Prevention of Strokes Caused By Sickle Cell Anemia, Ischemiaor Hemorrhage

Kang Cheng*

Department of Basic Medicine, Medical School, Qingdao Binhai University, Qingdao, P.R. China

---

*Corresponding Author: *Kang Cheng, Department of Basic Medicine, Medical School, Qingdao Binhai University, Qingdao, P.R. China,* **Email:** *Kangcheng.1@netzero.net*

Abstract:

Purposes: *To propose models of prevention of strokes caused by sickle cell anemia, Ischemiaor hemorrhageas well as models of blood (cells) velocities in arteries (or capillaries) with different cross sections.*

Methods: *Published hematologic data and hemadynamics theories are applied or referenced.*

Modeling Results: *When there are sickle cells, emboli (or thrombi) in or external obesity tissues around an artery (or capillary), the action and reaction forces between the blood vessel wall and the external fats increase. The forces reduce the compliance (or elasticity) of the vessel. The sickle cells, fats, emboli or thrombi narrow the artery (or capillary); increase the pressure and resistancewithin the vessel; block the blood (cells) flowing; cause anemia or ischemiastrokes; or raise the flowing velocities. The raised velocities increase risks of hemorrhage strokes. A hemorrhage strokeis modeled as an artery with hematoma or hypertensionand too little external fatty tissues. The models explain why or how fats increase and decrease probabilities of anemic, ischemic and hemorrhage strokes respectively*

Conclusions: *As long as we completely and moderately ingest nutrients daily as well as maintain our mental and physical health, we can prevent most strokes caused by sickle cell anemia, ischemia or hemorrhage. The smaller the cross section of a blood vessel, the faster the velocity, for the blood (cells) flowing.*

Keywords: *strokes, sickle cell, anemia, ischemia, hemorrhage, emboli, thrombi, obesity, hematoma*

Abbreviations: *CVR- Cerebrovascularaccident, RBC- Red blood cells, SCA- Sickle cell anemia, TCD - Transcranial Doppler, TMA- thrombotic microangiopathy, ICH- Intracerebral haemorrhage, BMI- Body mass index, VTE- Venous thrombo embolism, DVT-Deep vein thrombosis, PE- Pulmonary embolism*

1. INTRODUCTION

Neuronsare very sensitive to oxygen deprivation and will start to deteriorate within 1 or 2 minutes, and permanent damage (cell death) could result within a few hours. The loss of blood flow to part of the brain is known as astroke, or a cerebrovascular accident (CVA) [1-2]. Sickle cell anemia is a genetic disorder. A characteristic change of erythrocytes (red blood cells, RBC) is a sickle shape. It is caused by production of an abnormal type of hemoglobin, called hemoglobin S, which delivers less oxygen to tissues and causes erythrocytes to assume a sickle (or crescent) shape, especially at low oxygen concentrations. These abnormally shaped cells can then become lodged in narrow capillaries because they are unable to fold in on themselves to squeeze through, blocking blood flow to tissues and lead a stroke: a sickle cell anemic stroke. [1-2]. Cerebrovascular disease is an important complication in children with this condition. In sickle cell anemia, the peak incidence of overt stroke is 1.02 per 100 patient years between the ages of two and five years [3-4].Most cases of stroke in children with sickle cell anemia are associated with narrowing of large intracranial arteries. Transcranial Doppler (TCD) scanning demonstrated that high blood velocities in the middle cerebral artery (MCA) were strongly associated within creased risk of stroke [4-5]. Additionally, thrombotic microangiopathy (TMA) syndromes are characterized by endothelial dysfunction, microangiopathic hemolytic anemia, and micro vascular ischemia, with diverse etiologies that include drugs [6]. Anischemic strokeis the loss of blood flow to an area because vessels are blocked or narrowed. This is often caused by anembolus, which may be a blood clot, fat deposit [1-2, 7-10],a thrombus [4-5], thrombocythemia [11] or anatherosclerotic plaque [12]. A hemorrhagic stroke is bleeding into the brain because of a damaged blood

vessel. Accumulated blood fills a region of the cranial vault and presses against the tissue in the brain. Physical pressure on the brain can cause the loss of function, as well as the squeezing of local arteries resulting in compromised blood flow beyond the site of the hemorrhage [1-2]. A pooled analysis of 97 prospective cohorts with 1·8 million participants elucidate: obesity increases risks of strokes [11]. This analysis report is consistent with other research results [1-2, 7-10, 14-15]; and obesity has been found to be an independent risk factor for stroke [8]. Two critical reviews reported: within an individual, obesity may co-occur with anemia, due to shared underlying determinants or physiologic links. The co-existence of under- and over nutrition, a phenomenon known as the "dual burden", poses a novel public health challenge and a threat to children's health in low- and middle-income countries [16-17]. Hemorrhagic stroke is a severe stroke subtype with high rates of morbidity and mortality [18].The majority of non-traumatic intracerebral hemorrhages (ICHs, primary ICH) originate from the spontaneous rupture of small vessels damaged by chronic hypertension or amyloid angiopathy.ICH is well-known for its high overall stroke mortality and disability. It carries a 1-year fatality of >50% [19]. Obesity was associated with an increased risk of ischemic stroke and a decreased risk of hemorrhagic stroke (heterogeneity $p < 0.0001$) [20]. Based on above published data, I consider a comprehensive study and propose my models of prevention of strokes caused by sickle cell anemia, ischemia or hemorrhageas well as models of blood (cells) velocities in arteries (or capillaries) with different cross sections, in this article.

2. METHODS

Published hematologic data and hemadynamics theories [21-22] are applied or referenced. Obesity is defined by the body mass index (BMI), which is a measure of an individual's weight-to-height ratio. The normal, or healthy, BMI range is between 18 and 24.9 kg/m^2. Overweight is defined as a BMI of 25 to 29.9 kg/m^2,and obesity is considered to be a BMI greater than 30 kg/m^2 [1].

3. MODELING RESULTS

Compliance (or elasticity) allows an artery (or capillary) to expand when blood is going through it, and then to recoil after the surge has passed. This helps promote blood flow [1].

When there are sickle cells, emboli (or thrombi) in or external obesity tissues around an artery (or capillary), the action and reaction forces between the blood vessel wall and the external fats increase. The forces reduce the compliance (or elasticity) of the vessel. The sickle cells, fats, emboli or thrombi narrow the artery (or capillary); increase the pressure and resistance within the vessel; block the blood (cells) flowing; cause anemia or ischemia strokes (Figure 1 and 2); or raise the flowing velocities (Figure 3).
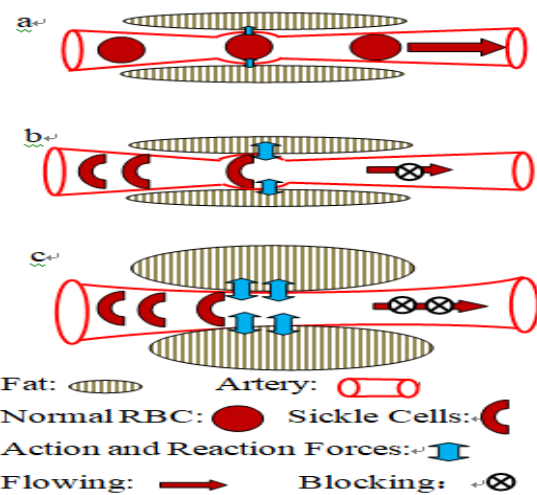

Figure1. *Strokes, normal RBC, sickle cells, external fats and arteries (or capillaries): (a) normal RBC are going through an artery with external normal fatty tissues; (b) sickle cells are blocked inan artery with external normal fatty tissues; (c) sickle cells are blocked inan artery with external obesity tissues. See the text. The draw is not to the scale*
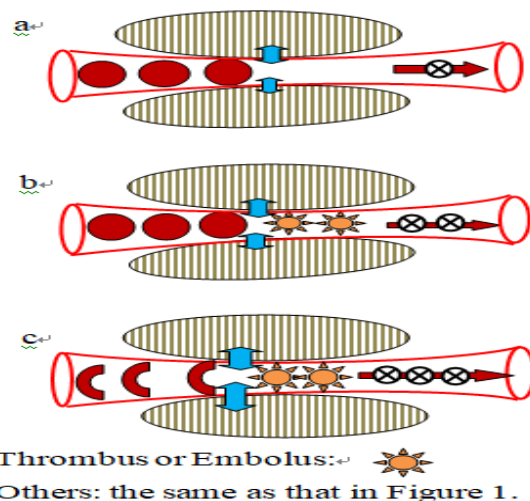

Figure2. *Strokes, normal RBC, sickle cells, emboli (or thrombi) and arteries (or capillaries) with external obesity tissues: (a) normal RBC are blocked in an artery; (b) normal RBC are blocked in an artery with emboli; (c) sickle cells are blocked in an artery with emboli. See the text. The draw is not to the scale*

Figure1 illustrates my models of strokes, normal RBC, sickle cells, and arteries (or capillaries) with external fats: (a) There is not any block when normal RBC are going through theartery with external normal fatty tissues; (b) when sickle cells are blocked in the artery with external normal fatty tissues, a stroke caused by an anemia or ischemia probably occurs; (c) when sickle cells are blocked in the artery with external obesity tissues, a stroke caused by an anemia or ischemia occurs more probably.

Figure 2 illustrates my models of strokes, normal RBC, sickle cells, fats, emboli (or thrombi) and arteries (or capillaries) with external obesity tissues: (a) when normal RBC are blocked in the artery, a stroke caused by an ischemia probably occurs; (b) when normal RBC are blocked in the artery with emboli, a stroke caused by an ischemia occurs more probably; (c) when sickle cells are blocked in the artery with emboli, a stroke caused by an anemia or ischemia occurs most probably. Here, the external fatty tissues play a role to increase the probability of anemia or ischemia strokes.

Figure 3 illustrates my models of blood (cells) velocities, normal RBC, sickle cells, fats, emboli (or thrombi) and arteries (or capillaries)with external obesity tissues: (a) when normal RBC are going through the artery, the flowing velocities increase if the blood vessel is narrowed; (b) when normal RBC are going through theartery with emboli, the flowing velocities increase more if the blood vessel is narrowed more; (c) when sickle cells are going through the artery with emboli, the flowing velocities increase most, if the blood vessel is narrowed most. Therefore, the smaller the cross section of a blood vessel, the faster the velocity, for the blood (cells) flowing. The raised velocities increase risks of hemorrhage strokes, especially in curved blood vessels, based on hemadynamics theories [21-22]

Figure 4 illustrates my models of strokes, normal RBC, arteries (or capillaries) with external fatty tissues and hematoma or hypertension: when normal RBC are going through an artery [18] and too little external fatty tissues(a), a stroke caused by a hemorrhage probably occurs more often compared to that with external normal fatty (b) and obesity (c)tissues [20]. Here, the external fatty tissues protect blood vessels from rupture or burst. Therefore, the fats play a role to decrease the probability of a hemorrhage stroke.

Published data showed, the emboli (or thrombi) and obesity strongly correlate the strokes [7-14]; and emboli and obesity are mostly caused by over intake of high energy nutrients [1-2]. Therefore, as long as we completely and moderately ingest nutrients daily as well as maintain our mental and physical health (not too slim and nor too fat) [23-24], we can prevent most strokes caused by sickle cell anemia, ischemia or hemorrhage.
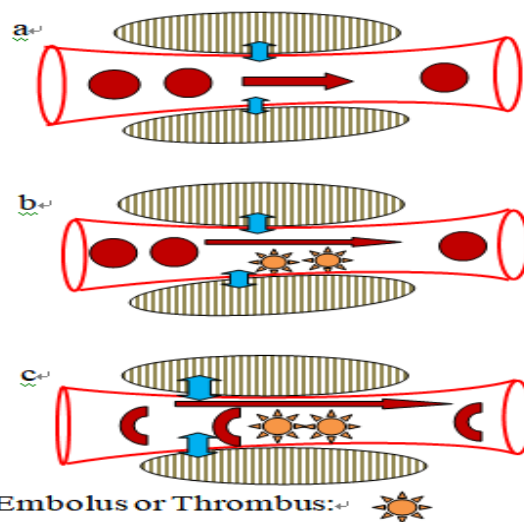

Figure3. *Blood (cells) velocities, normal RBC, sickle cells, fats, emboli (or thrombi) and arteries (or capillaries) with external obesity tissues: (a) normal RBC are going through an artery; (b) normal RBC are going through an artery with emboli; (c) sickle cells are going through an artery. See the text. The draw is not to the scale*
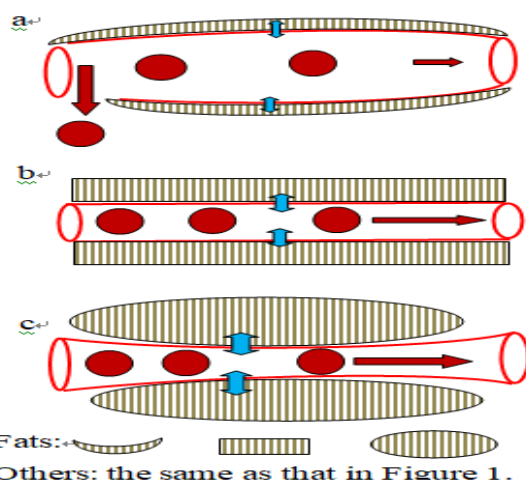

Figure4. *Strokes, normal RBC, fats and arteries (or capillaries) with external fatty tissues, hematoma or hypertension: (a) when normal RBC are going and (or) bleeding in an artery with too little external fatty tissues; (b) normal RBC are gonging through an artery with external normal fatty tissues; (c) normal cells are going through an artery with external obesity tissues. See the text. The draw is not to the scale*

4. DISCUSSIONS

For the co-occuring disease of obesity and anemia, we must remain committed to reducing under nutrition while simultaneously preventing over nutrition, through integrated health programs that incorporate prevention of infection, diet quality, and physical activity. [16-17].

Although my models in this paper focus on preventing a stroke or a cerebrovascular accident (CVA), I believe the principles in this study are also helpful to prevent other diseases, such as amyocardial infarction, or an atherosclerotic plaque (atherosclerosis); venous thrombo embolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) [25-26].

5. CONCLUSIONS

As long as we completely and moderately ingest nutrients daily as well as maintain our mental and physical health, we can prevent most strokes caused by sickle cell anemia, ischemia or hemorrhage. The smaller the cross section of a blood vessel, the faster the velocity, for the blood (cells) flowing.

REFERENCES

[1] OpenStax College, Anatomy &Physiology. OpenStax College. 2013. <http://cnx.org/content/col11496/latest/>.

[2] Young K, Human Physiology.Creative Commons Attribution-ShareAlike 3.0 Unported license. 2013. <http://de.wikibooks.org/wiki/Benutzer:Dirk_Huenniger/wb2pdf>.

[3] Ohene-Frempong K, Weiner SJ, Sleeper LA,Miller ST, Embury S, Moohr JW, et al.Cooperative study of sickle cell disease:cerebrovascular accidents in sickle cell disease:rates and risk factors. Blood1998; 91(1):288-94.

[4] Deane CR, Goss D, Colin R. Deane,Bartram J, et al. Extracranial internal carotid arterial disease in children with sickle cell anemia. Haematologica 2010; 95(8): 1287-1292.

[5] Adams RJ, McKie VC, Nichols FT, Carl E,Zhang DL, McKie K, et al. The use of transcranialultrasonography to predict strokein sickle cell disease. N Engl J Med 1992;326(9):605-10.

[6] Kavanagh D, McGlasson S, Jury A, Williams J, Scolding N, Bellamy C,Type I interferon causes thrombotic microangiopathy by a dosedependent toxic effect on the microvasculature. Blood 2016; 128(24): 2824–2833. doi: 10.1182/blood-2016-05-715987.

[7] Andersen KK, Steding-Jessen M,Dalton SO, Olsen TS. Socioeconomic Position and Incidence of Ischemic Stroke in Denmark 2003–2012. A Nationwide Hospital-Based Study. J Am Heart Assoc2014;3:e000762. doi: 10.1161/JAHA.113.000762

[8] Haley MJ, Lawrence CB. Obesity and stroke: Can we translate from rodents to patients?J Cereb Blood Flow Metab 2016; 36(12): 2007–2021.

[9] Xia X,et al. Prevalence and risk factors of stroke in the elderly in Northern China: data from the National Stroke Screening. Journal of Neurology 2019; 266:1449–1458.https://doi.org/10.1007/s00415-019-09281-5.

[10] Lee HJ. Risk of ischemic stroke in metabolically healthy obesity: A nationwide population-based study. PLoS One 2018; 13(3): e0195210. doi: 10.1371/journal.pone.0195210.

[11] Lazzaro MA, Cochran EJ, Lopes DK, Prabhakaran S. Moyamoya syndrome in an adult with essential Thrombocythemia. Neurology International 2011; 3: e3

[12] Teng Z, Sadat U, Brown AJ, Gillard YH.Plaque hemorrhage in carotid artery disease: Pathogenesis, clinical and biomechanical considerations J Biomech. 2014; 47(4): 847–858. doi: 10.1016/j.jbiomech.2014.01.013: 10.1016/j.jbiomech.2014.01.013.

[13] Danaei G. Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1·8 million participants. Lancet 2014; 383(9921): 970–983.doi: 10.1016/S0140-6736(13)61836-X: 10.1016/S0140-6736(13)61836-X.

[14] Olofindayo J, Peng H, Liu Y,et al. The interactive effect of diabetes and central obesity on stroke: a prospective cohort study of inner Mongolians. BMC Neurology 2015; 15:65 DOI 10.1186/s12883-015-0328-y.

[15] Kabootari M, Asgari S, Mansournia MA, Khalili D, Valizadeh M, Azizi F, Hadaegh F. Different weight histories and risk of incident coronary heart disease and stroke: Tehran lipid and glucose study. J Am Heart Assoc 2018; 7:e006924. DOI: 10. 1161/JAHA.117.006924.

[16] Tzioumis E, Adair LS.Childhood dual burden of under- and over-nutrition in low- and middle-income countries: a critical review.Food Nutr Bull 2014; 35(2): 230–243.

[17] Samper-Ternent R, Michaels-Obregon A,Wong R. Coexistence of obesity and anemia in older Mexican adults. Ageing Int 2011; 37(1): 104–117. Doi: 10.1007/s12126-011-9135-y.

[18] Chen S,Zeng L,Hu Z. Progressing haemorrhagic stroke: categories, causes, mechanisms and managements.J Neurol 2014;

261:2061–2078. DOI 10.1007/s00415-014-7291-1

[19] Tsai HH,Kim JS, Jouvent E, Gurole E. Updates on Prevention of Hemorrhagic and Lacunar Strokes. Stroke 2018; 20(2): 167-179. https://doi.org/10.5853/jos.2018.00787.

[20] Price AJ, Wright FL, Green J, Balkwill A, Kan SW, et al. Differences in risk factors for 3 types of stroke UK prospective study and meta-analyses.Neurology2018;90:e298-e306. doi:10.1212/WNL.0000000000004856.

[21] Fung YC.Biodynamics Circulation. Springer, New York, NY, USA, (1984).

[22] Fung YC.Biomechanics, Mechanics Properties of Living Tissues.Springer,New York, NY, USA, (1996).

[23] Cheng K. A model of primary and secondary preventions of lymphedema of superficial lymphatic system using warm running water and massage. Archives of Hematology and Blood Diseases 2018; 1(2): 25-27.

[24] Cheng K, Cheng V, Zou C. Modeling health oriented lifelong learning (HOLL) to prevent, delay and/or treat aging or aged dementias caused by less mentally stimulating activities. Frontiers Drug Chemistry Clinical Res 2018;1(2): 1-6, doi: 10.15761/FDCCR.1000107.

[25] Freeman AL, Pendleton RC, Rondina MT. Prevention of venous thromboembolism in obesity. Expert Rev Cardiovasc Ther 2010; 8(12): 1711–1721. doi:10.1586/erc.10.160.

[26] Cascio V, Hon M, Haramati LB, Gour A, Spiegler P, Bhalla S, et al. Imaging of suspected pulmonary embolism and deep venousthrombos is in obese patients. Br J Radiol 2018; 91: 20170956.