Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

(eg, if patients are planning pregnancy) and health (eg, if patients have cardiovascular and hepatometabolic comorbidities). For example, whereas prophylactic treatment could be prescribed in patients with episodic migraine and frequent attacks, acute treatments might be beneficial for patients with a low frequency of attacks. Given the wide variability of anti-CGRP and anti-CGRP receptor drugs that are now available, with different half-lives, the gepants could almost be considered to form a continuum between acute and prophylactic migraine treatment. This concept would be a departure from the distinction between acute and prophylactic treatment of migraine, and might help to address the fact that regular overuse of acutely acting drugs can induce medication-overuse headache.[17] If future studies confirm that gepants can be used in this way, the availability of more drugs that meet individual needs will provide a substantial improvement for migraine patients.

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1 Stovner LJ, Nichols E, Steiner TJ, et al. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018; **17:** 954–76.
2 Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology* 2007; **68:** 343–49.
3 Edvinsson L, Haanes KA, Warfvinge K, Krause DN. CGRP as the target of new migraine therapies – successful translation from bench to clinic. *Nat Rev Neurol* 2018; **14:** 338–50.
4 Silberstein SD. Emerging target-based paradigms to prevent and treat migraine. *Clin Pharmacol Ther* 2013; **93:** 78–85.
5 Goadsby PJ, Dodick DW, Ailani J, et al. Safety, tolerability, and efficacy of orally administered atogepant for the prevention of episodic migraine in adults: a double-blind, randomised phase 2b/3 trial. *Lancet Neurol* 2020; **19:** 727–37.
6 Negro A, Martelletti P. Gepants for the treatment of migraine. *Expert Opin Investig Drugs* 2019; **28:** 555–67.
7 Biohaven Pharmaceuticals. Rimegepant (Nurtec™ ODT): US prescribing information. 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212728s000lbl.pdf (accessed July 3, 2020).
8 Allergan USA. Ubrogepant (Ubrelvy™): US prescribing information. 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211765s000lbl.pdf (accessed July 3, 2020).
9 Rubio-Beltran E, Chan KY, Danser AJ, MaassenVanDenBrink A, Edvinsson L. Characterisation of the calcitonin gene-related peptide receptor antagonists ubrogepant and atogepant in human isolated coronary, cerebral and middle meningeal arteries. *Cephalalgia* 2020; **40:** 357–66.
10 Kielbasa W, Helton DL. A new era for migraine: pharmacokinetic and pharmacodynamic insights into monoclonal antibodies with a focus on galcanezumab, an anti-CGRP antibody. *Cephalalgia* 2019; **39:** 1284–97.
11 Ankrom W, Xu JL, Vallee MH, et al. Atogepant has no clinically relevant effects on the pharmacokinetics of an ethinyl estradiol/levonorgestrel oral contraceptive in healthy female participants. *J Clin Pharmacol* 2020; published online April 16. DOI:10.1002/jcph.1610.
12 Amgen Inc. Erenumab (Aimovig™): US prescribing information. 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761077s000lbl.pdf (accessed July 2, 2020).
13 Lundbeck Seattle BioPharmaceuticals, Inc. Eptinezumab (Vyepti™): US prescribing information. 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761119s000lbl.pdf (accessed July 2, 2020).
14 Teva Pharmaceuticals USA, Inc. Fremanezumab (Ajovy™): US prescribing information. 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761089s000lbl.pdf (accessed July 2, 2020).
15 Eli Lilly and Company. Galcanezumab (Emgality™): US prescribing information. 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761063s000lbl.pdf (accessed July 3, 2020).
16 DrugBank. Rimegepant (Accession number: DB12457). Updated on 2020 June 12. https://www.drugbank.ca/drugs/DB12457 (accessed July 3, 2020).
17 Kristoffersen ES, Lundqvist C. Medication-overuse headache: epidemiology, diagnosis and treatment. *Ther Adv Drug Saf* 2014; **5:** 87–99.

COVID-19 related stroke in young individuals

See **Rapid Review** page 767

Evidence is mounting on the diverse neurological presentations associated with COVID-19. In a Rapid Review in *The Lancet Neurology,* Mark Ellul and colleagues[1] nicely cover these findings, but we would like to emphasise the risk of associated stroke. As described in this Rapid Review, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be more likely to cause thrombotic vascular events, including stroke, than other coronavirus and seasonal infectious diseases. In fact, a 7·6-fold increase in the odds of stroke with COVID-19 compared with influenza was recently reported.[2] The reported incidence of cerebrovascular disease in patients testing positive for SARS-CoV-2 ranges from 1% to 6%, potentially equating to large numbers of individuals as the pandemic progresses in some countries.[1,3]

The proposed mechanisms for these cerebrovascular events include a hypercoagulable state from systemic inflammation and cytokine storm;[1] postinfectious immune-mediated responses;[1] and direct viral-induced endotheliitis or endotheliopathy, potentially leading to angiopathic thrombosis, with viral particles having been isolated from the endothelium of various tissue, including brain tissue.[4,5] Multiple regions with high COVID-19 prevalence have reported stable or increased incidence of large vessel stroke and increased incidence of cryptogenic stroke (patients with no found typical cause of stroke), despite observing a decrease in mild

stroke that is possibly secondary to quarantine and self-isolation.[6] This quarantine effect is supported by a nationwide analysis in the USA of automated stroke imaging processing software showing decreased imaging evaluation for stroke during the pandemic.[7] Our group observed that five patients younger than 50 years who tested positive for SARS-CoV-2, some with no vascular risk factors, were admitted with large vessel stroke to our hospitals during a 2-week period (March 23 to April 7, 2020) during the height of the pandemic in New York City (NY, USA).[8] This was a 7-fold increase in the rate of large vessel stroke in young people compared with the previous year, and the patients had laboratory findings that suggested a hypercoagulable state, leading to the postulation that stroke was probably related to the presence of SARS-CoV-2 in these young patients.[9]

Since then, this observation of COVID-19 related stroke in young patients has been supported by additional data from other centres worldwide. The mean patient age in several thrombectomy case series of COVID-19 (mean age of 52·8 years in a series from New York City [NY, USA],[10] mean age of 59·5 years in a series from Paris [France],[11] and mean age of 59·5 years in a combined series from New York City and Philadelphia [PA, USA][12]) is younger than the typical population having this procedure. Furthermore, in patients presenting with large vessel stroke during the pandemic, data from the Mount Sinai Health System in New York City confirm that patients who tested positive for SARS-CoV-2 were significantly younger, with a mean age of 59 years (SD 13), than patients who tested negative for SARS-CoV-2, who had a mean age of 74 years (SD 17),[13] mirroring the findings of the Paris group.[11] Patients with COVID-19 who had imaging confirmed stroke and were admitted to another large New York City medical centre were again found to be younger, with a mean age of 63 years (SD 17), than a control group of patients with stroke who tested negative for SARS-CoV-2 and had a mean age of 70 years (SD 18).[3] A case-control analysis of acute stroke protocol imaging from late March to early April, 2020, across a large New York City health system showed that, after adjusting for age, sex, and vascular risk factors, SAS-CoV-2 positivity was independently associated with stroke.

Many reports have documented an increased thrombosis risk early in COVID-19 and coagulation abnormalities in D-dimer and fibrinogen can be found in patients with mild symptoms. There are many reports of early COVID-19 presenting with thrombotic events, which has led to the consensus to start anticoagulation therapy early in the COVID-19 disease course before any thrombotic event. There are reports in the literature specifically addressing macrothrombosis in the internal carotid artery in patients with mild respiratory symptoms of COVID-19[14,15] and stroke as a presenting symptom of the disease.[12] A multicentre series of 26 patients with COVID-19 and either ischaemic or haemorrhagic events reported that 27% were younger than 50 years.[16] Additionally, the report stated that two of 15 patients with large vessel stroke were younger than 50 years and without previous stroke risk factors. In this study, consistent with other case series, patients with COVID-19 fare worse in terms of clinical outcomes than patients with stroke who do not have COVID-19.[6,12] This is probably related, in part, to the COVID-19 disease process.

In conclusion, data supporting an association between COVID-19 and stroke in young populations without typical vascular risk factors, at times with only mild respiratory symptoms, are increasing. Future prospective registries to study this association further, as well as studies of anticoagulation to prevent these potentially life devastating events, are underway.[1] We believe that, in otherwise healthy, young patients who present with stroke during the pandemic, the diagnosis of COVID-19 should be thoroughly investigated. Conversely, in patients with mild COVID-19 respiratory symptoms, a low threshold for investigation for stroke should be maintained if they present with new neurological symptoms.

We declare no competing interests.

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1 Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19. *Lancet Neurol* 2020; **19:** 767–83.
2 Merkler AE, Parikh NS, Mir S, et al. Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) *vs* patients with influenza. *JAMA Neurol* 2020; published online July 2. https://doi.org/10.1001/jamaneurol.2020.2730.
3 Yaghi S, Ishida K, Torres J, et al. SARS-CoV-2 and stroke in a New York healthcare system. *Stroke* 2020; **51:** 2002–11.
4 Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020; **395:** 1417–18.
5 Paniz-Mondolfi A, Bryce C, Grimes Z, et al. Central nervous system involvement by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). *J Med Virol* 2020; **92:** 699–702.
6 Siegler JE, Heslin ME, Thau L, Smith A, Jovin TG. Falling stroke rates during COVID-19 pandemic at a Comprehensive Stroke Center: cover title: falling stroke rates during COVID-19. *J Stroke Cerebrovasc Dis* 2020; **29:** 104953.
7 Kansagra AP, Goyal MS, Hamilton S, Albers GW. Collateral effect of COVID-19 on stroke evaluation in the United States. *N Engl J Med* 2020; **383:** 400–01.

8 Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. *N Engl J Med* 2020; **382:** e60.

9 Belani P, Schefflein J, Kihira S, et al. COVID-19 is an independent risk factor for acute ischemic stroke. *AJNR Am J Neuroradiol* 2020; published online June 25. https://doi.org/10.3174/ajnr.A6650.

10 Wang A, Mandigo GK, Yim PD, Meyers PM, Lavine SD. Stroke and mechanical thrombectomy in patients with COVID-19: technical observations and patient characteristics. *J Neurointerv Surg* 2020; **12:** 648–53.

11 Escalard S, Maïer B, Redjem H, et al. Treatment of acute ischemic stroke due to large vessel occlusion with COVID-19: experience from Paris. *Stroke* 2020; **51:** 2540–43.

12 Sweid A, Hammoud B, Bekelis K, et al. Cerebral ischemic and hemorrhagic complications of coronavirus disease 2019. *Int J Stroke* 2020; published online June 26. https://doi.org/10.1177/1747493020937189.

13 Majidi SFJ, Fifi JT, Ladner TR,et al. Emergent large vessel occlusion stroke during New York City's COVID-19 outbreak: clinical characteristics and paraclinical findings. *Stroke* 2020; published online July 31. https://doi.org/10.1161/STROKEAHA.120.030397.

14 Fara MG, Stein LK, Skliut M, Morgello S, Fifi JT, Dhamoon MS. Macrothrombosis and stroke in patients with mild Covid-19 infection. *J Thromb Haemost* 2020; published online May 28. https://doi.org/10.111/jth.14938.

15 Mohamud AY, Griffith B, Rehman M, et al. Intraluminal carotid artery thrombus in COVID-19: another danger of cytokine storm? *AJNR Am J Neuroradiol* 2020; published online July 2. https://doi.org/10.3174/ajnr.A6674.

16 Taylor BES, Khandelwal P, Rallo MS, et al. Outcomes and spectrum of major neurovascular events among COVID-19 patients: a 3-center experience. *Neurosurg Open* 2020; **1:** okaa008.

Thank you to our peer reviewers in 2019

The COVID-19 pandemic has led to unprecedented challenges. In particular, the impact of COVID-19 on neurological services and patients has been immense, as highlighted in a recent Editorial.[1] Despite the heightened burden felt by neurologists, the dedication of our authors and reviewers is not waning. Submissions to *The Lancet Neurology* between Jan 1 and June 14, 2020, increased by around 70% compared with the same period last year. Unabated expert advice from our clinical and statistical reviewers from around the world is ensuring the continued publication of the highest quality research and reviews for our readers.

The journal continues to strive towards the goal of the *Lancet* group of disseminating *the best science for better lives*. Our achievement is reflected by the continued placement of *The Lancet Neurology* as the leading clinical neurology journal, according to the 2019 Journal Citation Report. The names of everyone who reviewed papers for the journal throughout 2019 are listed in the appendix; those who reviewed five papers, or more, are marked with an asterisk. We extend our warmest gratitude to all these reviewers.

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1 The neurological impact of COVID-19. *Lancet Neurol* 2020; **19:** 471.

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