1 Understanding the Mechanisms and Dynamics of Cerebrovascular Events

"What does the term CVA "really" stand for? . . . Confused Vascular Assessment!"

Strokology 101

The time-honored use of a nonspecific term, CVA (cerebrovascular accident), by many of our colleagues underscores the need for patients suspected of having a stroke or a transient ischemic attack (TIA) to be seen by vascular neurologists to determine why these events are happening. This, in turn, will yield answers to the questions of how to treat and prevent stroke.

Our ability to diagnose the type of stroke (ischemic or hemorrhagic) relies solely on imaging, and patients with new symptoms suggestive of stroke should be granted emergency access to computed tomography (CT) and magnetic resonance imaging (MRI), depending on the clinical situation and resources available. Often both of these tests are done in sequence during their hospital stay or during observation/ outpatient diagnostic workup. Patients with stroke or TIA should also undergo several other tests. The reason is not only to see the parenchymal damage, if any, and tissue at risk of infarction but also to determine the pathogenic mechanism of the event because treatment options vary greatly (Figure 1.1). The focus of this book is the assessment of a stroke patient, linking the neurological findings with the evaluation of vessels, and, in turn, integrating these findings with parenchymal and perfusion imaging. This book will further explain how to obtain this information at the bedside, and how it can change patient management.

Lessons learned from cardiology and vascular medicine are invaluable for vascular neurology; however, these can only be applied to the brain vasculature to a certain extent. Unlike coronary vessels, the intracranial arteries are paper thin and cannot withstand too much mechanical or polypharmacological manipulations. They respond by vasodilation to a drop in blood pressure or volume in an attempt to maintain cerebral blood flow (CBF) as they also assure continuous diastolic flow, a feature of the low-resistance parenchymatous organs. When a patient develops stroke symptoms, this indicates that the blood flow to a specific area of the brain has dropped below the level that normally sustains neuronal function. Electrical function of neurons becomes affected at CBF falling below approximately 20 mL/100 g of brain tissue/min (Figure 1.2)[1–4]. Flattening of the electroencephalogram was seen in human subjects during endarterectomy when CBF was ≤19 mL/min [2]. The concept of ischemic penumbra emerged from studies correlating the neuronal electrical activity and CBF reduction thresholds [5]. It became clear that at certain CBF levels the neurons can remain structurally intact but functionally inactive. Without reperfusion treatment a further fall in CBF occurs, and the ischemic cascade may progress fast leading to influx of calcium and brain death. Further experimental research has focused on tissue viability thresholds [6, 7].

The neurological symptom onset has been long equated with the timing of a thromboembolic occlusion. In reality, this is not correct [8]. Symptom onset is the time of the collateral or residual flow failure. This failure can occur shortly after an acute occlusion or it can develop over time. Furthermore, the time lapse between symptom onset and initiation of reperfusion therapy was further treated as a substitute for recoverability. In general, this time dependency is applicable to large groups of patients in clinical trials: patients' chances to recover completely double

Neurovascular Examination: The Rapid Evaluation of Stroke Patients Using Ultrasound Waveform Interpretation, First Edition.
Andrei V. Alexandrov.

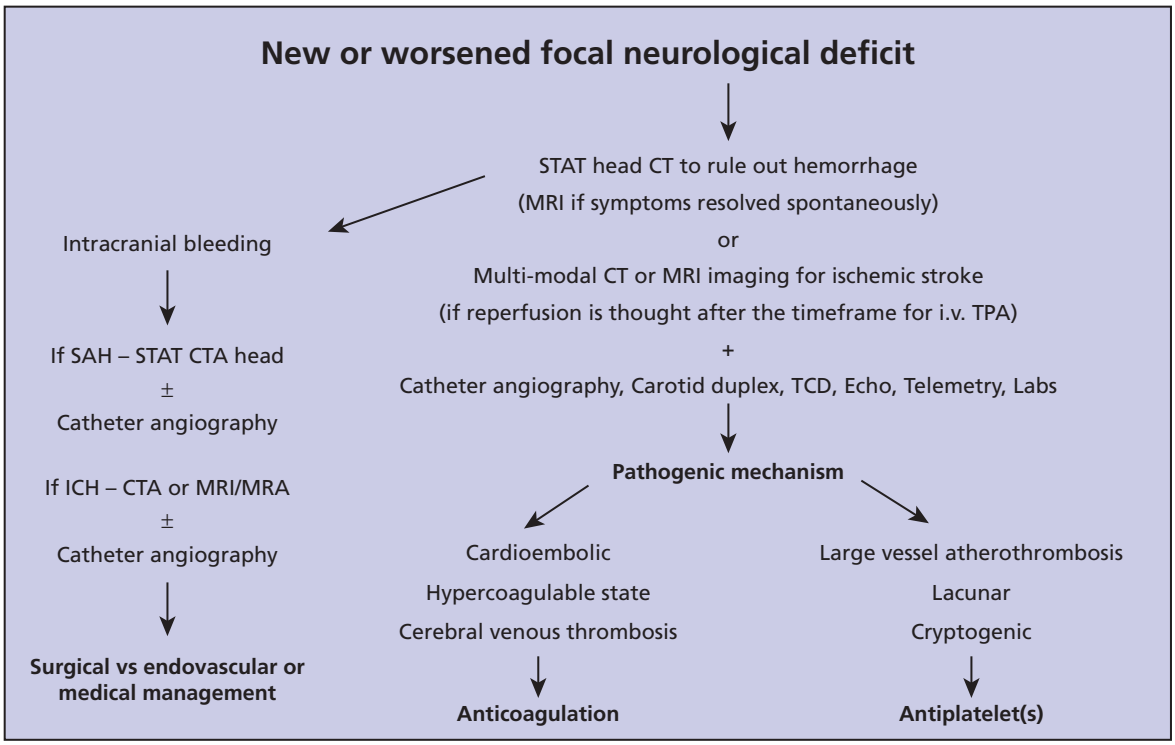

Figure 1.1 An overview of common sequences in the diagnostic workup and treatment options according to a specific pathogenic mechanism.

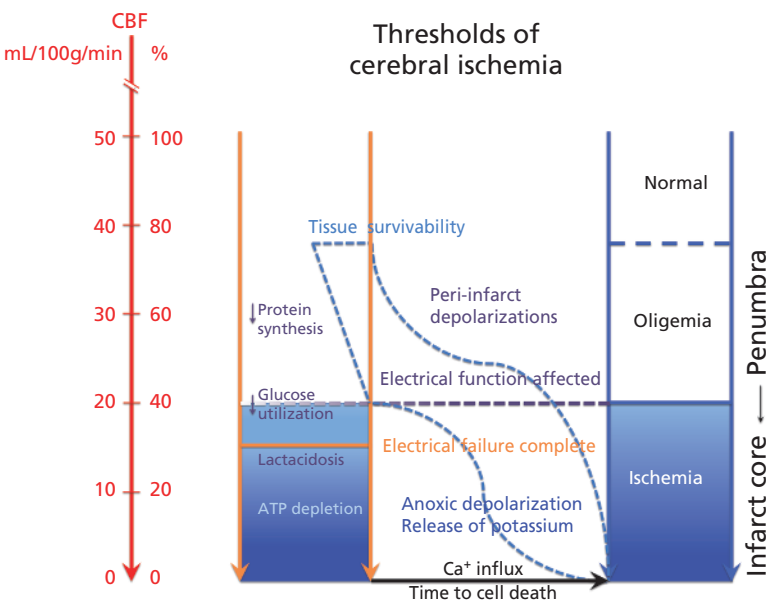

Figure 1.2 Neuronal dysfunction and levels of cerebral blood flow impairment. Two important concepts related to cerebral ischemia are schematically presented here. The decreasing levels of cerebral blood flow (CBF) due to occlusion or hypoperfusion can induce an oligemic state, subsequent electric cell dysfunction and failure, finally leading to cell death at very low CBF levels [1]. These thresholds of ischemia are hypothetically combined with the time to cell death and recoverability of tissue (dotted S-shape lines invoked from observations in reference [6]. The concepts arise from landmark studies of Austrup *et al*. [1] and Jones *et al*. [6].

Table 1.1 Main pathogenic types of ischemic stroke, or TOAST classification

Large-vessel atheromatous
≥50% stenosis or occlusion with pre-existing atheromatous plaque in an artery feeding the territory of cerebral ischemia
Cardioembolic
Identification of a known risk factor or source for cerebral embolization from the heart, i.e. atrial fibrillation, intracardiac thrombus, etc.
Lacunar
A typical lesion affecting perforating vessels in subcortical areas or pons/ brainstem
Other
Arterial dissection, paradoxical embolism, hypercoagulable state, vasculitis, etc.
Cryptogenic
No pathogenic mechanism was identified upon adequate workup or two or more etiologies were found, i.e. cortical lesion unilateral to a severe carotid stenosis in a patient with known atrial fibrillation

Data from Adams *et al*. [10].

if fibrinolytic treatment with intravenous tissue plasminogen activator (tPA) starts at 2 hours from symptom onset, and these chances diminish rapidly over time [9]. The decision making for systemic tPA is fairly straight forward and within the first few hours it applies to the majority of patients regardless of the cause of cerebral ischemia. However, a closer look at an individual patient reveals that ischemic stroke is remarkably heterogeneous (Table 1.1). We will examine in turn different stroke types and what tests are suitable to ascertain these mechanisms, commonly referred to as the TOAST classification of stroke pathogenic mechanisms [10]. Stroke remains an extremely time-sensitive process and if therapeutic attempts to restore blood flow are not done in time, most patients will loose their battles with obstructive arterial lesions. Traditional time frames for reperfusion, however, have nothing to do with the severity of ischemia and its variable mechanisms. The question is what else besides systemic tPA can you offer as treatment? This depends on why stroke is happening, and this in turn leads to the choice of imaging modalities. Even the use of systemic thrombolytics could be better gauged by rapid multimodal imaging [8, 11]. The stress here must be on "rapid," that is within minutes not half an hour to an hour to acquire imaging sequences.

Our ability to understand stroke by imaging the brain with X rays and MRI is constantly evolving, and the majority of current and future stroke specialists spend a great deal of time learning how to base their decisions on multimodal CT or MRI imaging. They also become familiar with carotid duplex ultrasound, at least to order it as a screening test for carotid pathology of the neck. Far fewer take the time and effort to master ultrasound tests themselves, particularly transcranial Doppler (TCD). In my practice, I use all available tests when appropriate or feasible, as they provide complimentary information. Furthermore, I find reasons to treat (not excuses to withhold treatment), an approach opposite to minimalistic or nihilistic views as to what we can offer stroke patients. The latter results in under-utilizing imaging and vascular assessment, often resulting in patient receiving treatment that is not based on a pathogenic mechanism specific to their event.

The following case scenarios will show how we approach typical patient problems, what key questions we ask to begin patient management, and the complimentary use of diverse ultrasound tests for the neurological examination and the standard of care CT or MRI scanning. A brief case presentation is followed by questions and answers that illustrate the thought process and supportive facts. So, as we say at the beginning of stroke rotation, welcome to the (neurovascular) plumbing service!

Case study 1.1

A 62-year-old man, current smoker with otherwise unremarkable past medical history and no primary care doctor, is seen for an episode of weakness in the left arm that lasted for 10 min and resolved spontaneously. The National Institutes of Health Stroke Scale (NIHSS) score (Appendix 1.1) is 0. A noncontrast head CT done within 20 min of arrival to the hospital is normal. His BP is 153/70 mmHg, pulse regular. $ABCD^2$ score (Tables 1.2 and 1.3) = 3 points [12].

Table 1.2 $ABCD^2$ score

Factor	Score
Age: ≥60 years	1
Blood pressure: ≥140/90 mmHg	1
Clinical features:	
Unilateral weakness	2
Speech impairment without weakness	1
Duration:	
≥60 min	2
10–59 min	1
Diabetes: Yes	1

Table 1.3 Stroke risk within 2 days after TIA as predicted by the total $ABCD^2$ score

Risk	$ABCD^2$ score (%)
Low	0–3 (1.0)
Medium	4–5 (4.1)
High	6–7 (8.1)

The $ABCD^2$ score is predictive of the risk of stroke after TIA and is being used to stratify patients according to this risk [12]. However, it bears no information as to pathogenic mechanism of the TIA, and it has certain other limitations. It should not be used instead of multimodal imaging such as MRI because our definition of the TIA is based on imaging of the brain parenchyma and noncontrast CT scan is not sensitive to stroke for several hours after symptom onset, particularly with spontaneous early symptom resolution.

Box 1.1 Current definition of TIA

Transient ischemic attack (TIA): a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.

Disclaimer: The definition of TIA proposed above is not constrained by limitations of DWI or any other imaging modality. The definition is tissue based, similar to the diagnoses of cancer and myocardial infarction. However, unlike the situation with cancer but similar to that with myocardial infarction, the histological diagnosis of brain infarction typically must be inferred from clinical, laboratory, and imaging data. The most appropriate clinical, laboratory, and imaging modalities to support the diagnosis of TIA versus stroke will evolve over time as diagnostic techniques advance. Specific criteria for the diagnosis of brain infarction also will evolve, just as the laboratory criteria for the diagnosis of myocardial infarction evolved as new serum markers were identified. However, the definition of the entity will not vary; ischemic stroke requires infarction, whereas TIA is defined by symptomatic ischemia with no evidence of infarction [13].

1. What is the diagnosis?
Likely a TIA (definition provided in Box 1.1[13]).
2. What is the highest yield test that should be done next?
Multimodal head MRI with head and neck magnetic resonance angiography (MRA).
3. When should this test should be done?
As soon as possible, because TIA is a medical emergency and patients with TIA are at risk of developing a stroke. MRI/MRA in combination with the $ABCD^2$ score can identify those at particularly high risk of both stroke (31%) and functional impairment (23%) within 90 days [14]. Furthermore, the diagnosis of TIA versus stroke depends on our evolving imaging ability to visualize brain tissue damage [13], and a noncontrast head CT has a low yield in patients with deficits that lasted just a few minutes as opposed to many hours.
4. What information can MRI/MRA provide?
If the diffusion weighted imaging (DWI) is negative, this would confirm the diagnosis of a TIA (but will

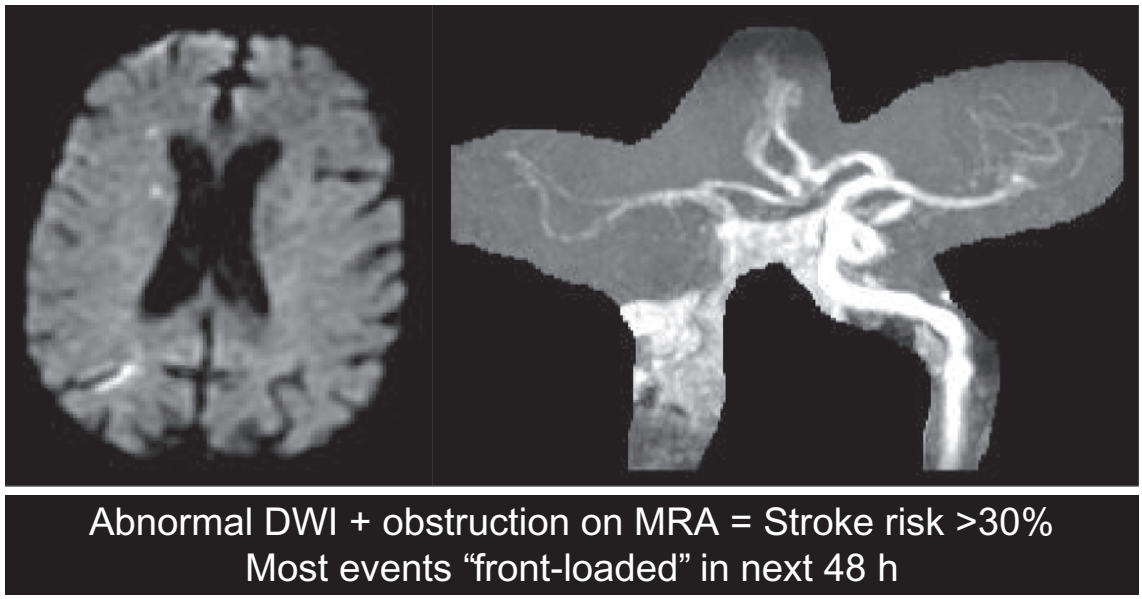

Figure 1.3 Clinical value of MRI/MRA in estimating stroke risk after TIA. Diffusion weighted imaging (DWI) showed a small ischemic lesion in the right hemisphere/watershed distribution between the middle and anterior cerebral arteries; magnetic resonance angiography (MRA) showed an obstruction extending from the proximal right internal carotid artery.

not completely rule out a small stroke or a stroke in the posterior circulation; see further explanation in Box 1.1). If MRA is abnormal, that is it may be showing persisting arterial obstruction, this would point to a high risk of stroke symptom recurrence. Also, brain perfusion sequences on MRI can identify patients with hypoperfusion even if the DWI is negative, and this finding should raise concern for possible neurological deterioration if cerebral hemodynamics is not improved.

If DWI is positive, that is showing a lesion in the appropriate distribution with corresponding changes on the apparent diffusion coefficient (ADC) sequence and the T2 shine-through artifact is ruled out, the patient has an ischemic stroke. Abnormal DWI and abnormal MRA findings identify patients with spontaneously resolved symptoms who are at the highest risk of stroke recurrence that is "front loaded" in the next couple of days (Figure 1.3)[15].

5. What is the impact of MRI/MRA on patient management?

MRI/MRA provide the initial ascertainment of the pathogenic mechanism of the current event for early initiation of an appropriate secondary stroke prevention, and can help determine the need for admission of the patient to the hospital (demonstration of an ischemic stroke despite symptom resolution and the high risk for early recurrence). CT-angiography/ CT-perfusion (CTA/CTP) and neurovascular ultrasound tests should also be considered if patients have contraindications for MRI.

6. What is the likely pathogenic mechanism for this event?

In Caucasian patients of this age group who are smokers, atheromatous stenosis of the proximal internal carotid artery should be ruled out first [16]. Atheromatous disease in the intracranial vessels should, in the first place, be suspected in African Americans, Asians, or Hispanics but also not entirely discounted in Caucasians [16–18]. MRA may show an abnormality in these vessels but it tends to overestimate the degree of the stenosis. An absent vessel segment on MRA may not necessarily be occluded, that is this false-positive finding ("flow gap" on MRA) may occur in the setting of near-occlusion with tenuous residual flow or flow reversal due to

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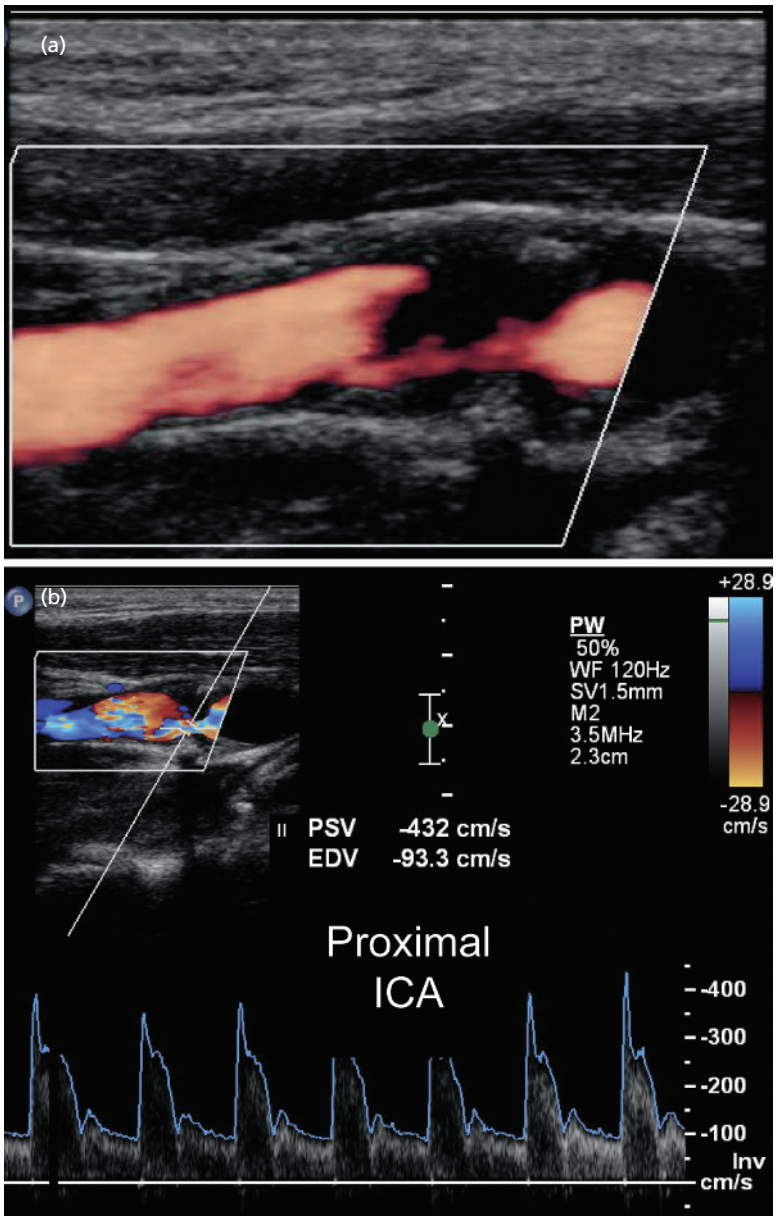

Figure 1.4 Carotid duplex findings with severe ICA atheromatous stenosis. Longitudinal views of the proximal ICA (left side of the image is oriented cephalad) show mostly hypoechoic atherosclerotic plaque and the residual lumen on power mode (**a**) and color flow (**b**). Angle-corrected velocity measurements are shown in (**b**) (PSV, peak systolic velocity; EDV, end diastolic velocity).

collateralization or in the presence of turbulence. This is why ultrasound examination of the precerebral and intracranial vessels should be done whether or not MRA shows a lesion. Looking just at reconstructed MRA images may also lead to false-negative results.

Ultrasound may show an atherosclerotic plaque (Figure 1.4), facilitating the diagnosis of atherosclerosis. This, in turn, will further support initiation of statin and antiplatelet therapy. Alternatively, ultrasound may show a thrombus without pre-existing atheroma (Figure 1.5), and this finding should prompt the search for an embolic source or a hypercoagulable state.

Ultrasound may show the presence of a ≥50% diameter reducing atheromatous stenosis in the vessel feeding the affected side of the brain (Figure 1.4). This finding will help identify patients with a large-vessel atheromatous mechanism of the event

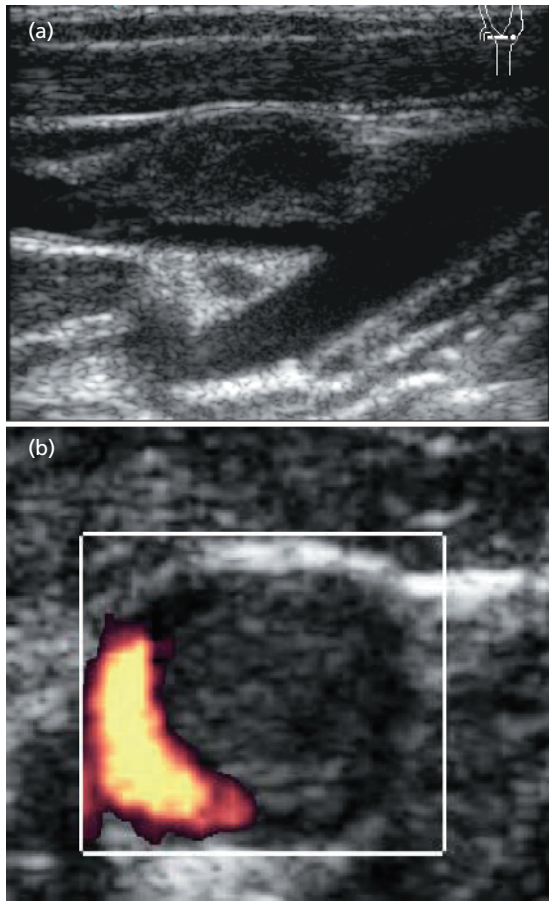

Figure 1.5 Carotid duplex visualization of a thrombus in the proximal ICA without underlying atheromatous stenosis. (**a**) Longitudinal brightness-modulated (B-mode) view of a large thrombus that is attached to the near wall occupying most of the carotid bulb. (**b**) Transverse view of the same thrombus with crescent moon-like appearance of the residual lumen on power Doppler.

(Table 1.1) and raise questions about further angiographic imaging to plan carotid revascularization for secondary stroke prevention. In fact, Figure 1.4 shows a lesion predictive of a ≥70% stenosis, according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[19], and these patients clearly benefit form carotid endarterectomy [19, 20]. Carotid stenting may be considered if surgery is deemed high risk [21, 22].

Spectral waveform assessment of the middle cerebral artery flow velocities (Figure 1.6)[23], emboli detection (Figure 1.7)[24], and vasomotor reactivity assessment (to be shown in subsequent chapters)[25, 26] with TCD can help identify patients who could be at higher risk of stroke recurrence. This information is complimentary to risk stratification or selection for revascularization based on the degree of the stenosis. I deploy these ultrasound tests to understand why TIA or stroke occurred, particularly if a patient was already receiving medical therapy currently deemed best for stroke prevention.

Another mechanism to consider across many patients, and particularly if the event occurred while on an antiplatelet agent, is cardiogenic embolism with conditions like atrial fibrillation that could be paroxysmal. Telemetry during the hospital stay and prolonged Holter-type (event detector) monitoring after discharge are helpful tools to detect atrial fibrillation. Electrocardiogram, if abnormal in our patient, should lend further support to pursue perhaps not only transthoracic (TTE) but also transesophageal echocardiography (TEE). Sonographers should be aware of possible paroxysmal dysrhythmias and should document an abnormal heart rhythm (Figure 1.8) apart from extra-systoli when seen during ultrasound tests – this would further raise suspicion for a cardioembolic mechanism of the event.

Lacunar, or small-vessel mechanism, should be considered next if DWI shows an appropriate small lesion in subcortical areas of white matter tracks and basal ganglia (Figure 1.9). However, despite such a convincing finding, other mechanisms should be considered because a small embolus can produce a subcortical or posterior circulation lesion mimicking lacune. Prognosis of a truly lacunar event is good but it should not preclude the workup for other risk factors that could be modifiable and that may necessitate treatment with more than aspirin and a statin.

Finally, less-common causes, such as an arterial dissection, paradoxical embolism, hypercoagulable state, etc., should be considered if the initial workup is negative for the more common mechanisms. Clues like recent trauma to the head and neck, events shortly after periods of prolonged immobility or trauma to the legs, unexplained weight loss, or

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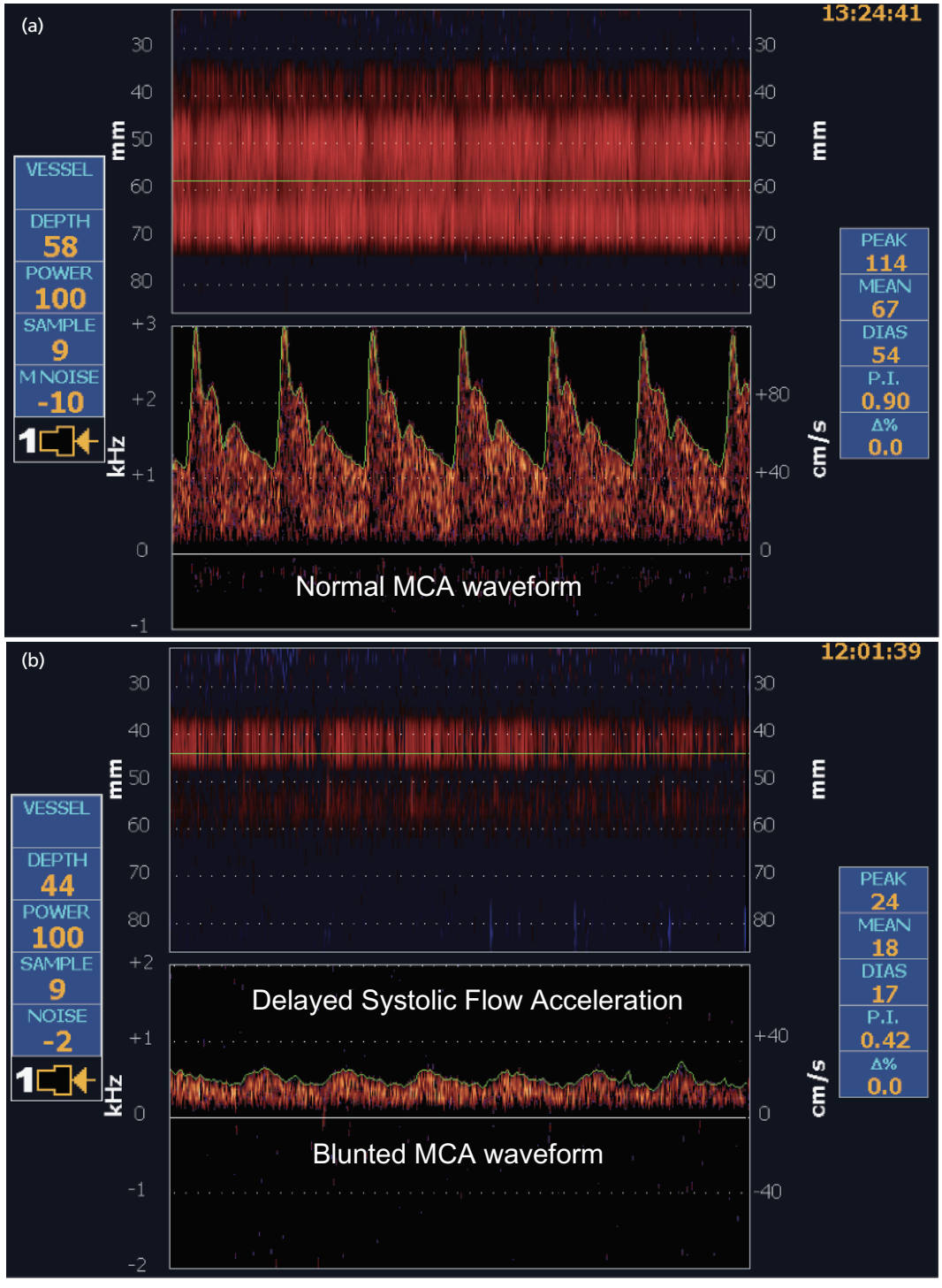

Figure 1.6 Power motion and spectral Doppler appearance of the normal and blunted MCA waveforms on transcranial Doppler. The upper part of (**a**) represents normal MCA appearance on motion display (vertical axis is the depth of insonation from the temporal window on the skull in mm). The lower part of (**a**) shows a typical spectral Doppler waveforms in the MCA with normal proximal ICA patency. (**b**) MCA appearance on motion display and spectral Doppler waveforms with hemodynamically significant ICA obstruction.

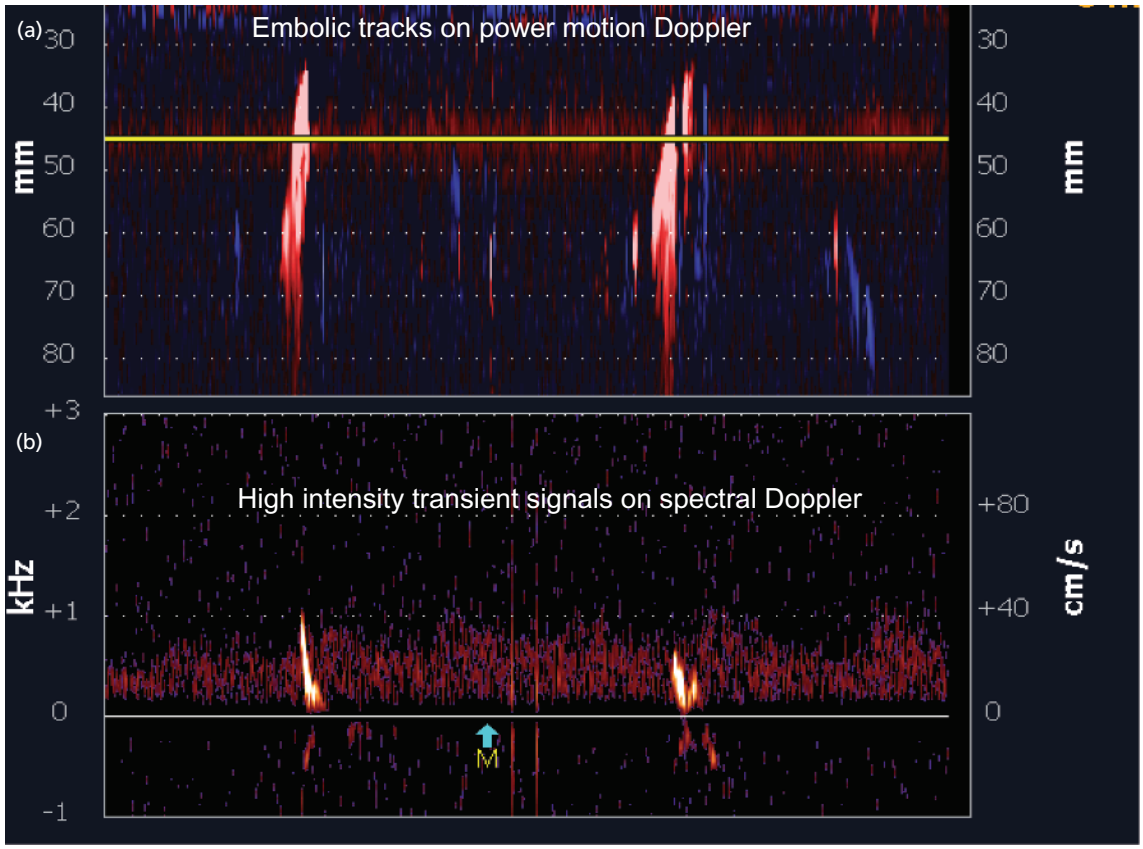

Figure 1.7 Embolic signals on power motion Doppler TCD. (**a**) The power motion display tracks emboli as they travel along cerebral vessels in real time (note the incline of tracks from right to left because the horizontal axis represents time and vertical axis represents the depth of vessel location in mm). (**b**) A spectral Doppler display of emboli at a single depth of insonation (the yellow line across motion display above).

recent history of deep venous thrombosis point to the need to consider such mechanisms. Additional vascular imaging, such as fat-suppression T2 MRI sequence, CTA, catheter angiography, and TCD emboli detection testing with agitated saline [27] (used as an echocontrast that is filtered out by lungs but detectable in the intracranial vessels in the presence of a right-to-left shunt), are helpful in these situations.

Upon completion of the diagnostic workup of our Case 1.1, a severe internal carotid artery (ICA) stenosis was found on carotid duplex corresponding to the 70–99% NASCET diameter reduction stenosis range caused by a heterogeneous plaque with an irregular surface (Figure 1.4). His low-density lipoprotein (LDL) was 182; MRI DWI was negative. This patient had a TIA due to large-vessel atheromatous disease. He was given 325 mg aspirin and 80 mg atorvastatin in the emergency room. During TCD testing, one microembolic signal was seen after receiving aspirin. His case was discussed with the endovascular neurosurgeon and he also received 300 mg clopidogrel load while his carotid revascularization procedure was planned. The decision to add clopidogrel to aspirin prior to revascularization was based on the clinical trial evidence that dual antiplatelet therapy

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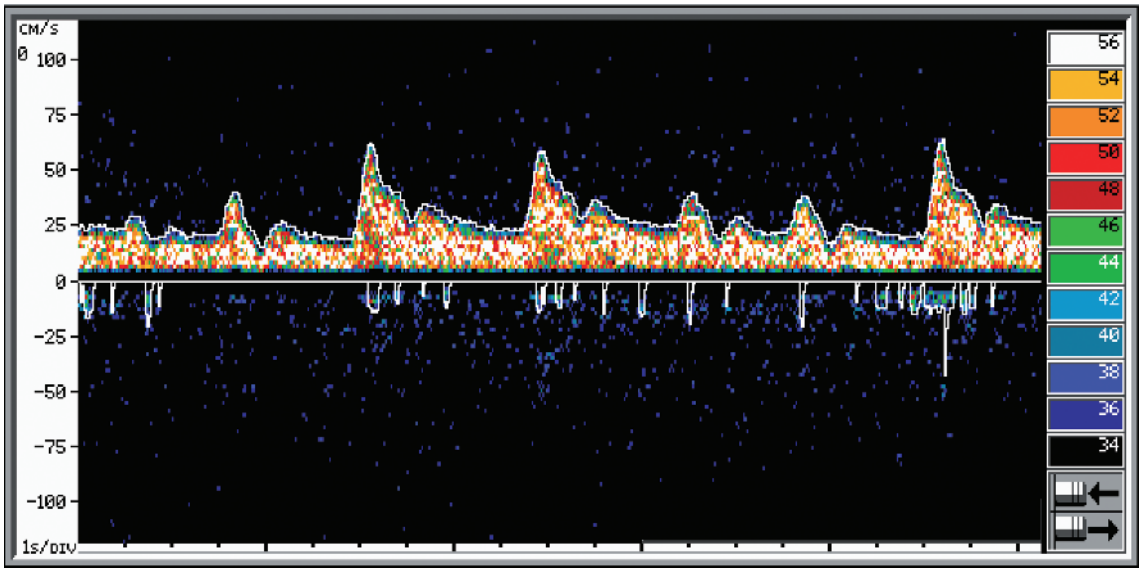

Figure 1.8 Atrial fibrillation appearance on spectral Doppler recording. Irregular-irregular rhythm recording was obtained from the MCA in a patient with acute stroke and paroxysmal atrial fibrillation. Sonographers should store abnormal waveforms like this if seen during diagnostic TCD or carotid duplex tests.

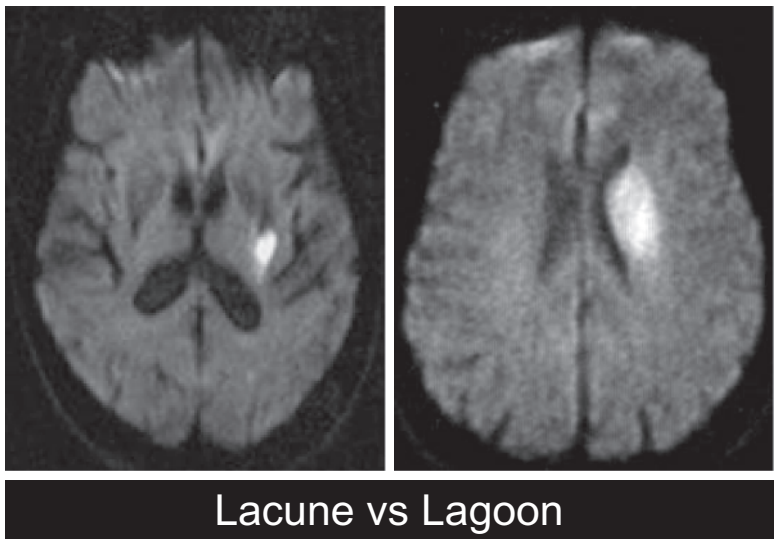

Figure 1.9 Typical lacunar stroke versus a subcortical infarction due to an embolus in the MCA.

reduce artery-to-artery embolization [28, 29], and differences in medical management in the CREST trial between surgical and stenting groups that could have led to higher perioperative myocardial ischemia events after carotid endarterectomy (CEA) on aspirin alone [22]. Carotid endarterectomy was done the next day. After surgery, he continued on clopidogrel and atorvastatin and he was encouraged to quit smoking. Of note, his ankle–brachial index (ABI) was 0.8.

Case study 1.2

A 70-year-old woman with a past medical history of arterial hypertension and coronary artery disease suddenly developed left-sided weakness. She called her daughter who then called 9-1-1 and the patient arrived 2 hours after symptom onset. Upon arrival, she reports that her strength has significantly improved mainly in her left hand. Her total NIHSS score is 2, for mild drift in the left arm and mild inattention to the left side with no gaze preference. Her symptoms continued to improve after CT scan, leaving her with only the drift at 2 hours and 25 minutes from symptom onset. No tissue plasminogen activator was given due to neurological improvement to a nondisabling level of the remaining symptoms. The patient passed the swallow test at bedside and was given 325 mg aspirin. She was then placed with the head of the bed flat and given 500 mL bolus of i.v. fluids. The patient was admitted to the Stroke Unit with neurological checks every hour for the next 6 hours, and every 2 hours thereafter for 24 hours. Her MRI at 4.5 hours from symptom onset showed a small cortical lesion on the DWI (Figure 1.10) that was also dark on the ADC sequence.

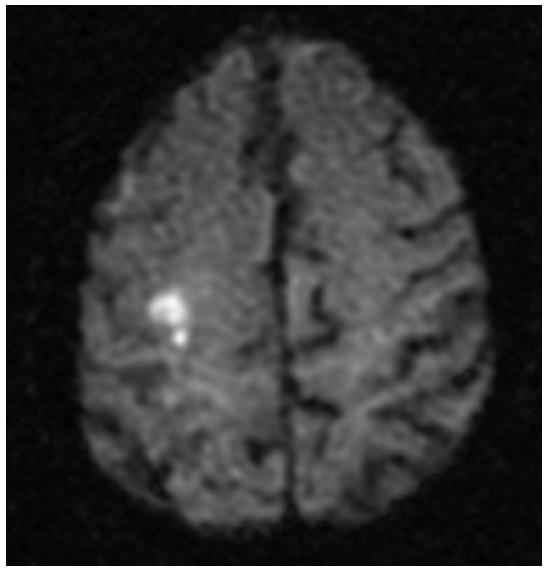

Figure 1.10 Small cortical lesion on DWI.

1. What is the diagnosis?
An acute ischemic stroke.
2. Should this patient have been offered reperfusion therapy?
Yes, if the remaining deficit after CT scan would still have been disabling, because the completeness of the "rapid" resolution of symptoms as a contraindication for intravenous tPA has not been defined or quantified.
3. What is the likely mechanism?
Likely an embolic event, either artery-to-artery or cardioembolic.
4. What is (are) the next test(s) that have the highest yield to identify this mechanism?
Carotid duplex to rule out carotid stenosis, and telemetry (admission ECG did not show atrial fibrillation (AFib)).
5. What are the risks for the patient now?
Neurological deterioration following spontaneous improvement or stroke progression/ recurrence.
6. What is the likelihood of such deterioration?
This clinical phenomenon has been reported in various trials and studies affecting as many as 13 to 37.5% of hyperacute stroke patients presenting within the time window for thrombolysis [30, 31].
7. What are the main predictors of possible deterioration following spontaneous improvement?
Persistence of an arterial occlusion, cardiac decompensation, early ischemic changes on admission CT scan, re-embolization/ re-occlusion, extension of an ischemic territory (stroke in evolution, brain swelling), baseline stroke severity, and elevated serum glucose [32–36].
8. What are the tests and their findings that can identify a patient at risk of stroke progression, recurrence or deterioration?

- MRA, CTA, or catheter-angiography or TCD/ carotid duplex for the presence/ persistence of an occlusion/ high-grade stenosis at the level supplying more brain tissue as compared to the extent of the DWI lesion (remember there may be a mismatch between mild symptoms and a larger area at risk);

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- perfusion deficit on MR greater than the DWI lesion;
- poor cardiac ejection fraction on echocardiography;
- arterial hypotension;
- embolic signals on TCD;
- diminished or exhausted vasomotor reactivity or intracranial arterial blood flow steal on TCD;
- the presence of a thrombus (with or without underlying atheromatous lesion) on carotid duplex or angiography.

The subsequent course and workup of our patient was as follows. Telemetry showed paroxysmal AFib, and repeated neurological examinations showed stable and complete symptom resolution. TCD at 8 hours from symptom onset showed complete spontaneous recanalization of the right M1 and proximal M2 middle cerebral artery (MCA) segments and no microembolic signals. Bed rest and flat head positioning were discontinued the next day. TEE showed a normal ejection fraction and no intracardiac thrombus. No heparin was administered. The patient was offered a direct thrombin inhibitor or warfarin for secondary stroke prevention in the setting of paroxysmal AFib and a small cortical stroke and no evidence of hemorrhagic transformation.

Case study 1.3

A 55-year-old man with a past medical history of diabetes and arterial hypertension noticed right-sided weakness when he woke up at night but chose not to call for help until the morning when he woke up completely flaccid on the right side. He was last seen normal at midnight the previous night, that is 7 hours before arrival to the hospital. Admission CT scan was normal with the Alberta Stroke Program Emergent CTScore (ASPECTS) of 10 points (Figure 1.11)[37]. (Figure 1.12, in contrast, shows an ASPECTS score of 1 where most areas of the middle cerebral artery territory are affected by early ischemic changes.) The NIHSS score was 8 points (pure motor weakness, arm equal to leg). No speech problems or other cortical signs were found.

1. What is the diagnosis?

Likely an acute ischemic stroke.

2. Why likely?

Since there is no intracranial bleeding and no hypoattenuation on head CT (given the time elapsed from last seen normal) to explain the patient's symptoms, there is a chance that it could be a stroke mimic.

3. If attributable to cerebral ischemia, what is the likely mechanism of this event?

Small-vessel or lacunar mechanism is likely in the setting of typical risk factors such as arterial hypertension and diabetes; however, other mechanisms should not be discounted.

4. What is (are) the test(s) that could help ascertain this mechanism or suspect others?

Since the patient presents 7 hours from last seen normal with definitely disabling deficit, emergent CTA of the head and neck or TCD and carotid duplex could be done to rule out an embolus or atherothrombotic lesion potentially amenable to intervention (normal head CT within the time window for a thrombectomy device deployment) even though the clinical examination points to a subcortical lesion. A partially occlusive thrombus in the M1 MCA may initially cause hypoperfusion in the perforator(s) originating from the M1 segment. If vessels are patent, the next test should be MRI, because it would be the most sensitive test to confirm lacunar stroke in the acute setting.

5. If MRI shows a subcortical lesion, should the patient receive the rest of a standard workup including echocardiography, telemetry, etc.?

Yes, the standard workup should be completed because a small embolus can produce a subcortical lesion that could be confused with a lacune. A subcortical lesion affecting several perforating vessels is colloquially called a "lagoon" or "macune" (an example was shown in Figure 1.9, right image), and

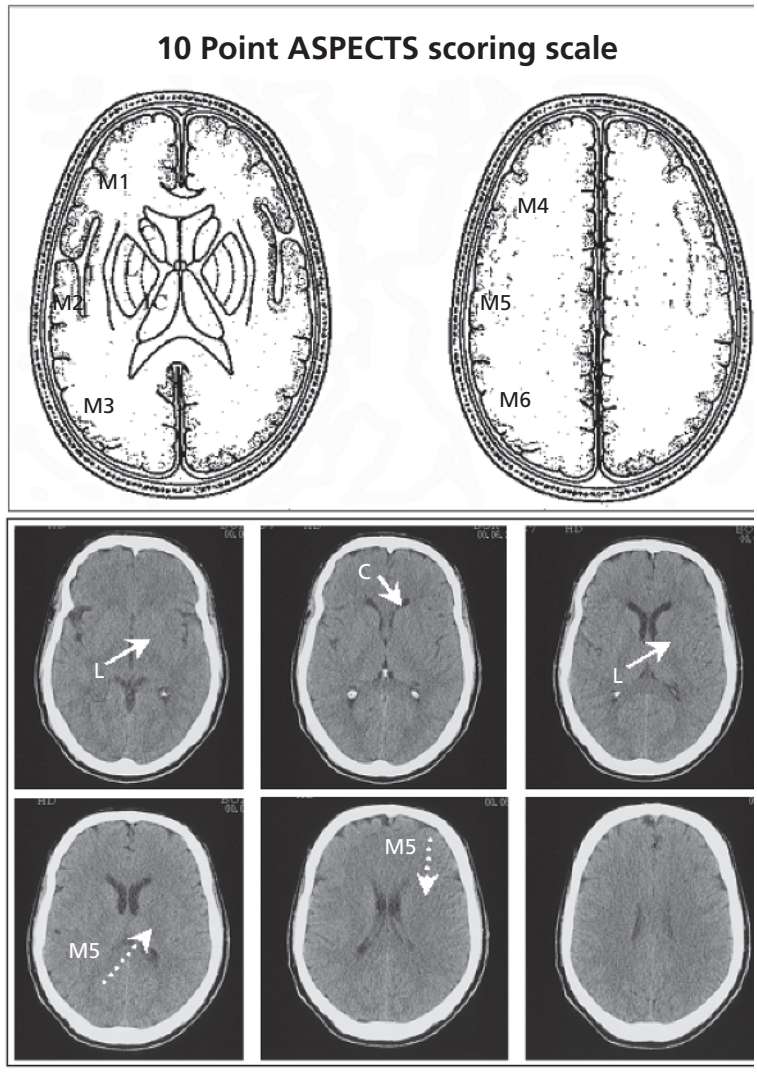

Figure 1.11 Alberta Stroke Program Emergent Computed Tomography Score (ASPECTS). A ten-point scoring system that focuses on the MCA territory over three ganglionic and three supraganglionic cuts. Each specific area is marked: I, insular ribbon; C, caudate nucleus; L, lentiform nucleus; IC, internal capsule; and M1, M2, M3, M4, M5, and M6 areas (this should not be confused with the order of MCA branches on angiography). If none are affected, the ASPECTS score is a maximum of 10 points.

this imaging finding should raise even more suspicion for possible embolic sources.

6. What if the DWI turns out to be negative?

If the DWI is negative and the patient's symptoms persist, it could be that time is needed for a small-vessel lesion to mature and appear on DWI [38] (sometimes it takes up to 3 days for a small lesion to appear on DWI particularly in the posterior circulation), or you may be dealing with hypoperfusion in the subcortical or posterior circulation area, or the patient has psychogenic symptoms.

The workup was completed and DWI showed a typical lacunar lesion while TCD in the emergency room was normal and so was the subsequent MRA. The patient was not currently taking aspirin, and he was given 325 mg on admission. He was then switched to aspirin plus extended-release dipyridamole for secondary stroke prevention. Tighter glycemic control and blood pressure medicines adjustment were recommended. He also was started on a statin.

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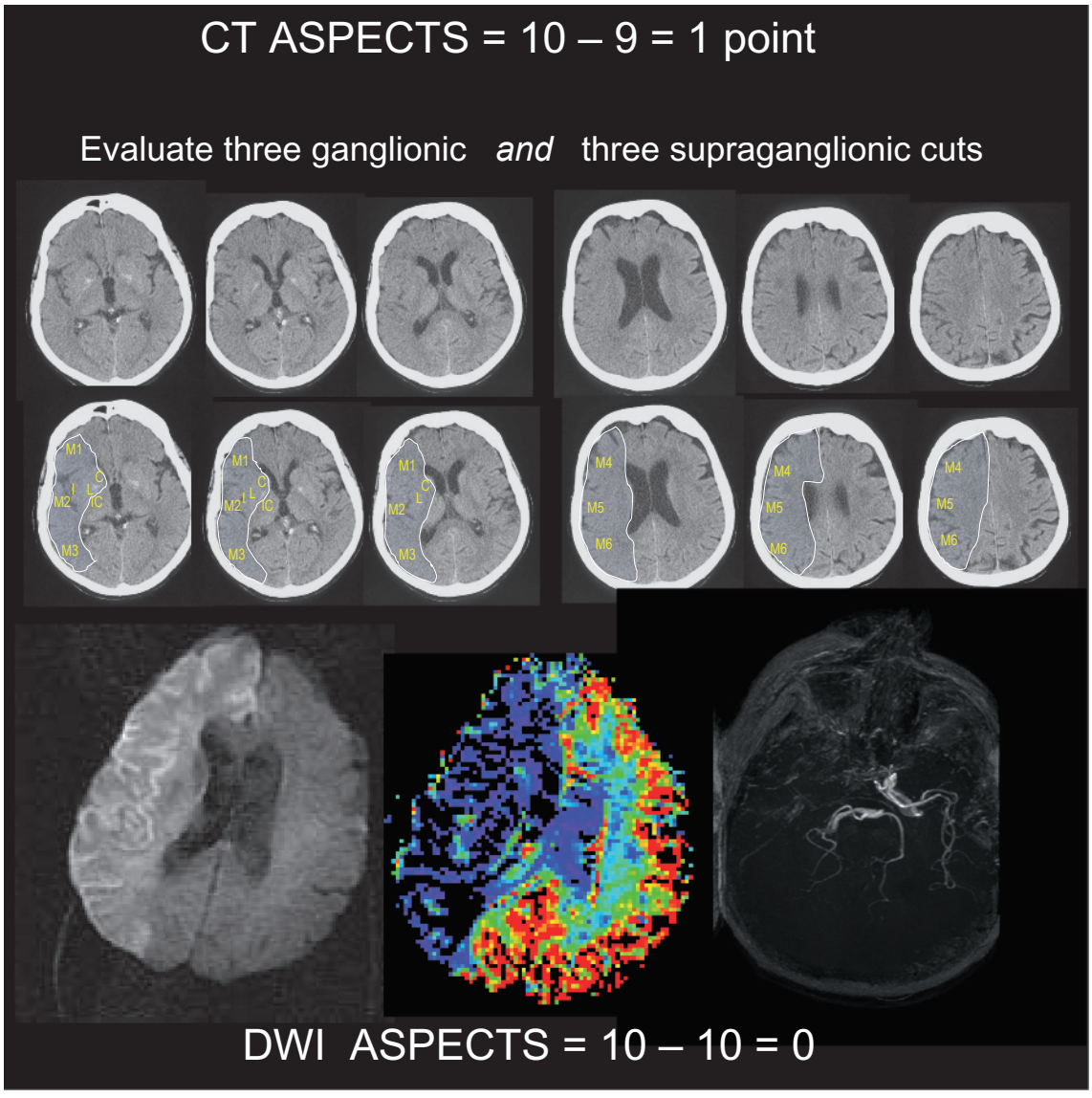


Figure 1.12 CT and MRI appearance of an extensive hemispheric ischemic lesion. All CT ASPECTS areas are affected by early ischemic changes except the internal capsule (images and interpretation courtesy of Andrew Demchuk, MD). For more information see www.aspectsinstroke.com (accessed Dec 11 2012). The bottom row of images show DWI, MR-perfusion, and MR-angiography findings in the patient with baseline ASPECTS score of 1.I, insular ribbon; C, caudate nucleus; L, lentiform nucleus; IC, internal capsule.

Case study 1.4

A 16-year-old female, who was taking a birth control pill and actively smoking, suddenly developed left-sided weakness (for additional discussion, see [39]). She was brought to an outside hospital and her CT scan was negative. The Emergency Medicine physician reported a focal neurological deficit with the total NIHSS score of 10 points at 2.5 hours from symptom onset. Even though the NINDS rt-PA Stroke Study did not enroll patients younger than 18 years of age, the disabling nature of the deficit in an adolescent prompted the decision to give intravenous tPA 0.9 mg/kg (10% bolus, 90% continuous infusion for 1 hour), and transfer her (or "drip'n ship") to the comprehensive stroke center. Upon arrival, and with tPA infusion just about to be completed, she regained most of her strength in the left side and still showed no cortical deficits (total NIHSS score of 4 points).

1. What is the diagnosis?

Despite her young age, it is likely an ischemic stroke due to her risk factors.

2. Should she be considered for additional catheter reperfusion?

Although the Interventional Management of Stroke (IMS) 3 trial [40] was stopped for futility, it did not properly test the latest technologies such as stentrievers [41]. Given her young age and the possibility of neurological worsening if the occlusion persists or the vessel re-occludes, an intra-arterial intervention (mechanical thrombus removal, i.e. thrombectomy) should be considered as an option. Urgent CTA of the head and neck or TCD will help determine if the MCA occlusion is still present. Rapid improvement during tPA infusion to the nondisabling level of her symptoms would be an argument against the risks of an endovascular intervention. The management will change should neurological worsening occur due to re-occlusion.

3. What is likely the mechanism?

Differential for stroke in the young is long and among other conditions pertinent to our acute case it includes paradoxical embolism, dissection, cardiogenic embolism, hypercoagulable state, and moya-moya.

4. What is (are) the next test(s) to confirm ischemic etiology and determine the pathogenic mechanism?

MRI of the brain and TCD "bubble" test (or emboli detection with intravenous contrast injection of 9 cc normal saline agitated with 1 cc room air) [27].

Her workup showed no ischemic changes on the noncontrast head CT upon arrival and patent right MCA at the end of the tPA infusion on TCD examination at bedside (Figure 1.13). Her TCD "bubble" test (or TCD emboli detection with contrast injection also done at the same time at the bedside, Figure 1.13) was positive for Spencer's grade III shunt at rest augmented to grade IV with Valsalva [42]. Her DWI showed a large subcortical ischemic lesion (or "lagoon"; Figure 1.14), and her MRA was normal. Her MRI sequences were extended to include a pelvic MR venogram that showed a thrombus (Figure 1.14). TEE showed patent foramen ovale (PFO) (Figure 1.14). She was instructed to quit smoking and stop taking the birth control pill. The risks and lack of evidence for PFO closure were discussed and she opted for closure of the shunt. She was started on 325 mg aspirin and 75 mg clopidogrel and received percutaneous PFO closure 1 month after her stroke. Her NIHSS was 0 and mRS was 0, and she gave birth to a healthy child 1 year later.

(*Continued*)

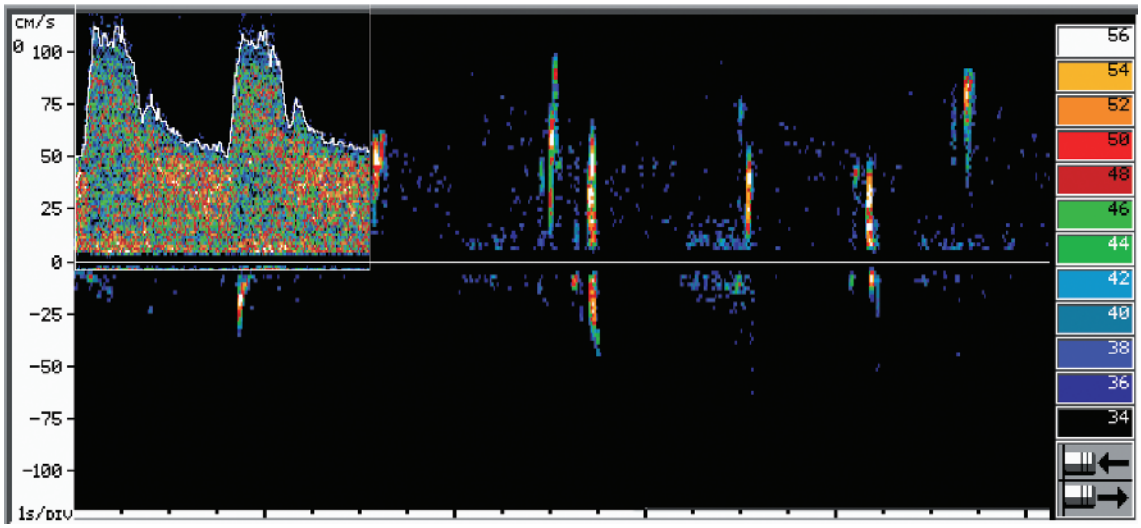


Figure 1.13 Spectral MCA waveform and embolic signals during TCD bubble test for right-to-left shunt. MCA waveforms (insert) are reflective of normal vessel patency. Air microbubble traces on spectral Doppler are seen as high-intensity transient signals (HITS). These HITS appeared after intravenous injection of agitated saline at rest. Gain was reduced to subtracted normal flow signals.

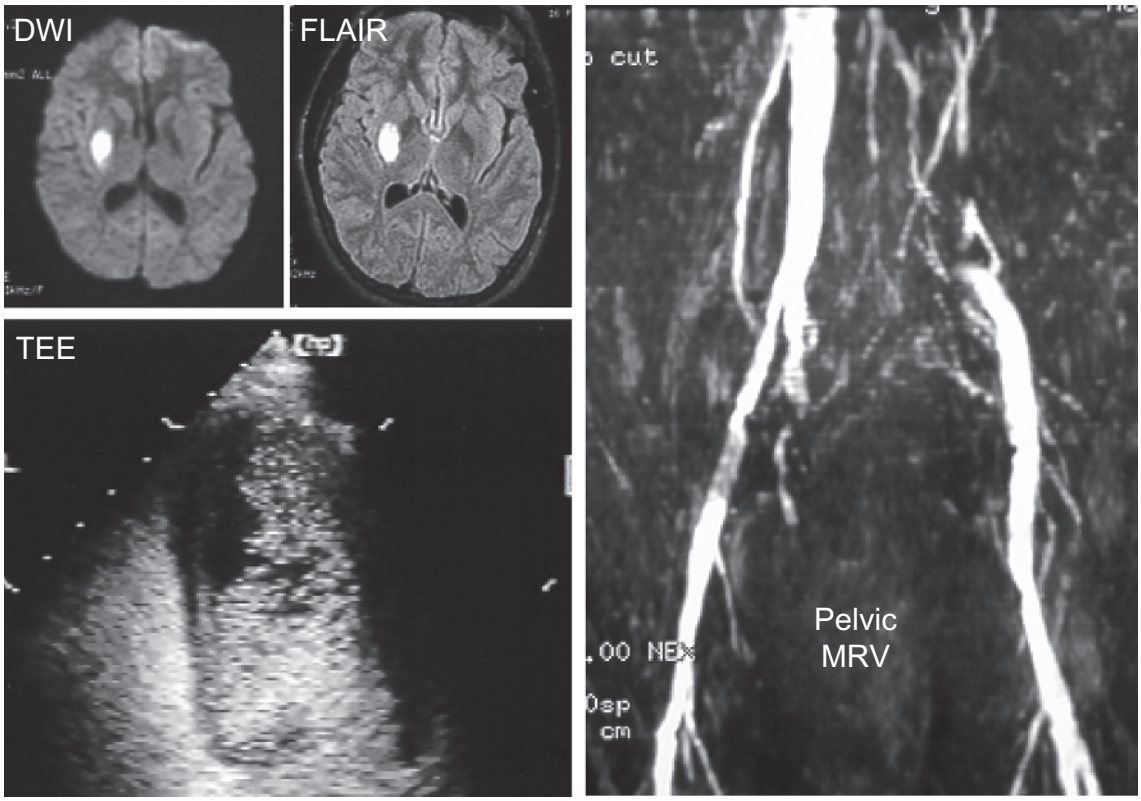


Figure 1.14 MRI findings in a young patient with paradoxical embolism and patent foramen ovale on transesophageal echocardiography (TEE). DWI and fluid-attenuated inversion recovery (FLAIR) show a subacute lesion despite complete symptom resolution at the time of MRI. MR venogram of the pelvis (right) shows flow void due to thrombus. TEE shows air bubble passage into the left ventricle after intravenous injection of agitated saline.

Case study 1.5

A 67-year-old man with a past medical history of coronary artery bypass graft (CABG), peripheral arterial disease, smoking (quit 3 years ago), and daytime sleepiness developed right-sided weakness 2 days ago that was getting worse at night/ morning and better during the day and that he attributed to his arthritis. He decided to seek help when his wife noticed the facial droop on the right and occasional problems finding the correct words. His NIHSS score was 3 upon arrival and his head CT showed a small cortical hypoattenuation in the left frontal lobe with no hemorrhage.

1. What is the diagnosis?

Subacute (greater than 24 hours from onset) ischemic stroke with fluctuating course and worsening of symptoms.

2. What is the likely mechanism?

This patient has polyvascular atheromatous disease, and carotid or intracranial stenoses should be suspected first. Although the course of his symptoms is not typical for an embolic stroke (when the symptoms are often most severe at onset followed by improvement as the embolus dissolves and moves distally), cardioembolism should still be a suspect. Finally, the presence of cortical symptoms (mild aphasia) argues against the small-vessel mechanism.

3. Which is (are) the test(s) that can help determine pathogenic mechanism?

MRI, carotid duplex, TCD, and CTA (if MRA/ultrasound results are discrepant) as well as telemetry and echocardiography should all be done because you suspect either hemodynamic changes in the setting or an extra- or intracranial stenosis, or artery-to-artery embolism, or cardiac embolism. Fluctuating symptoms are likely attributable to changing perfusion pressures and collateral supply rather then recurrent embolization into the same arterial territory. If telemetry is negative, this patient should also be referred for 1-month event detection (prolonged Holter monitoring) to detect paroxysmal atrial fibrillation.

4. Because the patient's symptoms fluctuate and worsen, should reperfusion therapy be considered?

This patient presents outside conventional time windows for systemic thrombolysis and towards the end of timeframes currently considered for endovascular interventions, that is 8 hours from symptom onset. At the moment, he has relatively mild deficit (right arm drift, mild word-finding difficulty and right facial droop). Consider the underlying mechanism of neurological fluctuation, such as a high-grade stenosis or an embolus. If found, these would indicate the possibility of clinical worsening to the point of a clearly debilitating deficit, which would justify the risk of endovascular reperfusion. The probability of neurological worsening can also be demonstrated by a perfusion defect on MRI or CT-perfusion larger than the hypoattenuation area on CT or a lesion on DWI. In parallel with consideration of aggressive reperfusion strategies and further multimodal imaging of a patient with mild deficits, medical management should be optimized, that is place with the head of the bed flat or even Tredelenburg, hydration with intravenous fluids, clopidogrel 300 mg load (he has been taking 81 mg of aspirin only), atorvastatin 80 mg, glycemic control, etc. On admission, his blood pressure should not be lowered (unless it exceeds 220/120 mmHg) until vascular imaging is completed and the mechanism of fluctuation/worsening is ascertained. I use bedside carotid duplex and TCD as an extension of my neurological examination to obtain the pathophysiological information in real time. Multimodal MRI/MRA or CTA/CTP can provide insights into the pathogenesis of his symptoms but lack information about vasomotor reactivity, recruitment of collaterals, and continuing embolization – information easily derived from the ultrasound tests.

5. What if both a significant carotid stenosis and atrial fibrillation are found in this patient?

If carotid duplex or angiography show ≥50% left ICA stenosis and telemetry reveals paroxysmal atrial fibrillation, both of these conditions can produce ischemic stroke and it would be hard to decide which one is the leading cause. If both conditions, each of which could lead to stroke, are confirmed, the patient's pathogenic mechanism of stroke is still deemed to be undetermined [12]. Secondary prevention strategies should nonetheless account for

(*Continued*)

both, that is this patient may be considered for carotid revascularization and take both an anticoagulant and an antiplatelet agent long term.

Upon completion of the diagnostic workup, a severe (70–99% NASCET range) stenosis was found on carotid duplex by the multidisciplinary consensus criteria [43] and telemetry showed paroxysmal atrial fibrillation. Applying TOAST the classification [12], the pathogenic mechanism remains cryptogenic or undetermined. However, the workup revealed risk factors that can be addressed. First, the patient is a candidate for carotid endarterectomy (CEA) or stenting (CAS) because he has a severe symptomatic carotid stenosis. Second, carotid revascularization should be done within 2 weeks of the stroke symptom onset to maximize the protective effect of carotid revascularization, as shown in CEA trials [44]. After carotid revascularization, the patient should receive anticoagulation (a direct thrombin inhibitor or warfarin) because paroxysmal atrial fibrillation places him at practically the same risk of ischemic stroke as persistent or permanent atrial fibrillation [45]. He also should continue on clopidogrel (without aspirin or with aspirin if stenting was performed) due to peripheral arterial disease and coronary artery disease. Unlike preventative measures after acute coronary syndrome, ischemic stroke patients are at a higher risk of bleeding on dual antiplatelet therapy long term in the absence of a larger stroke prevention benefit [46]. Short-term use of dual antiplatelet therapy may be advisable before CEA. Furthermore, blood pressure and lipid-lowering therapies as well as strict glycemic control, should be continued. The patient should receive a referral for a sleep study because sleep apnea is common among patients with stroke and can increase the risk of stroke, myocardial infarction, and sudden death, and it makes BP and glucose management more difficult [47].

These cases represent some of the many considerations that vascular neurologists have when we evaluate and manage patients with stroke and TIA. Imagine now how the pace of the evaluation and workup changes when patients arrive acutely, and quick decisions have to be made on how to reverse the stroke or stop worsening/ fluctuation with much less information at hand and with tools that have to be available in an emergency. The next chapter addresses how time becomes important for the brain to survive when ischemia starts because tissues become at risk of completing infarction and chaos increases when entropy follows the arrow of time. Meanwhile, time is also relative as every patient enters ischemia with different risk factors, abilities to collateralize, as well as differences is size and composition of the thromboembolic material and the location of steno-occlusive lesions. Real-time pathophysiological assessment provides clues as to what is happening and how each individual patient has a unique set of circumstances that may help tailor our management decisions.

Appendix 1.1 The National Institutes of Health Stroke Scale (NIHSS) score

(source: www.ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf; accessed Dec 11, 2012).

Note: the NIHSS is not a substitute for a complete neurological examination. NIHSS is used in emergency situations to document the severity of an ischemic stroke by assessing typical functions most commonly affected by the stroke. If NIHSS is 0 but the patient has neurological deficits, it is likely due to the fact that not all deficits are included into the NIHSS. For example, isolated diplopia, agraphia, acalculia, or thalamic pain. If a deficit cannot be scored, your assessment should document if this neurological problem is present and if it is disabling or not. The presence of a disabling deficit should prompt consideration of reperfusion therapies.

Furthermore, the NIHSS score was not developed for assessment and prognostication of the intracerebral hemorrhage (ICH). Though also applied to patients with ICH to document the severity of the neurological deficit, it should not be used in isolation. The well-established predictors of outcomes after ICH should be documented such as the Glasgow Coma Scale (GCS), ICH volume (cc), location (supra- or infratentorial, deep or lobar), and the presence of an intraventricular extension.

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

Time: ___ ___:___ ___ [ ]am [ ]pm

Person Administering Scale _____

Administer stroke scale items in the order listed. Record performance in each category after each subscale exam. Do not go back and change scores. Follow directions provided for each exam technique. Scores should reflect what the patient does, not what the clinician thinks the patient can do. The clinician should record answers while administering the exam and work quickly. Except where indicated, the patient should not be coached (i.e., repeated requests to patient to make a special effort).

Instructions	Scale Definition	Score
1a. Level of Consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = **Alert;** keenly responsive. 1 = **Not alert**; but arousable by minor stimulation to obey, answer, or respond. 2 = **Not alert**; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.	_____
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0 = **Answers** both questions correctly. 1 = **Answers** one question correctly. 2 = **Answers** neither question correctly.	_____
1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.	0 = **Performs** both tasks correctly. 1 = **Performs** one task correctly. 2 = **Performs** neither task correctly.	_____
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 = **Normal.** 1 = **Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = **Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.	0 = **No visual loss.** 1 = **Partial hemianopia.** 2 = **Complete hemianopia.** 3 = **Bilateral hemianopia** (blind including cortical blindness).	_____
4. Facial Palsy: Ask – or use pantomime to encourage – the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barriers obscure the face, these should be removed to the extent possible.	0 = **Normal** symmetrical movements. 1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling). 2 = **Partial paralysis** (total or near-total paralysis of lower face). 3 = **Complete paralysis** of one or both sides (absence of facial movement in the upper and lower face).	_____
5. Motor Arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** limb holds 90 (or 45) degrees for full 10 seconds. 1 = **Drift;** limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = **Some effort against gravity;** limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = **No effort against gravity;** limb falls. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **5a. Left Arm** **5b. Right Arm**	_____ _____
6. Motor Leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** leg holds 30-degree position for full 5 seconds. 1 = **Drift;** leg falls by the end of the 5-second period but does not hit bed. 2 = **Some effort against gravity;** leg falls to bed by 5 seconds, but has some effort against gravity. 3 = **No effort against gravity;** leg falls to bed immediately. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **6a. Left Leg** **6b. Right Leg**	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

		_____
7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.	0 = **Absent.** 1 = **Present in one limb.** 2 = **Present in two limbs.** UN = **Amputation** or joint fusion, explain: _____	_____
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.	0 = **Normal;** no sensory loss. 1 = **Mild-to-moderate sensory loss;** patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = **Severe to total sensory loss;** patient is not aware of being touched in the face, arm, and leg.	_____
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 = **No aphasia;** normal. 1 = **Mild-to-moderate aphasia;** some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = **Severe aphasia;** all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = **Mute, global aphasia;** no usable speech or auditory comprehension.	_____
10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested.	0 = **Normal.** 1 = **Mild-to-moderate dysarthria;** patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = **Severe dysarthria;** patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. UN = **Intubated** or other physical barrier, explain:_____	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

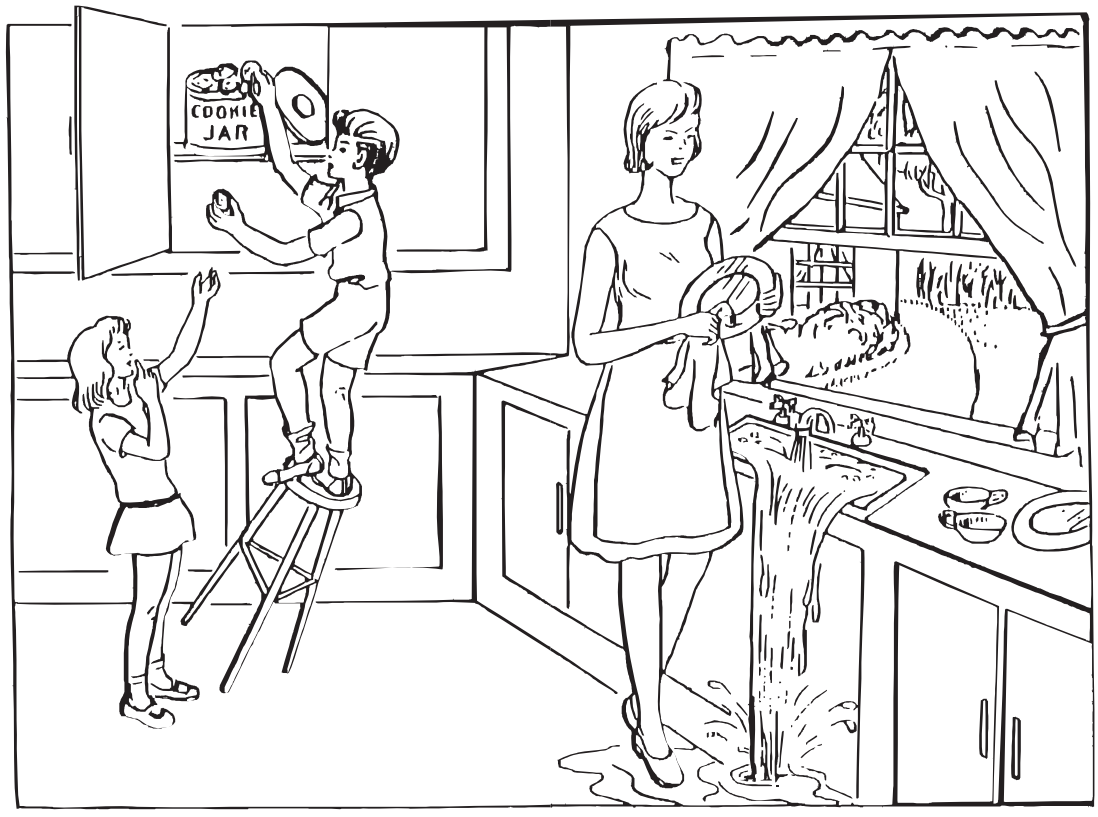
Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	0 = **No abnormality.** 1 = **Visual, tactile, auditory, spatial, or personal inattention** or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = **Profound hemi-inattention or extinction to more than one modality;** does not recognize own hand or orients to only one side of space.	_____

_____

_____



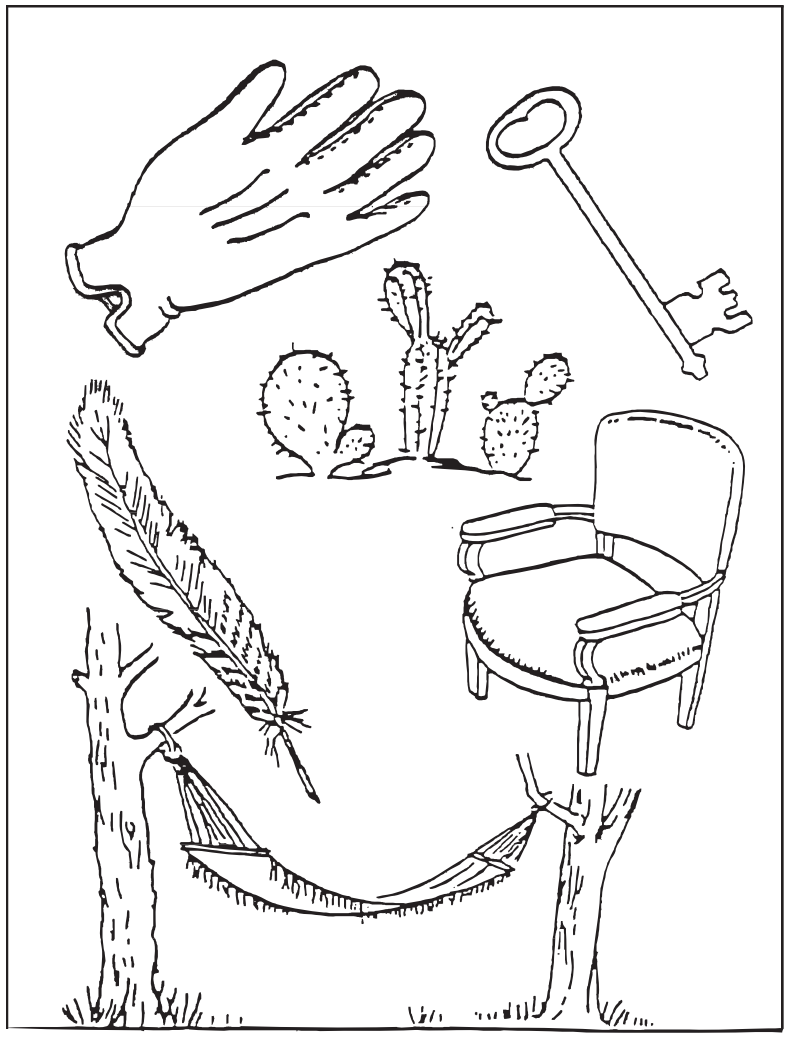
You know how.

Down to earth.

I got home from work.

Near the table in the dining room.

They heard him speak on the radio last night.



MAMA

TIP – TOP

FIFTY – FIFTY

THANKS

HUCKLEBERRY

BASEBALL PLAYER

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