G. Secondary Prevention of Stroke Educational Supplement

Manuel Murie-Fernandez MD, Andrew McClure, Katherine Salter, Robert Teasell MD FRCPC

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G1. Transient Ischemic Attack

G1.1 Case Study: TIA

Case Study

A 32 year old female patient presents to the Emergency Room and tells you that something strange happened one hour ago: She couldn't see out of her left eye for 50 minutes. Although she can see fine now, she and her family want to know what might have caused this temporary blindness.

Q1. What do you think happened and what it is your recommendation?

Q2. The patient and her family want to know more about the role of TIA as a possible risk factor for Stroke. What information can you give them?

Q3. Which clinical features are predictive of greater stroke risk with a TIA?

G2. Hypertension

Canadian Best Practice Recommendations (2008): Recommendation 2.2 – Management of High Blood Pressure

Hypertension is the single most important modifiable risk factor for stroke. Blood pressure should be monitored in all persons at risk for stroke.

2.2a. Blood pressure assessment

i. All persons at risk of stroke should have their blood pressure measured at each health care encounter, but no less than once annually [Evidence Level C] (CHEP, NICE, RCP).

ii. Proper standardized techniques, as described by the Canadian Hypertension Education Program, should be followed for blood pressure measurement (CHEP).

iii. Patients found to have elevated blood pressure should undergo thorough assessment for the diagnosis of hypertension following the current guidelines of the Canadian Hypertension Education Program [Evidence Level A] (ASA, CHEP, RCP).

iv. Patients with hypertension or at risk for hypertension should be advised on lifestyle modifications. [Evidence Level C]. Refer to recommendation 2.1, "Lifestyle and risk factor management," for details on lifestyle modifications.

2.2b. Blood pressure management

i. The Canadian Stroke Strategy recommends target blood pressure levels as defined by the Canadian Hypertension Education Program (CHEP) guidelines for prevention of first stroke, recurrent stroke, and other vascular events.
CHEP 2008 Recommendations for Management of Blood Pressure (excerpts used with permission; see www.hypertension.ca/chep for detailed information (Khan et al. 2008):
• For the prevention of first stroke in the general population the systolic blood pressure treatment goal is a pressure level of less than 140 mm Hg [Evidence Level C]. The diastolic blood pressure treatment goal is a pressure level of less than 90mm Hg [Evidence Level A].
• Blood pressure lowering treatment is recommended for patients who have had a stroke or transient ischemic attack to a target of less than 140/90 mm Hg [Evidence Level C].
• In patients who have had a stroke, treatment with an angiotensin-converting enzyme (ACE) inhibitor or diuretic is preferred [Evidence LevelB].
• Blood pressure lowering treatment is recommended for the prevention of first or recurrent stroke in patients with diabetes to attain systolic blood pressures of less than 130 mm Hg [Evidence Level C] and diastolic blood pressures of less than 80 mm Hg [Evidence Level A].
• Blood pressure lowering treatment is recommended for the prevention of first or recurrent stroke in patients with nondiabetic chronic kidney disease to attain a blood pressure of less than 130/80 mm Hg [Evidence Level C].

ii. Randomized controlled trials have not defined the optimal time to initiate blood pressure lowering therapy after stroke or transient ischemic attack. It is recommended that blood pressure lowering treatment be initiated (or modified) prior to discharge from hospital. For patients with

nondisabling stroke or transient ischemic attack not requiring hospitalization, it is recommended that blood pressure lowering treatment be initiated (or modified) at the time of the first medical assessment [Evidence Level B] (EXPRESS, PROGRESS).

iii. For recommendations on specific agents and sequence of agents, please refer to the current Canadian Hypertension Education Program guidelines (Khan et al. 2008).

G2.1 Case Study: Hypertension

Case Study

A 55 year old woman is admitted to the impatient rehabilitation unit with a lacunar infarct in the right thalamic/subcortical area. Her past medical records state that she has a history of hypertension which is not well controlled. The nurse notes that the patient's blood pressure (BP) is 145/90 mmHg and that she is not currently taking any antihypertensive medication.

Q1. What are the risk factors for this patient having a new stroke?

Q2. What BP level is considered normal?

Q3. The patient tells you that her current BP (145/90 mmHg) is normal for her and that she questions whether it needs to be treated because she doesn't want to have to take any "pills". What can you tell her?

Q4. After the patient agrees to be treated, the resident asks what pharmacological treatments are available for hypertension and which treatment would be most appropriate for this patient. What would be your initial treatment?

Q5. List the reasons why it is important to treat hypertension in stroke survivors?

Q6. Two important studies looking at the treatment of hypertension post-stroke were the PROGRESS and HOPE trials. Describe both of theses trials.

G2.2 Case Study: Intracerebral Hemorrhage and Hypertension

Case Study

34 year old obese male presented to hospital emergency room with aphasia, right hemiparesis and decreased level of consciousness. CT scan showed a large left intracerebral hemorrhage. BP was 236/124. Patient was admitted to the ICU.

Past medical history was a 2 year history of malignant hypertension complicated by two hypertensive crisis in the month before his stroke for which he was treated but he failed to follow through with his prescriptions. At the time of admission and in the ICU his BP proved extremely difficult to control and he was discharged from the ICU with a BP of 170/95.

Q7. What treatment options are available?

Case Study (continued)

He was admitted to rehabilitation and during his rehabilitation stay his blood pressure was generally running between 120-140 systolic and 70-90 diastolic with occasional BPs of 150-160 systolic and 90-100 diastolic.

Medication s for HBP while on the rehabilitation unit included Amlodipine 7.5 mg q12h, Metoprolol 150 mg q12h, Perindopril 2 mg OD, Prazosin 6 mg q6h with the suggestion of adding an additional 12.5 mg of Hydrochlorthiazide to further regulate the patient's blood pressure.

G3. Hyperlipidemia and Hypercholesterolemia

Canadian Best Practice Recommendations (2008): Recommendation 2.3 – Lipid Management

Lipid levels should be monitored in all persons at risk for stroke.

2.3a. Lipid assessment

i. Fasting lipid levels (total cholesterol, total glycerides, low-density-lipoprotein [LDL] cholesterol, high-density-lipoprotein [HDL] cholesterol) should be measured every 1 to 3 years for all men 40 years or older and for women who are postmenopausal and/or 50 years or older [Evidence Level C] (McPherson et al., VA/DoD). More frequent testing should be performed for patients with abnormal values or if treatment is initiated.

ii. Adults at any age should have their blood lipid levels measured if they have a history of diabetes, smoking, hypertension, obesity, ischemic heart disease, renal vascular disease, peripheral vascular disease, ischemic stroke, transient ischemic attack or asymptomatic carotid stenosis [Evidence Level C] (McPherson et al.).

2.3b. Lipid management

i. Ischemic stroke patients with LDL cholesterol of >2.0mmol/L should be managed with lifestyle modification and dietary guidelines [Evidence Level A] (AU, CSQCS, McPherson et al., VA/DoD)

ii. Statin agents should be prescribed for most patients who have had an ischemic stroke or transient ischemic attack to achieve current recommended lipid levels [Evidence Level A] (AU, CSQCS, McPherson et al., VA/DoD).

G3.1 Case Study: Hyperlipidemia

Case Study

A 68 year old man was admitted into the stroke rehabilitation program with an ischemic stroke on the left ACM territory. He has a history of hyperlipidemia and the cholesterol related results from a recent blood test are as follows:

- *Total cholesterol 4.1 mmol/L*
- *Triglycerides 0.74 mmol/L*
- *LDL 2.83 mmol/L*
- *HDL cholesterol 0.94 mmol/L*
- *Total cholesterol to HDL ratio 4.4*

Q1. When the patient asks about the cause of his stroke, the resident tells him that high cholesterol is a major risk factor and that it is the likely cause of his stroke. Do you agree with the resident and why?

Q2. After your explanation, the resident asks "if hyperlipidemia is not a major risk factor, do you still have to treat it"?

Q3. How would you treat the hyperlipidemia?

Q4. What are the target values for treating hyperlipidemia following stroke?

Q5. Why is it important to distinguish between LDLs, HDLs and total cholesterol in high risk patients?

Q6. Describe the pharmacological treatment of hypercholesterolemia.

Q7. Describe your treatment for each of the following cases.

Patient Description	**Lipid Profile**	**Proposed Treatment and Rationale**
Case a: Post Stroke – High Risk	Total cholesterol 4.75 LDL 2.4 mmol/L HDL 1.1 momol/L	
Case b: Post Stroke – High Risk	Total cholesterol 5.8 LDL 3.3 mmol/L HDL 1.4 mmol/L	

Case c: Post Stroke – High Risk	Total cholesterol 4.72 LDL cholesterol 3.0 mmol/L HDL 1.04 mmol/L	
Case d: Post Stroke – High Risk	Total cholesterol 5.2 LDL cholesterol 2.6 mmol/L HDL cholesterol 1.4 mmol/L	

G4. Diabetes

Canadian Best Practice Recommendations (2008): Recommendation 2.4 – Diabetes Management

2.4a. Diabetes Assessment

i. All individuals in the general population should be evaluated annually for type 2 diabetes risk on the basis of demographic and clinical criteria [Evidence Level C] (CDA).

ii. A fasting plasma glucose should be performed every 3years in individuals > 40 years of age to screen for diabetes [Evidence Level C] (CDA). More frequent and/or earlier testing with either a fasting plasma glucose or plasma glucose sample drawn 2 hours after a 75-g oral glucose load should be considered in people with additional risk factors for diabetes [Evidence Level C] (CDA). Some of these risk factors include family history, high-risk population, vascular disease, history of gestational diabetes, hypertension, dyslipidemia, overweight, abdominal obesity, polycystic ovary syndrome.

iii. In adults, fasting lipid levels (total cholesterol, HDL cholesterol, total glycerides and calculated LDL cholesterol) should be measured at the time of diagnosis of diabetes and then every 1 to 3 years as clinically indicated. More frequent testing should be performed if treatment for dyslipidemia is initiated [Evidence Level C] (CDA).

iv. Blood pressure should be measured at every diabetes visit [Evidence Level C] (CDA).

2.4b. Diabetes Management

i. Glycemic targets must be individualized; however, therapy in most patients with type 1 or type 2 diabetes should be targeted to achieve a glycated hemoglobin (Hb_{A1c}) level $\leq$7.0% in order to reduce the risk of microvascular complications [Evidence Level A] (CDA) and, for individuals with type 1 diabetes, macrovascular complications. [Evidence Level C] (CDA).

ii. To achieve an Hb_{A1c} $\leq$7.0%, patients with type 1 or type 2 diabetes should aim for a fasting plasma glucose or preprandial plasma glucose targets of 4.0 to 7.0 mmol/L [Evidence Level B] (CDA).

iii. The 2-hour postprandial plasma glucose target is 5.0–10.0 mmol/L [Evidence Level B]. If Hb_{A1c} targets cannot be achieved with a postprandial target of 5.0–10.0 mmol/L, further postprandial blood glucose lowering, to 5.0–8.0 mmol/L, can be considered [Evidence Level C] (CDA).

iv. Adults at high risk of a vascular event should be treated with a statin to achieve an LDL cholesterol $\leq$2.0mmol/L [Evidence Level A] (CDA).

v. Unless contraindicated, low dose acetylsalicylic acid (ASA) therapy (80 to 325 mg/day) is recommended in all patients with diabetes with evidence of cardiovascular disease, as well as for those individuals with atherosclerotic risk factors that increase their likelihood of cardiovascular events [Evidence Level A] (CDA).

G4.1 Case Study: Diabetes

Case Study

A 55 year old man was admitted into the rehabilitation unit with a right MCA ischemic stroke and he has no known history of medical problems or complications.

Q1. The nurse tells you that he has a fasting plasma glucose level of 127 mg/dL or 7.0 mmol/L. Is he diabetic?

Q2. His Hemoglobin A1C level is 8.2%. What is its significance?

Q3. Provide a classification for diabetes.

Q4. How is diabetes related to stroke?

Q5. Is glycemic control associated with secondary stroke prevention?

Q6. List three different groups of treatments recommended for glycemic control.

Case Study (continued)

The 55 year old man who was admitted into the rehabilitation unit with a right MCA ischemic stroke with no known history of medical problems or complications has now been diagnosed with type 2 diabetes. His fasting blood sugar is 7.0 mmol/L and his hemoglobin A1c is 8.2%. He has no other complications apart from the stroke.

Q7. Describe a glycemic control protocol for his new found Type 2 diabetes.

Case Study (continued)
Despite nutritional interventions and a structured physical activity program his Hemoglobin A1C still comes back at 8.3%.

Q8. What treatment is indicated now?

Q9. How important is BP control important in this diabetic patient post stroke?

G5. Lifestyle Modification

Canadian Best Practice Recommendations (2008): Recommendation 2.1 – Lifestyle and risk factor management

Persons at risk of stroke and patients who have had a stroke should be assessed for vascular disease risk factors and lifestyle management issues (diet, sodium intake, exercise, weight, smoking and alcohol intake). They should receive information and counselling about possible strategies to modify their lifestyle and risk factors [Evidence Level B] (AU, NZ, RCP, VA/DoD). Lifestyle and risk factor interventions should include:

i. *Healthy balanced diet:* High in fresh fruits, vegetables, low-fat dairy products, dietary and soluble fibre, whole grains and protein from plant sources and low in saturated fat, cholesterol and sodium, in accordance with Canada's Food Guide to Healthy Eating [Evidence Level B] (ASA, CHEP, RCP).

ii. *Sodium:* The recommended daily sodium intake from all sources is the Adequate Intake by age. For persons 9– 50 years, the Adequate Intake is 1500 mg. Adequate Intake decreases to 1300 mg for persons 50–70 years and to 1200 mg for persons > 70 years. A daily upper consumption limit of 2300 mg should not be exceeded by any age group [Evidence Level B]. See www.sodium101.ca for sodium intake guidelines.

iii. *Exercise:* Moderate exercise (an accumulation of 30 to 60 minutes) of walking (ideally brisk walking), jogging, cycling, swimming or other dynamic exercise 4 to 7days each week in addition to routine activities of daily living [Evidence Level A]. Medically supervised exercise programs are recommended for high-risk patients (e.g., those with cardiac disease) (ASA, CHEP, EBRSR, NZ).

iv. *Weight:* Maintain goal of a body mass index (BMI) of 18.5 to 24.9 kg/m^2 and a waist circumference of <88cm for women and < 102 cm for men [Evidence Level B] (ASA, CHEP, OCCPG).

v. *Smoking:* Smoking cessation and a smoke-free environment; nicotine replacement therapy and behavioural therapy [Evidence Level B] (ASA, CHEP, CSQCS, RCP). For nicotine replacement therapy, nortriptyline therapy, nicotine receptor partial agonist therapy and/or behavioural therapy should be considered [Evidence Level A] (ASA, AU).

vi. *Alcohol consumption:* Two or fewer standard drinks per day; and fewer than 14 drinks per week for men; and fewer than 9 drinks per week for women [Evidence Level C] (ASA, AU, CHEP).

G5.1 Case Study: Lifestyle Modification

Case Study

A 54 year old male patient is admitted to the rehabilitation unit. He has been a lifelong smoker and has a history of alcoholism. As well, he is overweight (with a BMI of 36kg/m2) and acknowledges that he rarely engages in physical activity.

Q1. What known modifiable risk factors does he have?

Q2. How can physical activity affect the risk of stroke?

Q3. Is the patient obese?

Q4. What can you tell the patient regarding obesity and diet in the secondary prevention of stroke?

Q5. The patient does not want to stop smoking. What can you tell him regarding smoke cessation in the secondary prevention of stroke?

Q6. The patient tells you that he is going to need help in order to avoid cigarette consumption. What can you suggest to help him?

Q7. What can you tell the patient regarding alcohol consumption as a risk factor for stroke?

G6. Homocysteine and Stroke

G6.1 Case Study: Homocysteine

Case Study

A 45 year old male presented with a right subcortical stroke. The neurologist feels that it was probably due to a high homocystine levels in his blood.

Q1. What is homocysteine and what are considered normal serum levels?

Q2. Is hyperhomocystinemia associated with secondary cardiovascular events?

Q3. What is the relationship between folic acid, vitamin B6, and Vitamin B12 levels and plasma homocysteine levels?

G7. Antiplatelet Agents

Canadian Stroke Guidelines (2008): Recommendation 2.5 – Antiplatelet therapy

All patients with ischemic stroke or transient ischemic attack should be prescribed antiplatelet therapy for secondary prevention of recurrent stroke unless there is an indication for anticoagulation [Evidence Level A] (ASA, AU, CSQCS, ESO, NZ, RCP, VA/DoD).

i. ASA, combined ASA (25 mg) and extended-release dipyridamole (200 mg), or clopidogrel may be used depending on the clinical circumstances [Evidence Level A].

ii. For adult patients on ASA, the usual maintenance dosage is 80 to 325 mg per day [Evidence Level A] (CSQCS, VA/DoD), and in children with stroke the usual maintenance dosage of ASA is 3 to 5 mg/kg per day for the prevention of recurrent stroke [Evidence Level C] (AHA-P).

iii. Long-term combinations of ASA and clopidogrel are not recommended for secondary stroke prevention [Evidence Level B] (CHARISMA, MATCH).

G7.1 Case Study: Antiplatelet Agents

Case Study

A 68 year old man with a right MCA is admitted into the rehabilitation unit. He has had a carotid ultrasound that shows a cholesterol plaque occluding 40% of the lumen of the right internal carotid vessel.

Q1. Assuming that he has had an atherotrombotic stroke, what treatment would you recommend to avoid a stroke recurrence?

Q2. What is the major adverse side-effect of antiplatelet therapy?

Q3. Knowing there may be an increased risk of bleeding, would this influence your decision to use antiplatelet treatment and why?

Q4. Describe the different types of antiplatelet therapy?

Q5. If antiplatelet therapy is the treatment of choice, which drug would be the initial choice?

Q6. The patient's family believe the patient should get at least 325 mg of Aspirin per day. How do you respond?

Q7. When should antiplatelet treatment be initiated and when should it be terminated?

Case Study (continued)

You tell the nurse that the patient is going to begin taking 81mg of aspirin/day but the nurse tells you that the patient is allergic to ASA.

Q8. Which other treatment options are available?

Q9. The nurse questions you about the difference between ASA and Clopidogrel in terms of effectiveness.

Q10. The nurse asks you why Clopidogrel is not used more often as the first line treatment.

Q11. Clopidogrel and Ticlopidine are both thienopyridines. Describe the differences between these two medications.

Q12. The resident asks about using combination therapy of different antiplatelet therapies.

G8. Atrial Fibrillation and Coumadin

Canadian Stroke Guidelines (2008): Recommendation 2.6 – Antithrombotic Therapy in Atrial Fibrillation

Patients with stroke and atrial fibrillation should be treated with warfarin at a target international normalized ratio of 2.5, range 2.0 to 3.0 (target international normalized ratio of 3.0 for mechanical cardiac valves, range 2.5 to 3.5) [Evidence Level A], if they are likely to be compliant with the required monitoring and are not at high risk for bleeding complications (ASA, AU, CSQCS, ESO, SIGN, VA/DoD).

G8.1 Atrial Fibrillation and Anticoagulation

Case Study

A 76 year old man is admitted to your rehabilitation unit with a left MCA stroke. In the emergency department atrial fibrillation was diagnosed and was thought to be the cause of the stroke.

Q1. What is the relationship between atrial fibrillation and the development of stroke?

Q2. What are some other cardiac disorders that could lead to an embolic stroke?

Q3. Once a patient with AF has had a stroke, what is the risk for recurrence of stroke?

Q4. Describe some contraindications for anticoagulant therapy?

Q5. Which drug would you use for anticoagulant therapy in this patient?

Q6. The patient's daughter asks you if treatment with warfarin is effective and also wants to know the optimal range of INR.

Q7. The patient's daughter asks you when treatment should be initiated.

Q8. The nurse asks you to explain to the patient any negative side effects associated with warfarin.

Q9. The resident asks why not use ASA alone as treatment for atrial fibrillation.

G9. Patent Foramen Ovale

G9.1 Case Study: PFO

Case Study

You see a 45 year old woman in your outpatient clinic. She has had a TIA and her echocardiogram shows a patent foramen ovale (PFO).

Q1. What it is a PFO?

Q2. Is PFO a stroke risk factor?

Q3. How can PFO be treated?

Q4. The resident asks you if it is necessary to close the PFO.

G10. Carotid Artery Stenosis

Canadian Stroke Guideline (2008): Recommendation 2.7 – Carotid Intervention

2.7a Symptomatic carotid stenosis

Patients with transient ischemic attack or nondisabling stroke and ipsilateral 70%–99% internal carotid artery stenosis (measured on a catheter angiogram or by 2 concordant noninvasive imaging modalities) should be offered carotid endarterectomy within 2 weeks of the incident transient ischemic attack or stroke unless contraindicated [Evidence Level A] (ASA, AU, CSQCS, ESO, NZ, SIGN 14).

i. Carotid endartarectomy is recommended for selected patients with moderate (50%–69%) symptomatic stenosis, and these patients should be evaluated by a physician with expertise in stroke management [Evidence Level A] (ASA, AU, CSQCS, NZ, SIGN 14).

ii. Carotid endarterectomy should be performed by a surgeon with a known perioperative morbidity and mortality of < 6% [Evidence Level A] (ASA, CSQCS, ESO, NZ).

iii. Carotid stenting may be considered for patients who are not operative candidates for technical, anatomic or medical reasons [Evidence Level C].

iv. Carotid endarterectomy is contraindicated for patients with mild (< 50%) stenosis [Evidence Level A] (ASA, CSQCS, SIGN 14).

2.7b Asymptomatic carotid stenosis

Carotid endarterectomy may be considered for selected patients with asymptomatic 60%–99% carotid stenosis.

i. Patients should be less than 75 years old with a surgical risk of < 3%, a life expectancy of > 5 years and be evaluated by a physician with expertise in stroke management [Evidence Level A] (AAN, AHA, AU, CSQCS).

G10.1 Case Study: Carotid Endarterectomy (CEA)

Case Study

A 62 year old woman was admitted to your rehabilitation unit with a left MCA ischemic stroke. 75% stenosis of the left internal carotid artery due to atherosclerotic plaque was found on carotid ultrasound.

Q1. What issues must be considered when deciding on therapeutic options?

Q2. In this case, what will be your recommendation and why?

Q3. The medical student asks you why you think carotid endarterectomy (CEA) should be used instead of carotid artery stenting (CAS).

Case Study (continued)
The radiologist revises his report; the grade of stenosis was 60%, not 75%.

Q4. Does this change your treatment decision?

Q5. How long after the symptomatic event do you recommend performing the CEA?

G10.2 Case Study: Symptomatic Stenosis (>50%)

Case Study

A 62 year old woman was admitted to your rehabilitation unit with a left MCA ischemic stroke. A 40% stenosis due to atherosclerotic plaque was found on the carotid ultrasound.

Q6. What will be your recommendation in this case and why?

G10.3 Case Study: Non-symptomatic Stenosis

Case Study

You see a 55 year old man in your outpatient clinic. He has an asymptomatic 55% stenosis in his right internal carotid artery.

Q7. What is the risk of stroke for this patient?

G10.4 Case Study: Recurrent Carotid Stenosis

Case Study

You see a 52 year old man in your outpatient clinic who was treated with CEA for his symptomatic 70% stenosis of his left internal carotid artery. In his new ultrasound you find a restenosis of 80% and he is complaining about recurrent numbness in his right side

Q8. Which treatment do you recommend in this situation, carotid endarterectomy or carotid artery stenting?