

Cerebrovascular manifestations of Covid- 19

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Covid-19

- ▶ A novel coronavirus
- ▶ Resembling SARS-Co in many ways, specially they shared the same receptor, angio-tension converting enzyme-2
- ▶ Typical manifestations: fever, cough, diarrhea, fatigue
- ▶ Neurological manifestations: (36.4%)
 - 1.CNS(dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia, seizure)
 - 2.PNS (taste/smell impairment, vision impairment, nerve pain)
 - 3.Skeletal muscular injury

Pathophysiology

Neuroinvasion and neurovirulence

- ▶ Access may be achieved via two main routes: hematogenous or transneuronal through the olfactory bulb
- ▶ hematogenous route involves directly infecting the blood–brain barrier (BBB) or access via a Trojan such as leukocytes

ACE2 receptor and angiotensin (1-7) (ANG (1-7))

- ▶ ACE2 is a carboxypeptidase that converts angiotensin I into ANG (1-7), which is an essential component of the renin-angiotensin system
- ▶ ANG (1-7) : synthesized in endothelial cells and has a downstream effect stimulates the release of prostaglandin and nitric oxide, enhances the metabolic actions of brady kinin, and inhibits smooth muscle cell growth
- ▶ binding of SARSCoV-2 to the ACE2 receptor may inhibit its downstream effect via pathway down regulation or cell lysis, ultimately decreasing ANG (1-7) synthesis counteract neuroprotective properties and blood pressure auto-regulation (increase in sympathetic activity)

Hypercoagulable state

- ▶ hypercoagulable state causes by the virus-induced cytokine storm
- ▶ critically ill COVID-19 patients had increased proinflammatory cytokines, including IL-2 and TNF- α , which can up-regulate the coagulation system.
- ▶ In a recent Dutch study, there was a 31% incidence of thrombotic complications in patients with COVID-19 admitted to the ICU, mainly consisting of acute pulmonary embolism, deep vein thrombosis, ischemic stroke, myocardial infarction, and systemic arterial embolism

Features of Covid-19 associated ischemic stroke

- ▶ large vessel occlusion
- ▶ multiterritory infarcts
- ▶ Venous thromboembolism
- ▶ raised inflammatory markers
- ▶ antiphospholipid antibody production
- ▶ a younger age of presentation
- ▶ concurrent severe systemic inflammation with organ failure
- ▶ reported incidence of stroke in COVID-19 hospitalized patients is 0.9–2%, with an increased incidence in the young

Features of Covid-19 associated hemorrhagic stroke

- ▶ Relatively young with a mean age of 52.2 years (range 41 – 64 years with morbidity mortality generally increases with advancing age)
- ▶ lobar predominance (Lobar ICH occurs in 15 – 30% of conventional cases, and is predominantly associated with an underlying vascular abnormality)
- ▶ having evidence of a period of prolonged inflammation, as demonstrated firstly by markedly raised D-Dimer values and secondly by severe end organ damage

Risk factors for ischemic stroke

- ▶ Older age
- ▶ Black
- ▶ Higher frequency of HTN
- ▶ Diabetes
- ▶ Hyperlipidemia
- ▶ Arterial fibrillation
- ▶ Congestive heart failure
- ▶ Organ failure
- ▶ More severe symptoms, less response to TPA

Risk factors for intra-cerebral hemorrhage

- ▶ Older age
- ▶ Caucasian race
- ▶ Respiratory failure requiring mechanical ventilation
- ▶ Anticoagulation

Take home message

- ▶ Clinicians should have a low threshold for suspicion and investigation particularly those younger individuals receiving organ support beyond two weeks of their COVID-19 illness, who are also being treated with anticoagulants
- ▶ Acute ischemic stroke patients with suspected COVID-19 have to be evaluated under the assumption that they have COVID-19

Covid-19 vaccines

	Pfizer ¹⁴	Moderna ¹⁹	AstraZeneca ¹⁵	Johnson & Johnson ¹⁶	Gamaleya ¹⁷
Vaccine name	BNT162b2	mRNA-1273	ChAdOx1	Ad26.COV2.S	Ad26/Ad5
Vector	mRNA	mRNA	Adenovirus	Adenovirus	Adenovirus
Dosage	2 doses, 3 wks apart	2 doses, 4 wks apart	2 doses, up to 12 wks apart	1 dose	2 doses, 3 wks apart
Efficacy against infection	%95	%95	%90–%62	%70	%92
Efficacy against severe COVID-19	%95	%94.1	Up to 100%	%85	%90
Storage	–70 °C	–20 °C	4 °C	4 °C	4 °C

Neurological complications

- ▶ most common neurological symptoms: dizziness, headache, pain, muscle spasms, myalgia, and paresthesias
- ▶ Rare symptoms: tremor, diplopia, tinnitus, dysphonia, seizures, and reactivation of herpes zoster
- ▶ There are also cases of stroke ,GBS ,facial palsy, transverse myelitis and acute disseminated encephalomyelitis



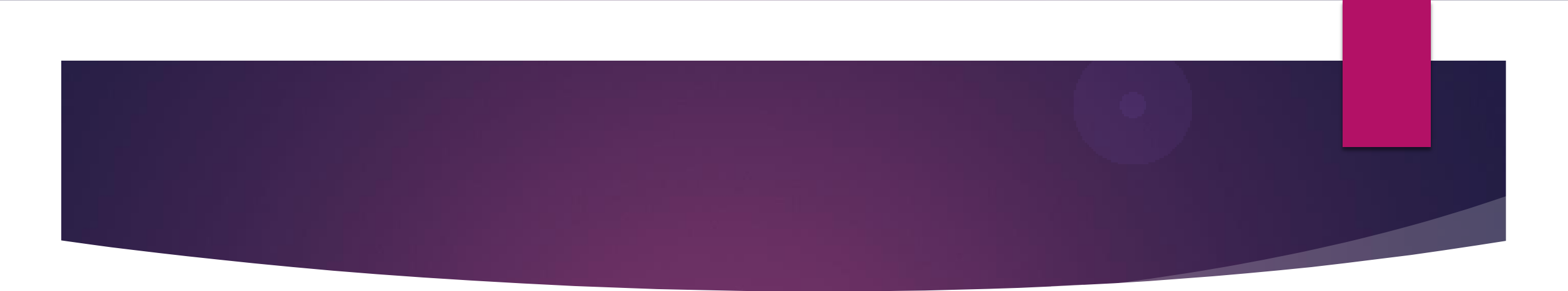
▶ LIMITATIONS:

1. passive surveillance

2. the large numbers of patients being vaccinated and the background rate of neurological conditions in a population

3. some cases of neurological conditions will occur within the post-vaccination window by chance alone

▶ To date, there has not been a signal suggesting higher rates of neurological disease associated with the COVID-19 vaccines

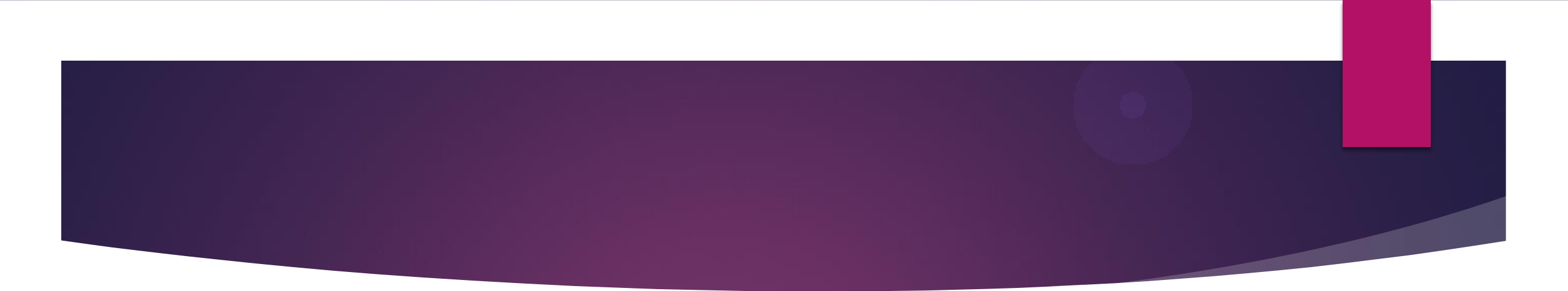
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- ▶ No neurological condition is an absolute contraindication to COVID-19 vaccination
 - ▶ there are special considerations around COVID-19 vaccines for patients who take immunosuppressive medications
 1. At increased risk for severe COVID-19
 2. Immunosuppressive medications may attenuate immune responses to vaccine antigens

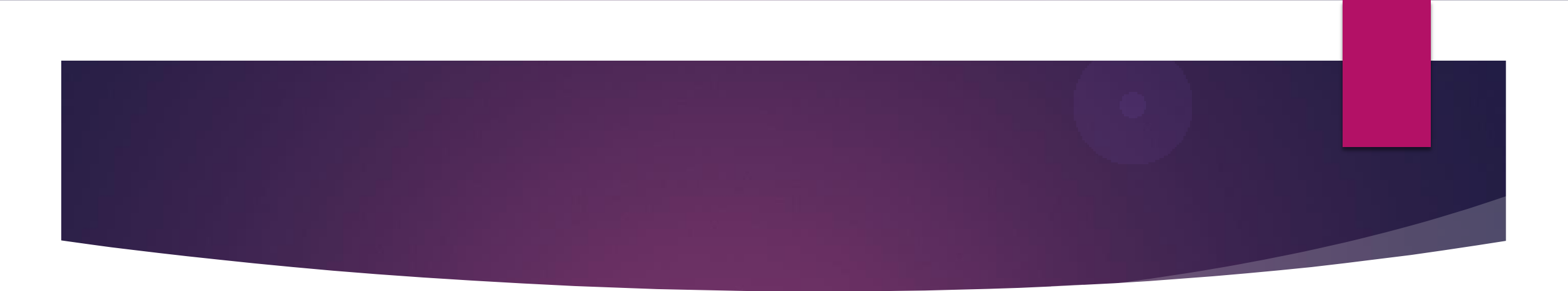
Covid-19 vaccine induced thrombosis

- ▶ Thromboses in the cerebral and splanchnic veins among patients vaccinated in the preceding 4 weeks were described in 17 patients out of 7.98 million recipients of the Johnson & Johnson vaccine (with 3 fatalities related to cerebral vein thrombosis) and 169 cases of cerebral vein thrombosis among 35 million AstraZeneca vaccine recipients
- ▶ autoimmune vaccine response: anti PF4 (platelet factor 4)
- ▶ unusual thrombotic complications with thrombocytopenia
- ▶ Unlike the related heparin-induced thrombotic thrombocytopenia, with an estimated incidence of <1:1000 patients treated with heparin, and a mortality rate of 25%, vaccine-induced immune thrombotic thrombocytopenia has been reported in 1:150 000 ChAdOx1 recipients and 1:470 000 Ad26.COV.2 recipients, with a reported mortality rate of 20% to 30%.

Diagnostic evaluation of CVT and VITT

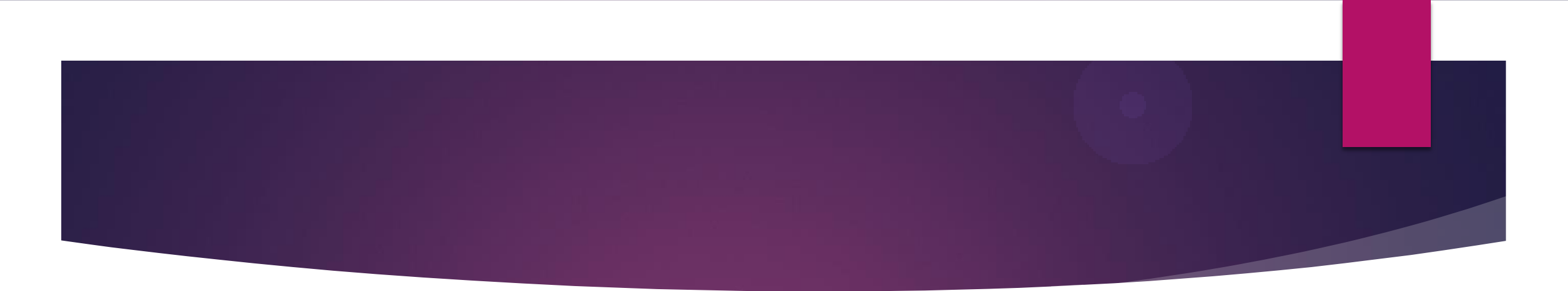
- ▶ A high index of suspicion is important in the detection of CVT with VITT
- ▶ patients who present within 4 weeks of adenovirus-mediated vaccination
- ▶ Patients with new severe headache, subacute encephalopathy, visual loss, seizure, or focal neurological deficit

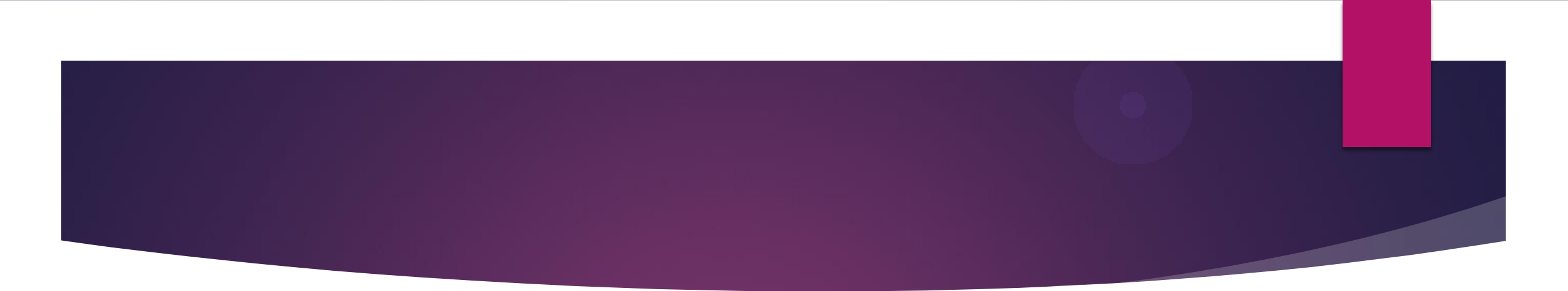
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- ▶ a complete blood count and head computed tomography with venography with or without angiography or magnetic resonance imaging with a venogram is recommended
 - ▶ If either the platelet count is $<150\,000/\mu\text{L}$ or the neuroimaging is suggestive of CVT, the patient will be tested for anti-PF4, preferably an anti-PF4 ELISA
 - ▶ Patients with thrombocytopenia should be verified for platelet clumping and recent heparin exposure as alternative mechanisms to explain the low platelets

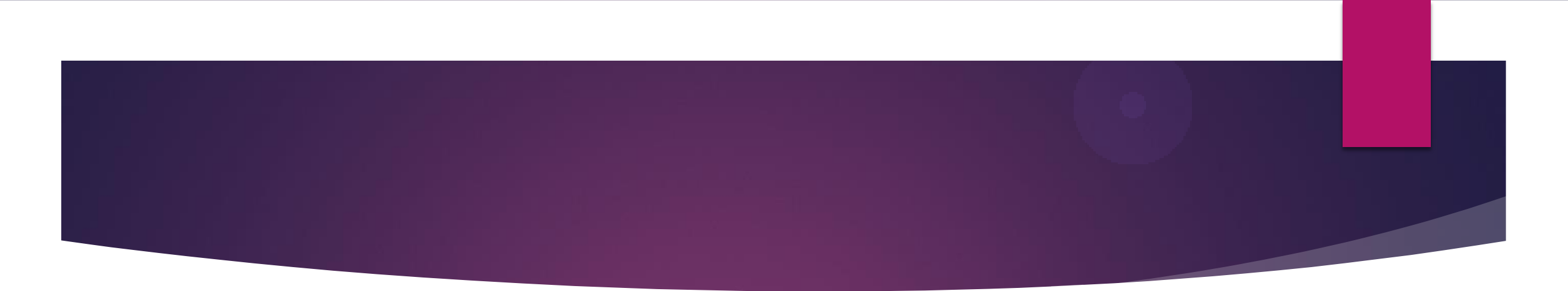
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- ▶ American Heart Association/American Stroke Association recommend testing for SARS-CoV-2 by nasopharyngeal polymerase chain reaction, as present vaccines are not fully protective against viral infection, and as COVID-19 has been associated with a low but significant risk of CVT
 - ▶ Other causes and risk factors of CVT ought to be considered

Treatment

- ▶ IVIg (intravenous immunoglobulin) 1g/kg daily for 2 days
- ▶ High-dose corticosteroids, plasma exchange, and fibrinogen substitution may be considered for severe thrombocytopenia
- ▶ Although there is no evidence that administering heparin for CVT related to VITT is harmful, **nonheparin-based intravenous anticoagulants** (argatroban, bivalirudin, fondaparinux) are considered due to the presence of anti-PF4 antibodies and overlapping mechanisms with HIT

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- ▶ **Oral anticoagulants** (rivaroxaban, apixaban, dabigatran) may be considered after clinical stabilization
 - ▶ Anticoagulation with a direct oral anticoagulant or with a vitamin K antagonist should continue for 3 to 6 months or until radiographic resolution of the CVT
 - ▶ The American Heart Association/American Stroke Association guidelines recommend anticoagulation be initiated or continued in the presence of hemorrhagic venous congestion , although this remains debated

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- ▶ Hemicraniectomy or hematoma evacuation to prevent fatal herniation : in patient with edema and large hematoma
 - ▶ Alternatively, endovascular thrombectomy
 - ▶ Platelet transfusions are **not recommended** for thrombocytopenia in VITT, unless a life-threatening hemorrhage is present

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- ▶ In patients who are at higher risk for developing VTE (eg, family history, hypercoagulable state, oral contraceptives, prior VTE), it is not known whether they are at risk of developing VITT. However, when alternative vaccines may be available, a preferential strategy to offer these patients mRNA vaccines may be advised
 - ▶ Due to the relatively low risk of severe coronavirus disease 2019 (COVID-19) in young women (<50 years), it is reasonable to recommend an alternative vaccine if one is available

THANK YOU FOR
YOUR ATTENTION

