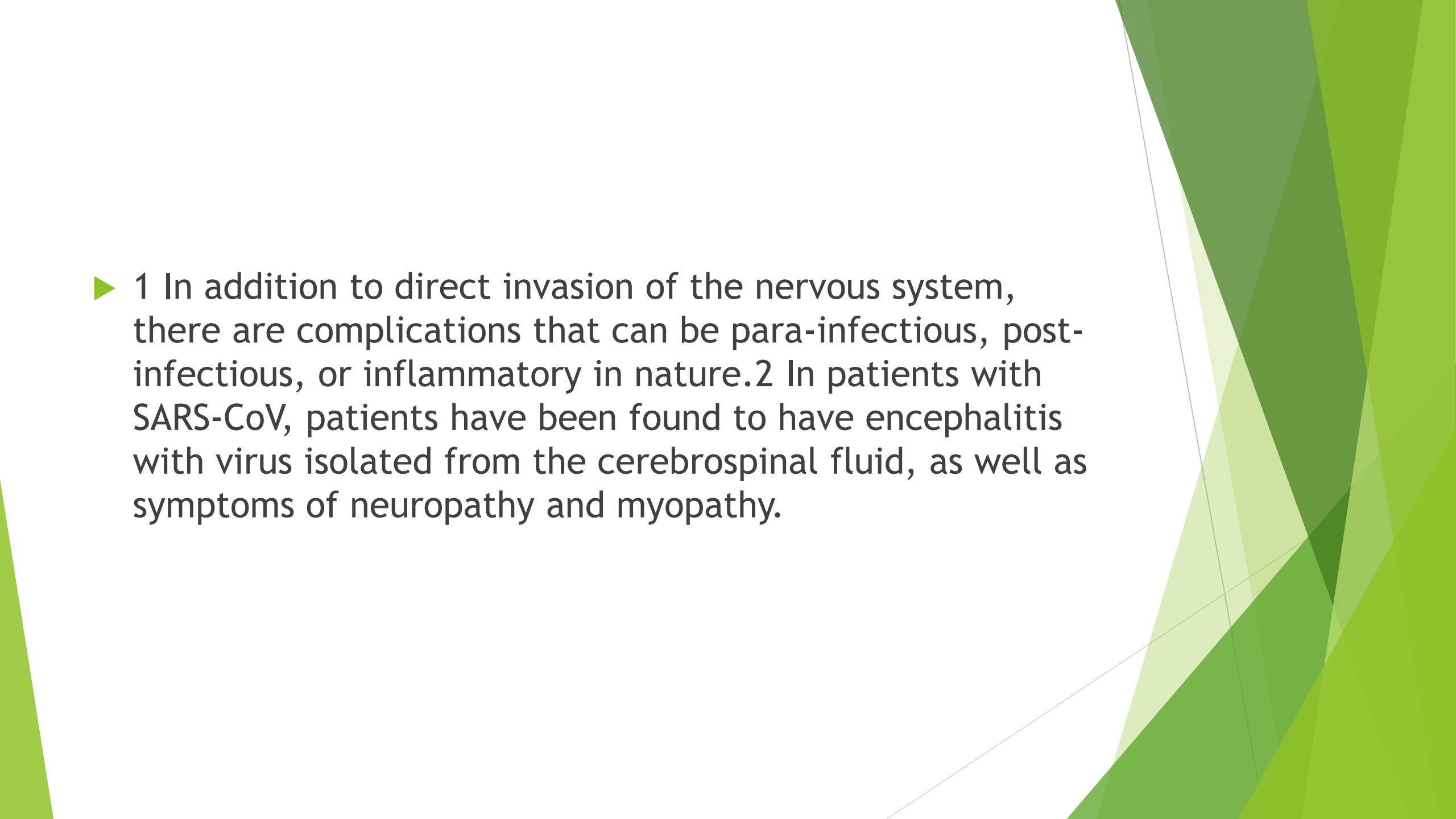
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- The background of the slide features abstract, overlapping green geometric shapes, primarily triangles and polygons, in various shades of green, creating a modern and dynamic visual effect.
- ▶ Although most of the severe coronavirus disease 2019 (COVID-19) infections have occurred in the adult population, children have also been affected, although in smaller number

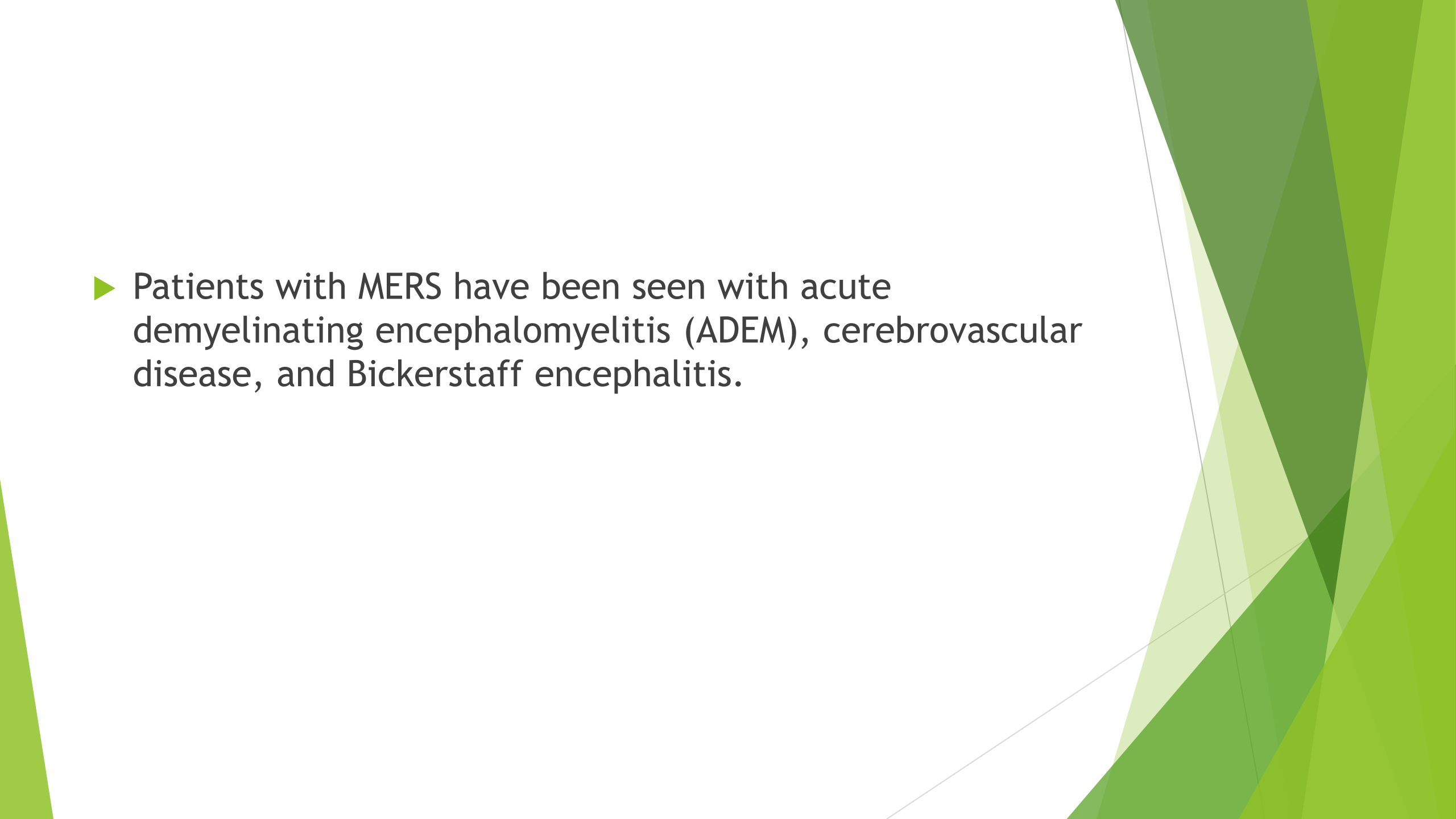
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- The background of the slide features abstract, overlapping green geometric shapes, primarily triangles and polygons, in various shades of green, creating a modern and dynamic visual effect.
- ▶ Neurological symptoms in children have been infrequently reported, and the majority of these are nonspecific, consisting of headache, myalgias, and fatigue

- ▶ There are, however, a few cases of more severe neurological illness reported in children with COVID-1

- ▶ the beta-coronaviruses are large, positive strand RNA viruses that are most well understood as a cause of seasonal upper respiratory infections (URIs), accounting for 15% to 30% of all seasonal cases of the common cold

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- ▶ Severe acute respiratory syndrome (SARS) caused by the original SARS-associated coronavirus (CoV) and the Middle East respiratory syndrome (MERS) caused by MERS-CoV both are well documented to cause significant neurological complication

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- ▶ 1 In addition to direct invasion of the nervous system, there are complications that can be para-infectious, post-infectious, or inflammatory in nature.² In patients with SARS-CoV, patients have been found to have encephalitis with virus isolated from the cerebrospinal fluid, as well as symptoms of neuropathy and myopathy.

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- ▶ Patients with MERS have been seen with acute demyelinating encephalomyelitis (ADEM), cerebrovascular disease, and Bickerstaff encephalitis.

- ▶ The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus responsible for the COVID-19 pandemic is thought to demonstrate neuro-tropism as well.

- ▶ The mechanism of viral entry into cells is via angiotensin converting enzyme 2 (ACE2) receptors, as the viral spike protein binds to the ACE2 receptor

In children, there is some clear overlap with regard to neurological complications of COVID-19. Given the lower incidence of SARS-CoV-2 disease presentations in children, to date there have been fewer severe complications

the adult data show the wide spectrum of disease of which we need to be aware, including direct CNS infection, cerebrovascular complications, central and peripheral demyelination, CNS edema, myopathy, and seizures.

similar to the widespread hyperinflammatory condition in adults with COVID-19, the most severe cases in children present with multi-system inflammatory

common neurological symptoms in patients presenting with this syndrome are headache, malaise, and dizziness

in one larger meta-analysis up to 10% of patients presented with altered mental status. The data regarding anosmia/ageusia are less robust, with some studies reporting rates as high as 62% (similar to the adult data), and others reporting minimal incidence of these symptoms,⁸ which presents a challenge in trying to accurately assess the rates of these complications in children

In a large systematic review of COVID-19 in children that included 3,707 patients, approximately 1% had definite neurological complications, including 25 patients with encephalopathy, 12 with seizures, and 17 with meningeal signs.

In this review, it was noted that there was a single child with intracranial hemorrhage who had died. There are also reports of individual children with AIDP that responded favorably to conventional management

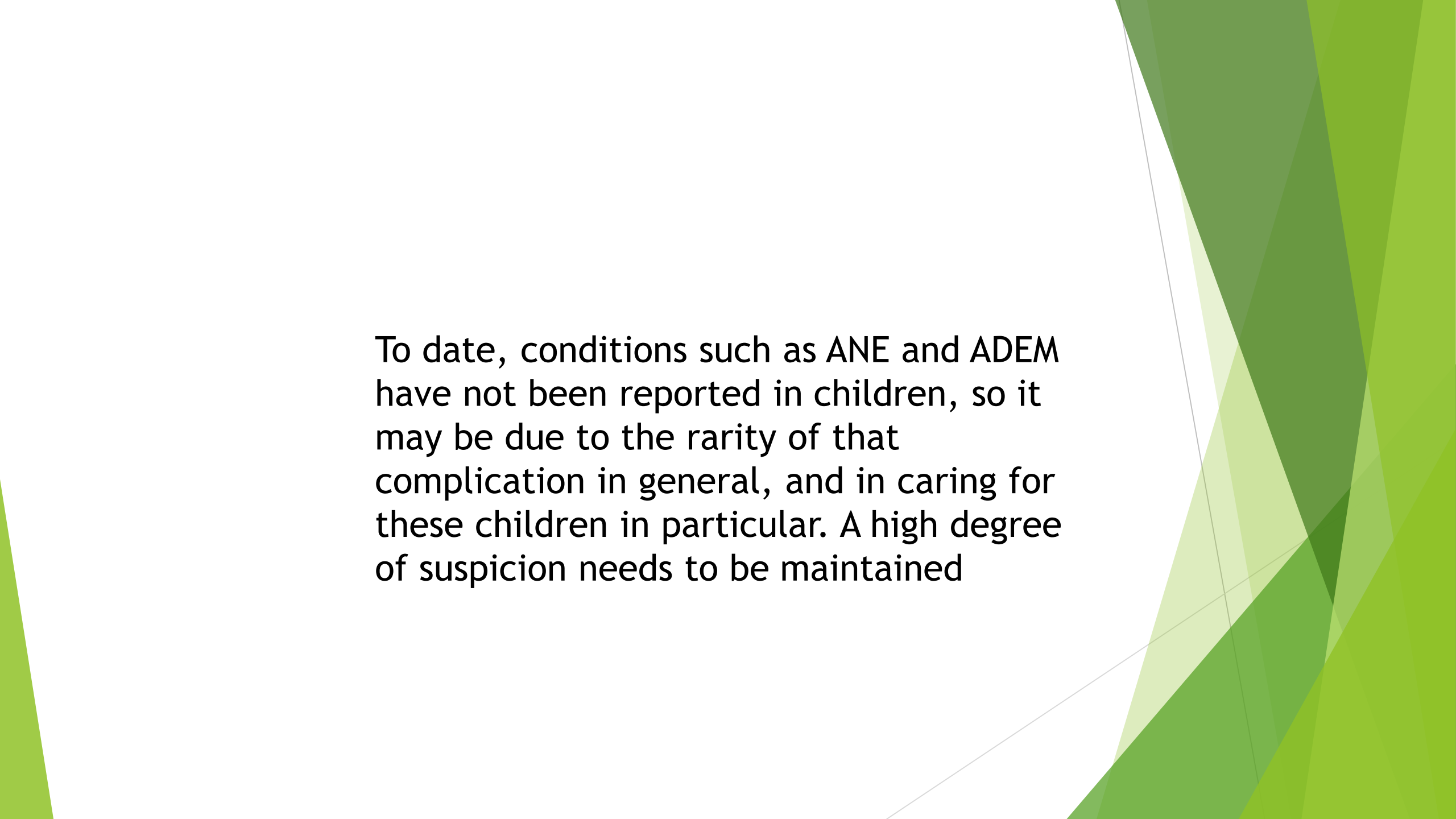
Notably, the high rate of cardiac involvement seen in children with multisystem inflammatory syndrome in children is striking—up to 54% in one case series.¹⁰ This would predispose children to cardioembolic events in the future

the neonatal population, the neurological symptoms are even more challenging to discern. Some case series describe neonates and infants presenting days to weeks after birth with altered behavior and hypotonia, sometimes with seizure like activity

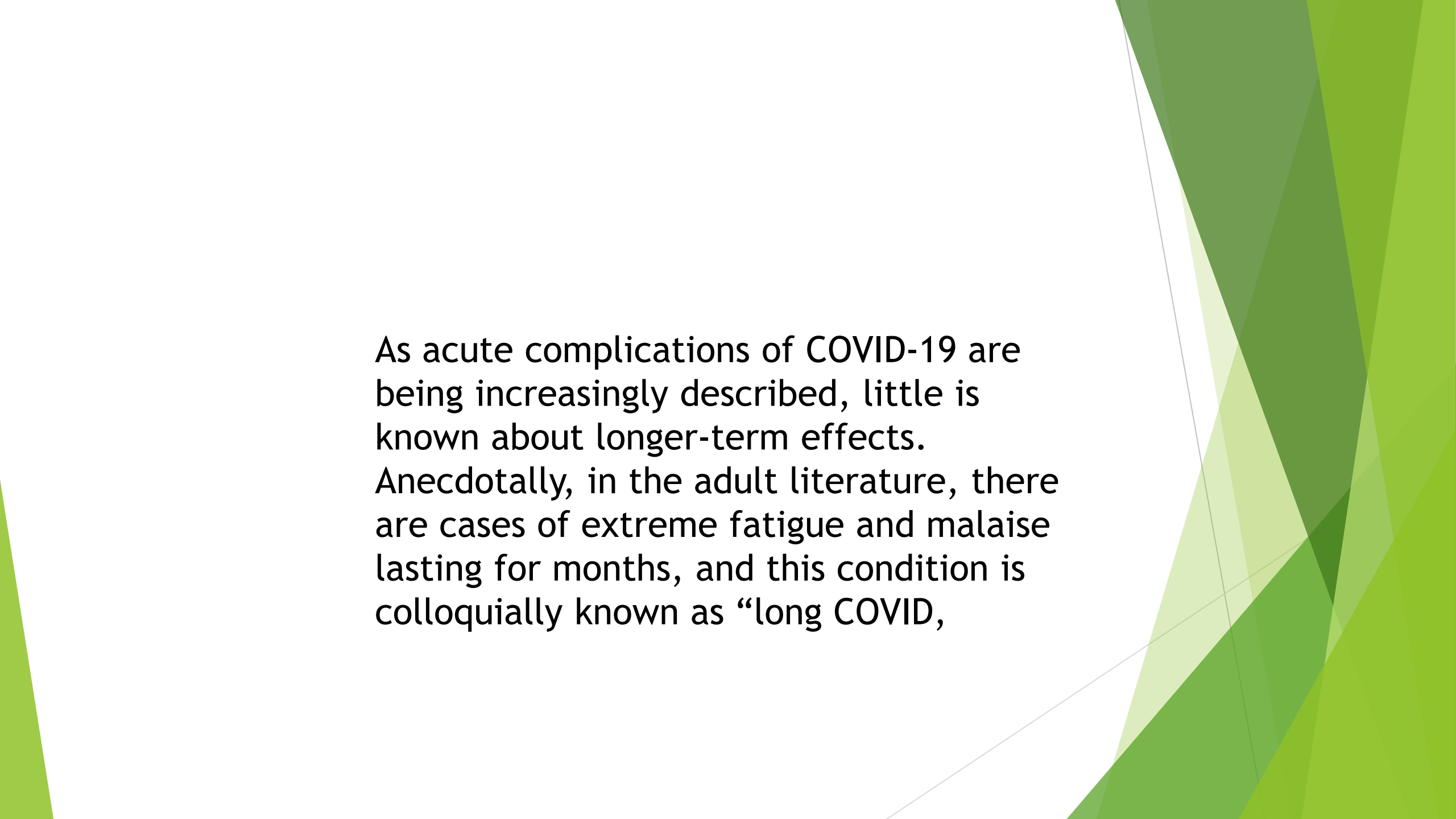
All infants with post-natal exposure
improved spontaneously within day 11

There was a case of transplacental transmission of a 35-week premature infant with SARS-CoV-2 polymerase chain reaction testing being positive at 1 hour of postnatal life. This infant presented with opisthotonic posturing, poor feeding and irritability, and some nonspecific T2 hyperintensities on magnetic resonance imaging (MRI).¹² This infant gradually improved over several weeks, and at the 2-month follow-up the MRI also showed improvement

Although similarities with the adult population exist, there seem to be distinct differences between neurological complications between the two groups. In children, at least, neurological complications seem to be associated more with severe disease. In the adult population, the neurological manifestations were at times the primary manifestation and delayed the diagnosis of COVID-19.

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To date, conditions such as ANE and ADEM have not been reported in children, so it may be due to the rarity of that complication in general, and in caring for these children in particular. A high degree of suspicion needs to be maintained

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As acute complications of COVID-19 are being increasingly described, little is known about longer-term effects. Anecdotally, in the adult literature, there are cases of extreme fatigue and malaise lasting for months, and this condition is colloquially known as “long COVID,

These include evidence of persistent cardiac inflammation, fatigue, weakness, headaches, and cognitive struggles such as concentration difficulties and confusion. There are mounting data that these symptoms may also be present in children and may proceed from an asymptomatic or minimally symptomatic acute infection

Longer term, prospective data are needed to assess the frequency and severity of these symptoms in children, but as data emerge, we may be facing a dramatic rise in complaints of confusion/memory problems, chronic fatigue, increased symptoms of attention-deficit/ hyperactivity disorder (ADHD), and executive functioning difficulties in the pediatric population