Diabetes and Stroke: Making the Connection

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
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Faculty

Diane Thompson, RN, MSN, CDE, CLNC, has an extensive history in nursing and nursing education. She possesses a strong background in diabetes and cardiac care, starting her professional career at the cardiac care area of the Cleveland Clinic in Cleveland, Ohio. Ms. Thompson took the knowledge and experience she learned from the Cleveland Clinic and transferred it into the home health arena in rural Ohio, after which she moved to Florida and obtained further knowledge while working as a PRN nurse in all areas, including medical/surgical, intensive care, emergency, critical care, and cardiology. With a desire to have a specific area to concentrate her profession, Ms. Thompson accepted a position as a pneumonia case manager, which led into a diabetes case manager career.

Ms. Thompson has been employed in diabetes care since 2001, when she was hired as a diabetes case manager. After the completion of 1,000 hours of education to diabetes patients, Ms. Thompson earned her certification as a diabetes educator in 2003. From 2006 to 2018, Ms. Thompson was the Director of Diabetes Healthways at Munroe Regional Medical Center in Ocala, Florida. As the director of the diabetes center, Ms. Thompson was responsible for the hospital diabetes clinicians, hospital wound care clinicians, and out-patient education program. Today, she is the nurse manager of a heart, vascular, and pulmonary ambulatory clinic at Metro Health System in Cleveland, Ohio. Ms. Thompson has also lectured at the local, state, and national level regarding diabetes and the hospital management of hyperglycemia. Ms. Thompson is a member of the ADA, AADE, Florida Nurses Association, and the National Alliance of Certified Legal Nurse Consultants.

Ms. Thompson acknowledges her family as her greatest accomplishment. She is a wife of more than 30 years and a mother of a daughter and son, of which she is very proud. Ms. Thompson credits her husband for the support needed to set a goal and achieve it. He has been by her side through nursing school and completion of her Bachelor's degree and Master's degree, which she was awarded in 2015 from Jacksonville University in Florida.

Faculty Disclosure

Contributing faculty, Diane Thompson, RN, MSN, CDE, CLNC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Division Planner/Director Disclosure

The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

A complete Works Cited list begins on page 12.

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Audience
This course is designed for nurses in all practice settings who care for patients with diabetes.

Accreditations & Approvals
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Disclosure Statement
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Course Objective
Due to the widespread and potentially life-threatening nature of this issue, having a firm understanding of the implications of diabetes and how they relate to stroke is paramount. The purpose of this course is to provide nurses with the information necessary to identify patients with diabetes who are at risk for stroke and intervene early.

Learning Objectives
Upon completion of this course, you should be able to:

1. Outline the prevalence and diagnosis of diabetes.
2. Evaluate the etiology and presentation of stroke in patients with diabetes.
3. Identify treatment options for acute stroke.
4. Describe primary stroke prevention strategies for patients with diabetes.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Both diabetes and stroke are major public health issues in the United States. An estimated 34.2 million American children and adults, or 10.5% of the total population, have diabetes [1]. Cerebrovascular disease is one of the most common complications of diabetes and is an area of serious concern as the population ages and the trend for diabetes to be diagnosed at an earlier age continues.

The risk of stroke is two to four times greater for individuals with diabetes compared to those without. As of 2016, 313,000 (18.9 per 1,000) patients discharged with documented stroke also had diabetes [1]. Due to the widespread and potentially life-threatening nature of this issue, having a firm understanding of the implications of diabetes and how they relate to stroke is paramount.

AN OVERVIEW OF DIABETES

EPIDEMIOLOGY

Diabetes is a progressive disease process influencing fuel metabolism [2]. Carbohydrate, protein, and fat metabolism are altered when insulin, the mediator of fuel, is not available. This insulin deficiency can result from defects in insulin secretion and/or diminished tissue response to insulin, resulting in hyperglycemia [3]. The chronic metabolic dysregulation associated with diabetes can result in long-standing damage to various organs, including the eyes, kidneys, nerves, heart, and blood vessels [2].

According to the American Diabetes Association (ADA), the prevalence of diabetes increased 382% between 1988 and 2014. However, the incidence of diabetes appears to have peaked in 2008 with an incidence of 8.4 per 1,000 adults in 2008; it has since decreased to an incidence of 6.7 per 1,000 adults in 2018 [1; 4]. As stated, 10.5% of the U.S. population, or 34.2 million Americans, have a diagnosis of diabetes. In addition, an estimated 7.3 million adults have diabetes but remain undiagnosed [1]. By 2045, it is predicted that 36 million American adults will have diagnosed or undiagnosed diabetes or impaired glucose tolerance, an increase of 1.8 million adults from current rates [5].

The scope of the diabetes problem is vast and diverse, particularly among geographical regions. In 2018, the prevalence of diabetes in the United States varied from 6.6% in Colorado to 13.4% in West Virginia [6]. Genetics, race, age, and lifestyle significantly influence the onset and progression of the disease process [1]. Although all races and ethnicities can develop diabetes, the prevalence is greatest (14.7%) among Native Americans/Alaska Natives. This group also has a risk for development of type 2 diabetes that is nearly two times greater than that of White Americans [1]. The prevalence of diabetes is 12.5% in Hispanic Americans, 11.7% in non-Hispanic Black Americans, 9.2% in Asian Americans/Pacific Islanders, and 7.5% in non-Hispanic White Americans [1]. Compared to non-Hispanic White Americans, African Americans and Hispanics are 40% to 50% more likely to have diabetes [4]. The highest prevalence of diabetes in the United States is observed in Native Americans in certain areas of the Southwest, where more than 30% of the population has the disease [1].

Diabetes is considered to be one of the most important risk factors for ischemic stroke, especially in individuals younger than 65 years of age. Individuals with diabetes who experience an ischemic stroke are typically younger than those without diabetes and often also have signs of hypertension, myocardial infarction (MI), and hyperlipidemia [7]. In 2016, after adjusting for age, the percentage of adults with diabetes who reported stroke was lowest among Hispanics (7.3%) compared with White (7.6%) or Black (9.4%) adults [8].

DIAGNOSIS OF DIABETES

The most common types of diabetes are type 1 and type 2. However, gestational diabetes is also relatively common and is a source of significant morbidity and mortality. Gestational diabetes is first recognized in pregnancy, usually after 27 weeks' gestation, and typically resolves after the birth of the child [9]. Other less common types of diabetes include [5; 10]:

- Maturity-onset diabetes of the young: A genetic, autosomal-dominant defect of the pancreatic beta cells resulting in insulin deficiency and decreased insulin release without the presence of insulin resistance and obesity. This form of diabetes typically develops in patients younger than 25 years of age. It is a different clinical entity than type 2 diabetes of the adolescent, which presents with insulin resistance.
- Diabetes related to diseases of the exocrine pancreas, such as cystic fibrosis, and various endocrine diseases, such as Cushing syndrome, acromegaly, and chromocytoma
- Drug-induced diabetes resulting from the use of certain medications, particularly high-dose corticosteroids

According to 2022 recommendations from the American Diabetes Association, all adults older than 35 years of age should be screened for type 2 diabetes every three years, or sooner with symptoms or in the presence of risk factors [9]. In addition, individuals of any age who are at risk for or are suspected of having diabetes should be screened. Established risk factors for type 2 diabetes include [9]:

- Age older than 35 years
- Body mass index (BMI) greater than or equal to 25, or greater than or equal to 23 in Asian Americans
- Family history of type 2 diabetes
- Habitual physical inactivity
- Race/ethnicity (e.g., African American, Hispanic American, Native American, Alaska Native, or Pacific Islander)
- Impaired glucose tolerance or elevated fasting glucose
- Previous history of gestational diabetes or giving birth to a child weighing more than 9 pounds
- Hypertension (i.e., blood pressure greater than 140/90 mm Hg in adults)
- Abnormal lipid levels (i.e., high-density lipoprotein [HDL] level <35 mg/dL and/or triglyceride level >250 mg/dL)
- Polycystic ovary syndrome
- History of vascular disease
- Acanthosis nigricans (most common among individuals of African descent)

The diagnostic criteria for type 2 diabetes are fairly straightforward and are based on fasting plasma glucose and postprandial plasma glucose levels (***Table 1***). After a diagnosis of type 2 diabetes has been definitively made, education on self-care management is necessary in order to obtain euglycemia and prevent complications related to the detrimental effects of hyperglycemia [9]. It is estimated that as many as 90% of patients with type 2 diabetes will require oral medications to achieve adequate glucose control within five years of diagnosis [9]. When glucose levels cannot be adequately controlled with oral medications, the use of injectable medications is necessary. If elevated blood glucose levels are untreated and continue to rise, the result can be hyperosmolar hyperglycemic nonketotic syndrome and ultimately death [11].

DIAGNOSTIC CRITERIA FOR TYPE 2 DIABETES			
Stage	**Fasting Plasma Glucose Level**	**Two-Hour Postprandial Plasma Glucose Level**	**Glycated Hemoglobin (HbA1c)**
Euglycemia	≤100 mg/dL	<140 mg/dL	<5.7%
Prediabetes	>100 mg/dL but <126 mg/dL	≥140 mg/dL but <200 mg/dL	5.7% to 6.4%
Diabetes[a]	≥126 mg/dL	≥200 mg/dL	≥6.5%
[a]A random blood glucose level ≥200 mg/dL with symptoms of hyperglycemia is also indicative of diabetes.			
Source: [9; 10; 11]			*Table 1*

CEREBROVASCULAR DISEASE AND DIABETES

The main cause of cerebrovascular disease in patients with diabetes is atherosclerosis, or thickening of artery walls. It is generally believed that patients with diabetes are at an increased risk for atherosclerosis due to endothelial dysfunction. The endothelium is the biologically active lining of the blood vessel that functions to [12]:

- Provide a mechanical lining
- Maintain vascular patency
- Prevent platelet aggregation and thrombosis
- Promote fibrinolysis

Endothelial dysfunction is the earliest vascular abnormality seen in patients with diabetes and is associated with blood vessel constriction, aggregation of platelets, and a proinflammatory state, with the accumulation of leukocytes and coagulation products on the endothelium [12]. This inflammatory response is mainly caused by the chronic effects of hyperglycemia and specifically the formation of biologically active glycated proteins and lipids that promote inflammation [13]. Visceral obesity, hypertension, and hyperlipidemia also contribute to oxidative stress, which can damage the endothelium [14].

The normal metabolic response to a glucose load is an increase in free fatty acids and insulin. These changes result in a transient decrease in endothelium-derived nitric oxide production and in endothelium-mediated vasoconstriction. In persons without diabetes, endothelial nitric oxide production and vasodilation returns to normal within two hours. In the presence of diabetes, endothelial-mediated vasoconstriction extends for hours [15].

In addition to vasoconstriction, aggregation of platelets and an increase in leukocytes and coagulation products on the endothelium also occur. Fibrinolysis is decreased, and thrombosis is increased. As the secretion of prostacyclin and nitric oxide induce vasoconstriction, plasma cytokine and prothrombin levels increase, making the plasma markedly procoagulant and antifibrolytic and promoting atherosclerosis [12]. These changes at the microvascular and macrovascular levels lead to reduced vascular reactivity and impaired blood flow to end organs [15].

Defects in endothelial function may be further compounded by the hypercoagulable state of the patient with diabetes. Plasminogen activator inhibitor-1, antithrombin III (which inhibits fibrinolysis), and tissue plasminogen activator antigen (a marker of impaired fibrinolysis) are consistently elevated in individuals with diabetes or insulin resistance [16]. Over time, these changes may lead atheromatous plaques to form at branching and curves in the cerebral circulation. The smooth stenotic area can degenerate, resulting in an ulcerated area of the vessel wall. Platelets and fibrin adhere to the damaged wall and a clot forms, gradually occluding the artery and eventually causing a stroke [17].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American Diabetes Association asserts that cardiovascular disease risk factors should be identified and treated in all patients with prediabetes or type 2 diabetes.

(https://diabetesjournals.org/care/issue/45/Supplement_1. Last accessed May 20, 2022.)

Level of Evidence: Expert Opinion/Consensus Statement

TYPES OF CEREBROVASCULAR ACCIDENTS

The two primary types of stroke are ischemic and hemorrhagic. In the United States, approximately 87% of all strokes are ischemic and 13% are hemorrhagic [18]. An ischemic stroke occurs when any artery that supplies the brain with oxygen becomes stenosed or occluded, resulting in infarction [19]. In the case of hemorrhagic stroke, bleeding occurs below the arachnoid, the location of the brain's blood supply, allowing blood to directly contact and damage brain tissue. Research has linked diabetes (particularly poorly controlled type 2 diabetes) with ischemic stroke, a result of the disease's impact on vascular health and predisposition for atherosclerosis, as discussed [20]. The link between diabetes and hemorrhagic stroke is not well established. Therefore, the focus of this course will be on ischemic stroke.

Ischemic stroke can be further classified as either thrombolic or embolic depending on its origin. A thrombotic stroke occurs when a thrombus impairs cerebral blood flow by further narrowing or blocking an artery, typically around an atherosclerotic plaque. The stenosed or occluded artery may be a large vessel (e.g., carotid artery systems, vertebral arteries, the circle of Willis) or a small vessel (e.g., branches of the circle of Willis, the posterior circulation). Approximately 21% to 27% of ischemic strokes arise from atherosclerotic disease of the large vessels [21; 22]. In these cases, the cerebral artery branch points, especially those of the internal carotid artery, are the most vulnerable [23]. Small-vessel disease is associated with 21% to 25% of ischemic strokes [21; 22]. Thrombotic strokes caused by small-vessel disease are traditionally associated with lacunar infarcts, small, deep, subcortical lesions 15 mm or less in diameter resulting from occlusion of a single penetrating artery [24; 25]. As many as 20% of older individuals who are otherwise healthy have asymptomatic lacunar infarcts unrelated to an ictal event [26]. These silent infarctions were previously believed to be benign with a good long-term prognosis. However, they now have been linked to increased risks of stroke and death and can lead to debilitating cognitive impairments such as vascular dementia [26; 27]. Independent risk factors for lacunar infarcts include hypertension, gender, age, diabetes, smoking, and a history of transient ischemic attack (TIA) [26; 28].

An embolic stroke occurs when an embolus (i.e., any circulating clot or particle originating from a distal point) blocks an artery that supplies oxygen to the brain. Stroke registries indicate that 26% to 29% of ischemic strokes are embolic [21; 22]. Emboli include blood clots, fatty deposits, atherosclerotic plaque fragments, and cancerous cells or infectious materials emanating from conditions such as atrial myxoma and endocarditis, respectively. Clinical symptoms of the resulting infarct correspond to the location of the embolus, not its type. The region of the middle cerebral artery is most frequently blocked by emboli [29].

RISK FACTORS

As discussed, diabetes is a well-established risk factor for stroke, particularly ischemic stroke, and cerebrovascular disease. In addition to diabetes, other risk factors include [17; 30; 31]:

- Advanced age (older than 65 years)
- Positive family history
- Arterial hypertension (elevated systolic and/or diastolic blood pressure)
- Carotid artery disease
- Cigarette or cigar use
- Physical inactivity

GENERAL REGIONS OF ISCHEMIC STROKE AND CORRESPONDING NEUROLOGIC DEFICITS	
Affected Region	**Common Signs and Potential Sequelae**
Left anterior hemisphere	Aphasia (especially difficulty reading, writing, and calculating) Right limb weakness and sensory loss Right field visual defect
Right anterior hemisphere	Limb motor weakness or loss Left field visual neglect Unable to determine two-point stimuli on left side
Left posterior cerebral artery	Aphasia (esp. difficulty reading and naming objects) Right visual field defect Occasionally, right-sided numbness
Right posterior cerebral artery	Left limb sensory loss Left-sided neglect Left field visual defect
Vertebrobasilar territory (posterior circulation)	Bilateral vision disturbances and nystagmus Dysarthria and dysphagia Ataxia Dizziness, vomiting, headache No cortical deficits (e.g., aphasia and cognitive impairments)
Caudate nucleus, thalamus, frontal lobe (anterior circulation)	Sudden abnormal behavior
Thalamus (posterior circulation)	Numbness, decreased sensation in the face, arm, leg on same side
Source: [33; 34]	*Table 2*

- Hyperlipidemia
- Obesity
- Atrial fibrillation
- Cardiac conditions other than atrial fibrillation
- History of myocardial infarction or TIA
- Asymptomatic carotid stenosis
- Atherosclerosis of the aortic arch
- Postmenopausal hormone replacement therapy
- Polycythemia and thrombocythemia
- Alcohol or drug abuse
- Sleep-disordered breathing

SIGNS AND SYMPTOMS

The National Institute of Neurological Disorders and Stroke has identified the following signs and symptoms of stroke [17; 30; 32]:

- Sudden unilateral weakness or numbness of the face, arm, or leg
- Sudden loss of vision or dimming of vision
- Sudden aphasia or confusion
- Sudden severe headache
- Sudden falling, gait disturbance, or dizziness
- Hemiparesis or paralysis
- Homonymous hemianopia

The physical signs, symptoms, and sequelae of ischemic stroke are usually unilateral because of the circulatory anatomy of the brain (***Table 2***).

Because neurons surrounding the ischemic or infarcted tissues undergo changes that disrupt the plasma membranes, cellular edema ensues, resulting in further compression of capillaries. Cerebral edema reaches its maximum in about 72 hours and takes about two weeks to subside. Most individuals survive an initial hemispheric ischemic stroke cerebral vascular accident unless there is massive cerebral edema, which is typically fatal [17].

TREATMENT OF STROKE

Individuals who present with symptoms of cerebrovascular accident should have a full neurologic assessment by a practitioner [30]. After etiology is determined, treatment related to the causative source may be initiated. In thrombotic strokes, treatment is directed at prevention of ischemic injury [15]. Occlusions treated within 90 minutes of the onset of symptoms show the most improvement. Tissue plasminogen activator (t-PA) is recommended for select patients who may be treated within three hours after the onset of symptoms [24; 31]. In 2009, the American Heart Association/American Stroke Association (AHA/ASA) revised guidelines for administration of rt-PA after acute stroke, expanding the window of treatment from 3 hours to 4.5 hours. Eligibility criteria for treatment during this later period are similar to those for treatment within three hours, but also include the following exclusion criteria [24; 36; 37; 38]:

- Age older than 80 years
- Use of oral anticoagulants, regardless of the international normalized ratio (INR)
- Baseline score on the National Institutes of Health Stroke Scale (NIHSS) >25
- History of stroke and diabetes

As time goes on, there is a diminishing effect of treatment, and there may be almost no benefit when treatment is initiated more than six hours after onset [24; 39].

Between 31% and 50% of patients treated with rt-PA have a 4-point or greater NIHSS score improvement by three months after the stroke [24]. These clinical improvements do not recede for at least one year after the stroke. In general, the best response to rt-PA has been found for patients who are younger than 75 years of age and have a baseline NIHSS score greater than 20 [24].

The most common serious medical complication of rt-PA is secondary brain hemorrhage, which occurs in 6% of patients [24; 40]. Yet, the risk does not outweigh the benefits of rt-PA [41; 42]. In most cases, the mortality rate for patients receiving treatment or placebo is comparable at three months (17% compared with 20%) and one year (24% compared with 28%) [43; 44]. Other dangerous complications of rt-PA, although rare, are angioedema, anaphylaxis, systemic hemorrhage, and if rt-PA is administered soon after an acute MI, myocardial rupture [45].

MECHANICAL EMBOLECTOMY

Mechanical embolectomy may be an option for patients with acute stroke who are ineligible for intravenous rt-PA or who fail to respond to intravenous rt-PA [32; 46]. This procedure consists of a device that is threaded through the artery to remove the thrombus and restore blood flow. Mechanical embolectomy can remove a clot in a matter of minutes, compared with pharmaceuticals, which may take as long as two hours to dissolve a thrombus [47]. The procedure is effective for up to eight hours after the onset of symptoms [46]. Several different devices are available, and more are under review [32].

In 2004, the Merci Retriever became the first mechanical stroke device to be approved by the U.S. Food and Drug Administration (FDA) [47]. Although the Merci is still in use, in 2015, and again in 2019, the AHA/ASA issued updated guidelines for treatment of acute stroke, recommending the use of stent retrievers due to higher recanalization rates and better outcomes than those seen with the Merci [24; 47; 48; 49]. Newer stent retrievers include [47; 50; 51]:

- The Penumbra System
- The Stryker Trevo stent retriever
- The Solitaire stent retriever system

ANTICOAGULANTS

The AHA Task Force reviewed and discussed several studies addressing the use of heparin or low-molecular-weight heparin and danaparoid as an adjunct to a thrombolytic agent in the treatment of stroke [24]. In general, the Task Force concluded that early administration of heparin or low-molecular-weight heparin and danaparoid is inadvisable partly due to the increased risk of bleeding complications, especially the hemorrhagic transformation of ischemic strokes. Additionally, early administration has not been shown to prevent recurrent stroke, lessen the risk of neurologic worsening, or improve patient outcomes [24].

ANTIPLATELETS

Data combined from two large clinical trials suggest that administration of aspirin (160–300 mg) within 48 hours after the onset of stroke slightly reduces mortality and morbidity by preventing early recurrent stroke in some patients [52; 53]. A 2014 Cochrane review found that the daily administration of aspirin (160–300 mg) within 48 hours of onset of stroke reduced the risk of early recurrent stroke without a major risk of early hemorrhagic complications. Long-term outcomes were also improved [54]. Although no new data have emerged since the publication of these results, the 2018 AHA guideline recommendations for antiplatelet therapy have changed to include the administration of aspirin in patients with acute ischemic stroke within 24 to 48 hours after onset. For patients treated with IV alteplase, aspirin administration is generally delayed until 24 hours later but might be considered in select patients [24]. Other oral antiplatelet therapies (e.g., ticlopidine, clopidogrel, dipyridamole) have not been tested sufficiently in the setting of acute ischemic stroke. The efficacy of intravenous glycoprotein IIb/IIIa receptor blockers in combination with other interventions or alone is under investigation. These agents may accelerate spontaneous recanalization and improve microvascular patency [55]. If administered alone, these agents have been shown to have an adequate safety profile [56].

PREVENTION

Primary stroke prevention relies primarily on lifestyle changes to reduce the impact of modifiable risk factors, and this should be a part of the treatment plan for all patients with diabetes. Elimination of tobacco use via cigarettes or cigars should be stressed. In addition to smoking cessation, stress management techniques should be investigated to attempt to control hypertension. If these techniques do not succeed, medications may be necessary [12]. The combination of hyperglycemia and hypertension is thought to increase the risk of stroke [57]. The AHA recommends that the target blood pressure for individuals with diabetes be less than 130/80 mm Hg [57]. Pharmacologic therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) has been shown to be safe and effective in this population [57]. A low-cholesterol diet should be encouraged in order to address dyslipidemia [46]. In addition, lipid-lowering statins reduce the risk of first-time strokes in patients with diabetes, irrespective of the baseline lipid levels, pre-existing vascular conditions, or glycemic control [57]. Niacin, bile acid sequestrants, ezetimibe, or fibric acid derivatives may also be considered for individuals with known coronary heart disease and low levels of HDL cholesterol, such as people in whom target cholesterol levels cannot be achieved

with statins or tolerate statin therapy; however, their effectiveness in decreasing stroke risk has not been established [57]. Furthermore, statin therapy may increase the risk of type 2 diabetes in people at high risk of developing the disease. As such, patients taking statins should be monitored for hyperglycemia.

The ADA recommends that pioglitazone be considered for people with a history of stroke and evidence of insulin resistance and prediabetes, as this agent may lower the risk of stroke or myocardial infarction [69]. However, this benefit needs to be balanced with the increased risk of weight gain, edema, and fracture.

Obesity and excess weight place pressure on the entire circulatory system and are associated with hyperlipidemia, hypertension, and diabetes—all of which create an increased risk for cerebrovascular accidents. Adopting healthy eating habits and increasing physical activity can help reduce stroke risk in these patients [46].

Glycemic control is also essential in the prevention of stroke or extension of the injury. Intracellular acidosis resulting from hyperglycemia increases lactate, leading to glial and neuronal membrane damage due to reactive oxygen species generation and impaired vasodilatation. Potentially viable neurons in the ischemic penumbra are more likely to infarct under conditions of hyperglycemia, and research has demonstrated a disruption of the blood brain barrier associated with greater degrees of hemorrhage and cerebral edema. Hyperglycemia with or without a diagnosis of diabetes is associated with transformation from ischemic to hemorrhagic stroke [59]. Therefore, patients with diabetes should be encouraged to monitor their blood glucose levels regularly and remain compliant with prescribed medications.

KNOWLEDGE OF STROKE WARNING SIGNS

Although public knowledge regarding the warning signs and risks of stroke has improved, the majority of the general public is still unaware that early treatment can prevent severe disability and death [60; 61]. According to one estimate, five out of six people are unable to name the signs that signify a stroke [62]. Estimates vary widely, however. The International Stroke Trial found that only 4% of patients suffering an acute ischemic stroke arrive at the emergency department (ED) within three hours after the onset of symptoms, and a separate study found that 21% to 25% of individuals with acute ischemic stroke arrive at an ED within the same timeframe [63; 64]. Of these individuals, 2% to 4% receive thrombolytic treatment [65; 66]. It has been estimated that if all individuals called for emergency help at the onset of symptoms, as many as 29% could realistically receive treatment within three hours [65]. If all patients arrived at the ED within one hour after known symptom onset and received optimal treatment, the projected rate of thrombolysis would be 57%.

To improve the rate of early arrival in the ED, public education campaigns designed to help individuals recognize a stroke and seek early treatment often use the "five sudden warning signs" devised by the Brain Attack Coalition or "FAST," a mnemonic device created by study investigators on the basis of the Cincinnati Prehospital Stroke Scale [67; 68]. FAST was designed to focus on fewer common signs of stroke onset (face numbness, arm numbness, and slurred speech) and to include an action component (time) for lay persons who may have trouble recalling the warning signs and the appropriate action.

A retrospective study exploring the capacity of the FAST campaign to facilitate the recognition of stroke suggests that it leads to the identification of approximately 89% of individuals who have a stroke or TIA [68]. The most common stroke symptoms were related to the face, arm, and speech/language. The same study found that a modified version of FAST (with removal of the word "numbness") decreased the number of TIAs identified and targeted ischemic stroke more readily than hemorrhagic stroke. Ultimately, it is unknown whether the general public is more likely to remember FAST or the five sudden warning signs.

Another education program—Hip-Hop Stroke (HHS)—is a school-based, child-mediated, stroke communication intervention designed to improve stroke literacy among school-aged children and their parents in low-income urban communities [35]. Researchers recruited 3,070 fourth- through sixth-grade schoolchildren and 1,144 parents from 22 schools, randomized to the HHS intervention or attentional control (i.e., nutritional classes) [58]. Among the children, an estimated 1% of controls and 2% of the intervention group demonstrated optimal stroke preparedness (i.e., perfect scores on the knowledge/preparedness test) at baseline. This increased to 57% immediately following the program in the intervention group compared with 1% among controls. At three-month follow-up, 24% of the intervention group retained optimal preparedness, compared with 2% of controls. Only 3% of parents in the intervention group could identify all four letters of the stroke FAST acronym at baseline, which increased to 20% immediately post-test and to 17% at three months post-test. There were no significant changes among controls. Among children in the intervention group, four called 911 for real-life stroke symptoms, in one instance over-ruling a parent's wait-and-see approach [58].

CONCLUSION

Every year, thousands of individuals will die as a result of their diabetes complications, and stroke is one of the leading causes of death in this population. Good control of diabetes and of other causes of cerebrovascular disease can reduce the associated morbidity and mortality and improve patients' quality of life. Healthcare professionals play a crucial role in identifying patients with diabetes who are at risk for stroke and intervening to address modifiable factors. This course is intended to raise nurses' awareness of the connection between diabetes and stroke in order to improve patient care.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

Works Cited

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. Available at https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf. Last accessed May 1, 2022.
2. Cornell S, Halstenson C, Miller DK (eds). *The Art and Science of Diabetes Self-Management Education: Desk Reference*. 5th ed. Chicago, IL: American Association of Diabetes Educators; 2020.
3. International Diabetes Federation. What Is Diabetes? Available at https://www.idf.org/aboutdiabetes/what-is-diabetes. Last accessed May 17, 2022.
4. Diabetes Pro. Fast Facts: Data and Statistics About Diabetes. Available at https://professional.diabetes.org/content/fast-facts-data-and-statistics-about-diabetes. Last accessed May 10, 2022.
5. Saeedi P, Petersohn I, Salpea P, et al. *Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas*. 9th ed. Amsterdam, Netherlands: Diabetes Research and Clinical Practice; 2019.
6. Centers for Disease Control and Prevention. Diagnosed Diabetes. Available at https://gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html. Last accessed May 10, 2022.
7. Kissela BM, Khoury J, Kleindorfer D, et al. Epidemiology of ischemic stroke in patients with diabetes: the greater Cincinnati/northern Kentucky stroke study. *Diabetes Care*. 2005;28(2):355-359.
8. Centers for Disease Control and Prevention. Prevalence of Cardiovascular Disease: Stroke. Available at https://gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html. Last accessed May 10, 2022.
9. American Diabetes Association. Standards of medical care in diabetes—2022. *Diabetes Care*. 2022;41(Suppl 1):S17-S38.
10. Childs BP, Cypress M, Spollett G (eds). *Complete Nurse's Guide to Diabetes Care*. 3rd ed. Alexandria, VA: American Diabetes Association; 2017.
11. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2016;39(Suppl 1):S1-S106.
12. Westerfield J, Holcomb S, Jensen S (eds). *Current Trends in Diabetes Management: A Guide for the Healthcare Professional*. 7th ed. Nashville, TN: Healthways; 2008.
13. Southerland JH, Taylor GW, Offenbacher S. Diabetes and periodontal infection: making the connection. *Diabetes Care*. 2005;23(4):171-178.
14. Madhu SV. Endothelial dysfunction and diabetes. *JAPI*. 2010;58:475-476.
15. Lorber D. Macrovascular disease in diabetes. In: Mensing C (ed). *The Art and Science of Diabetes Self-Management Education: A Desk Reference for Healthcare Professionals*. Chicago, IL: American Association of Diabetes Educators; 2006:475-510.
16. Air EL, Kissela BM. Diabetes, the metabolic syndrome, and ischemic stroke: epidemiology and possible mechanisms. *Diabetes Care*. 2007;30(12):3131-3140.
17. Boss BJ, Huether SE. Alterations in cognitive systems, cerebral hemodynamics, and motor function. In: Huether SE, McCance KL, Brashers VL (eds). *Understanding Pathophysiology*. 7th ed. St. Louis, MO: Mosby; 2020: 351-383.
18. Centers for Disease Control and Prevention. Stroke Facts. Available at https://www.cdc.gov/stroke/facts.htm. Last accessed May 11, 2022.
19. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol*. 2003;2(1):43-53.
20. Hyvärinen M, Tuomilehto J, Mähönen M, et al. Hyperglycemia and incidence of ischemic and hemorrhagic stroke: comparison between fasting and 2-hour glucose criteria. *Stroke*. 2009;40(5):1633-1637.
21. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of incidence and risk factors. *Stroke*. 1999;30(12):2513-2516.
22. Grau AJ, Weimar C, Buggle F, et al. Risk factors, outcome, and treatment in subtypes of ischemic stroke: the German Stroke Data Bank. *Stroke*. 2001;32(11):2559-2566.
23. Frishman W, Ismail A. Role of infection in atherosclerosis and coronary artery disease: a new therapeutic target? *Cardiol Rev*. 2002;10(4):199-210.
24. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50(12):e344-e418.
25. Donnan G, Norrving B, Bamford J, Bogousslavsky J. Classification of subcortical infarcts. In: Donnan G, Norrving B, Bamford J, Bogousslavsky J (eds). *Subcortical Stroke*. 2nd ed. Oxford: Oxford Medical Publications; 2002: 27-34.
26. Vermeer SE, Longstreth WT Jr, Koudstaal PJ. Silent brain infarcts: a systematic review. *Lancet Neurol*. 2007;6(7):611-619.
27. Bokura H, Kobayashi S, Yamaguchi S, et al. Silent brain infarction and subcortical white matter lesions increase the risk of stroke and mortality: a prospective cohort study. *J Stroke Cerebrovasc Dis*. 2006;15(2):57-63.

28. Tuttolomondo A, Pinto A, Salemi G, et al. Diabetic and non-diabetic subjects with ischemic stroke: differences, subtype distribution and outcome. *Nutr Metab Cardiovasc Dis*. 2008;18(2):152-157.
29. Olsen TS. Regional cerebral blood flow after occlusion of the middle cerebral artery. *Acta Neurol Scand*. 1986;73(4):321-337.
30. Davis FA (ed). *Taber's Cyclopedic Medical Dictionary*. 24th ed. Philadelphia, PA: FA Davis Company; 2021.
31. Jauch EC. Ischemic Stroke Treatment and Management: Mechanical Thrombectomy. Available at https://emedicine.medscape.com/article/1916852-treatment. Last accessed May 12, 2022.
32. National Institute of Neurological Disorders and Stroke. Transient Ischemic Attack Information Page. Available at https://www.ninds.nih.gov/Disorders/All-Disorders/Transient-Ischemic-Attack-Information-Page. Last accessed May 12, 2022.
33. Hewko C. Acute ischemic stroke: swift assessment and quick action produce optimal outcomes. *JAAPA*. 2004;17(7):19-25.
34. Savitz SI, Caplan LR. Vertebrobasilar disease. *N Engl J Med*. 2005;352(25):2618-2626.
35. Williams O, Leighton-Hermann E, DeSorbo A, et al. Hip Hop Stroke: study protocol for a randomized controlled trial to address stroke literacy. *J Clin Trials*. 2015;5(5):pii:242.
36. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*. 2008;359(13):1317-1329.
37. Del Zoppo GJ, Saver JL, Jauch EC, Adams HP Jr. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator: a science advisory from the American Heart Association/American Stroke Association. *Stroke*. 2009;40(8):2945-2948.
38. Wahlgren N, Ahmed N, Dávalos A, et al. Thrombolysis with alteplase 3–4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. *Lancet*. 2008;372(9646):1303-1309.
39. Emberson J, Lees KR, Lyden P, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. *Lancet*. 2014;384(9958):1929-1935.
40. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Intracerebral hemorrhage after intravenous t-PA therapy for ischemic stroke. *Stroke*. 1997;28(11):2109-2118.
41. Diedler J, Ahmed N, Sykora M, et al. Safety of intravenous thrombolysis for acute ischemic stroke in patients receiving antiplatelet therapy at stroke onset. *Stroke*. 2010;(2):288-294.
42. Xian Y, Federspiel JJ, Grau-Sepulveda M, et al. Risks and benefits associated with prestroke antiplatelet therapy among patients with acute ischemic stroke treated with intravenous tissue plasminogen activator. *JAMA Neurol*. 2016;73(1):50-59.
43. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med*. 1995;333(24):1581-1587.
44. Kwiatkowski TG, Libman RB, Frankel M, et al. for the National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator Stroke Study Group. Effects of tissue plasminogen activator for acute ischemic stroke at one year. *N Engl J Med*. 1999;340(23):1781-1787.
45. Lyden PD. *Thrombolytic Therapy for Acute Stroke*. 3rd ed. Totowa, NJ: Humana Press; 2015.
46. National Stroke Association. Stroke Treatments. Available at https://www.stroke.org/en/about-stroke/treatment. Last accessed May 16, 2022.
47. Lutsep HL. Mechanical Thrombolysis in Acute Stroke. Available at https://emedicine.medscape.com/article/1163240-overview. Last accessed May 16, 2022.
48. Powers WJ, Derdeyn CP, Biller J, et al. 2015 AHA/ASA focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46(10):3020-3035.
49. Hassan AE, Aman MM, Chauhdry SA, et al. Value of other endovascular techniques among patients with MERCI device failure during the treatment of acute ischemic stroke: what to do when MERCI fails? *J Vasc Interv Neurol*. 2013;5(2):27-31.
50. Jeffrey S. Solitaire Device for Stroke Gets FDA Nod. Available at https://www.medscape.com/viewarticle/759773. Last accessed May 16, 2022.
51. Stryker.com. Stryker's Trevo Retriever Becomes First and Only Device Indicated for Treatment Up to 24 Hours, Aligning with New AHA/ASA Guidelines. Available at https://www.stryker.com/us/en/about/news/2018/stryker_s-trevo-retriever-becomes-first-and-only-device-indicat.html. Last accessed May 16, 2022.
52. Chinese Acute Stroke Trial (CAST) Collaborative Group. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. *Lancet*. 1997;349(9066):1641-1649.
53. International Stroke Trial Collaborative Group. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. *Lancet*. 1997;349(9065):1569-1581.
54. Sandercock PA, Counsell C, Tseng MC, Cecconi E. Oral antiplatelet therapy for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2014;3:CD000029.

55. Lapchak PA, Araujo DM. Therapeutic potential of platelet glycoprotein IIb/IIIa receptor antagonists in the management of ischemic stroke. *Am J Cardiovasc Drugs*. 2003;3(2):87-94.
56. Abciximab Emergent Stroke Treatment Trial (AbESTT) Investigators. Emergency administration of abciximab for treatment of patients with acute ischemic stroke: results of a randomized phase 2 trial. *Stroke*. 2005;36(4):880-890.
57. Kleindorfer DO, Towfighi A, Chaturvedi S. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. Stroke. 2021;52(7):e364-e467.
58. Williams O, Leighton-Herrmann Quinn E, Teresi J, et al. Improving community stroke preparedness in the HHS (Hip-Hop Stroke) randomized clinical trial. *Stroke*. 2018;49(4):972-979.
59. Bloomgarden ZT. Inpatient diabetes control: approaches to treatment. *Diabetes Care*. 2004;27(9):2272-2277.
60. Müller-Nordhorn J, Nolte CH, Rossnagel K, et al. Knowledge about risk factors for stroke: a population-based survey with 28,090 participants. *Stroke*. 2006;37(4):946-950.
61. Schneider AT, Pancioli AM, Khoury JC, et al. Trends in community knowledge of the warning signs and risk factors for stroke. *JAMA*. 2003;289(3):343-346.
62. Miller-Hoover S. Stroke Awareness: Act F.A.S.T. Available at https://www.rn.com/nursing-news/stroke-awareness-act-fast. Last accessed May 16, 2022.
63. Rosamond WD, Gorton RA, Hinn AR, Hohenhaus SM, Morris DL. Rapid response to stroke symptoms: the Delay in Accessing Stroke Healthcare (DASH) study. *Acad Emerg Med*. 1998;5(1):45-51.
64. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. *Lancet*. 1997;349(9065):1569-1581.
65. California Acute Stroke Pilot Registry (CASPR) Investigators. Prioritizing interventions to improve rates of thrombolysis for ischemic stroke. *Neurology*. 2005;64(4):654-659.
66. Wattigney WA, Croft JB, Mensah GA, et al. Establishing data elements for the Paul Coverdell National Acute Stroke Registry. Part 1: proceedings of an expert panel. *Stroke*. 2003;34(1):151-156.
67. Kothari R, Pancioli A, Liu T, Brott T, Broderick J. Cincinnati Prehospital Stroke Scale: reproducibility and validity. *Ann Emerg Med*. 1999;33(4):373-378.
68. Kleindorfer D, Miller R, Moomaw CJ, et al. Designing a message for public education regarding stroke: does FAST capture enough stroke? *Stroke*. 2007;38(10):2864-2868.
69. ElSayed NA, Aleppo G, Aroda VR, et al. Prevention or delay of type 2 diabetes and associated comorbidities: Standards of Care in Diabetes—2023. *Diabetes Care*. 2023;46(Supplement_1):S41–S48.

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