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ISKANDAROVA DILNOZAKHON ERGASHENA'S

"EARLY, MODERN WAY OF DIAGNOSIS AND TREATMENT OF CHILDREN'S STROKE"

5A 510205 -"CHILDREN'S NEUROLOGY"

Dissertation was written to get master's degree

Scientific advisor: docent Abdukadirov U.T.

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Annotation

The urgency of the problem.

Stroke has been increasingly recognized in children in recent years, but diagnosis and management can be difficult because of the diversity of underlying risk factors and the absence of a uniform treatment approach.

The World Health Organization definition of stroke (a clinical syndrome of rapidly developing focal or global disturbance of brain function lasting >24 hours or leading to death with no obvious nonvascular cause) is far from ideal for children. Children with symptoms compatible with a transient ischemic attack (TIA), for example, commonly have a brain infarction shown by brain imaging despite the transient nature of their symptoms. Children with cerebral venous sinus thrombosis (CVST) commonly present with headache or seizures. "Stroke-like episodes" without an obvious vascular cause may occur in migraine or metabolic disease but may require specific treatment. Prior illness (e.g., infection) or events (e.g., head trauma) need not preclude a diagnosis of stroke. Although extra-axial

hematomas, neonatal intraventricular hemorrhages (IVHs), and periventricular leukomalacia arise from cerebrovascular dysfunction in a broad sense, they are not considered in detail here.

Pediatric stroke affects 25 in 100,000 newborns and 12 in 100,000 children under 18 years of age. High rate of complications leading to invalidation of children with acute disorder of the blood circulation in the brain and recurrence of stroke in 20% of cases require specific method in determining it at early stages. This pathology leads to death in 14% of cases and there is stable neurologic deficit in 70% of cases. The best prevention against stroke is control and management of risk factors.

There are 2 main types of stroke: ischemic and haemorrhagic.

Pediatric arterial ischemic stroke (AIS) is an important cause of long-term morbidity and is among 1 of the top 10 reasons for death in children [1, 2]. Although it occurs in 2 to 3 children per 100,000 children per year, with an increased incidence of about 1 in 4000 during the perinatal or neonatal period, accurate diagnosis is commonly delayed or missed [2]. As such, increasing recognition of the signs and symptoms of this significant cause of morbidity and mortality in children is critical to improving diagnosis and providing optimal treatment.

Pediatric hemorrhagic stroke has an incidence of 1.1 per 100,000 person-years and encompasses subarachnoid hemorrhage and intracerebral (parenchymal) hemorrhage. Given the rarity of the condition and the under-recognition of cerebrovascular disease in children, it is not surprising that hemorrhagic stroke in children has not been well studied. This thesis will focus on information needed to move the field forward in terms of predicting hemorrhagic stroke etiology and outcome, as well as on improving treatment options [27].

With an incidence of 2–3/100,000 children, stroke is among the top ten causes of death in childhood [28, 29], and is as common as brain tumor in children [30]. A study of a California-wide hospital discharge database found an incidence rate of 1.1 per 100,000 person-years for hemorrhagic stroke and 1.2 per 100,000

person-years for ischemic stroke [31]. Thus, nearly half of pediatric strokes are hemorrhagic. Typically, the term “hemorrhagic stroke” (HS) includes spontaneous intraparenchymal hemorrhage (IPH) and non-traumatic subarachnoid hemorrhage (SAH). Patients with traumatic IPH, primary subdural or epidural hematomas, or hemorrhagic transformation of ischemic stroke are usually not considered to have a hemorrhagic stroke [32, 33]. For the purposes of this article, we will focus on IPH, the most common type of HS. Non-traumatic SAH is most often due to intracranial aneurysm and is evaluated and treated differently, though like IPH, recommendations for childhood SAH are based on the adult literature. Two recent pediatric intracranial aneurysm case series and reviews of the literature are available [34, 35].

The purpose of the research

To define the modern early way of diagnosing, revealing an optimal treatment, preventing measures and evaluating patients with children’s stroke diagnosis.

The tasks

1. Checking, comparing and analyzing patients and case history with children’s stroke diagnosis in the children’s multi-disciplinary medical center of Andijan region during 2014-2015 years.
2. To learn etiology of children’s stroke.
3. To examine changes at MRI and ultra sound duplex scanner analyses.
4. To estimate effects of neuprotective drugs on optimal treatment of childhood stroke.

Materials

We had examined 78 children from the 1-month of life to 16 years old with acute disorder blood circulation of the brain and its complication in the children’ medical center of Andijan region during 2013-2015 years. There were 20 practical healthy children.

Methods of investigation

1. Anamnesis and clinical-neurological examination.
2. Investigation with medical instruments (MRI, USDS, laboratory analyses).

3. Information of statistics.

Main results and conclusion:

1. According to clinical-neurological and neurovisual results, it had been done differential diagnosis acute disorder of blood circulation in the brain between ischemic and hemorrhagic types in children, as such, in newborns.

2.Neurological statues of ADBCB characterized with hemiplegia, psychomotorical and intellectual developing were late.

3. Occupational effects of complex rehabilitation were estimated positively on clinical-neurological and hemodynamically parameters of brain in children with ADBCB and its influence.

4. It had been defined and worked statistical analyses.

Scientific newness

1. Children's stroke statistical analyzed and gave conclusion for these years.
2. Etiology of children's stroke learned etiology of children's stroke and preventive measure revealed for childhood stroke.
3. The hearth of defeat in the brain determined, comparing due to MRT, USDS and increased effect of treatment of children's stroke.
4. Effects of neuroprotectors at treatment of ChS estimated.

The practical significance:

Determining algorithm of diagnosis, treatment of ChS and prophylactic measures, which can give us possibility preventing invalidation, increase badly results of polyprogmazy.

Printed results.

Results of the research were printed according to 26 scientific works: 8 scientific articles (4 foreign), 10 theses, 3 practical recommendations, 3 racionalizator's invitation, 1 methodologies hand book and 1 patent.

Volume and structure of the dissertation:

Work is presented in 65 pages of computer text and consists of an introduction, literature review, three heads of research, including materials and methods of research, findings, conclusions, practical recommendations and literature index,

comprising 88 sources, including 71 on foreign languages. Work is illustrated with 5 tables, 4 charts and 2 pictures.

Scientific advisor, doc.: Abducadirov U.T.

Student of master's degree: Iskandarova D.E.

ЎЗБЕКИСТОН РЕСПУБЛИКАСИ ОЛИЙ ВА ЎРТА МАҲСУС ТАЪЛИМ ВАЗИРЛИГИ

ЎЗБЕКИСТОН РЕСПУБЛИКАСИ СОҒЛИҚНИ САҚЛАШ ВАЗИРЛИГИ

АНДИЖОН ДАВЛАТ ТИББИЁТ ИНСТИТУТИ

Факультет: педиатрия

Мутахассислик: болалар неврологияси

Кафедра: неврология ва болалар неврологияси

Илмий рахбар, доцент:

Абдукадиров У.Т.

Магистратура талабаси:

Искандарова Д.Э.

Ўқув йили: 2013-2016-йиллар

Мавзу долзарблиги: Болалар церебрал инсульти - 1 ойликдан 18 ёшгача бош мияда қон айланишининг ўткир бузилиши бўлиб, 24 соат ва ундан кўп вақт давомида марказий нерв системасида зарарланишнинг турғун белгилари ривожланиши билан ифодаланади ва бугунги кунболалар неврологиясининг кам ўрганилган долзарб муаммоларидан биридир (Шнайдер Н.А. 2010, Амос Е.Г., Потяшин А.Е., 2001).

Турли адабиётларда келтирилган маълумотларга кўра, церебрал инсульт билан хасталанган болалар АҚШда йилига 1 ёшгача бўлган ҳар 100000 та боланинг 7,8 та; 1-18 ёш орасида 2-3 та, Россияда 7,8 та; Саудия Арабистонида 29,7 тасига тўғри келади. Геморрагик нсульт билан хасталаниш йилига ҳар 100 минг та болага 1,5-5,1 (ўртача 2,9) холатда тўғри келади. Бунда ўғил болалар ва қизлар орасидаги нисбат 1,5/1 ни ташкил этади. Ишемик инсульт ташхиси йилига ҳар 100 минг та болага 0,6-7,9 холатда тўғри келади. Бунда ўғил болалар ва қизлар орасидаги нисбат 1,5/1 ни ташкил қилади (Cardo E., Monros E., Colome C. 2000).

Инсульт ўказган болаларда ўлим даражаси ўртача 7-28 % ни ташкил этиб(S. Lanthier, 2000; H. Fullerton, 2002), АҚШ да 100 минг аҳолига 1-15

ёшгача 0,6 та холатни ташкил этган. Бунда ўғил болалар ва негроид иркдаги болалар сони юқори кўрсаткичга эга (Fullerton H.J., Chetkovich D.M. 2002). 20 % холатларда эса болаларда инсультнинг қайталаниши кузатилган (S.Kittner, 2002).

Олиб борилаётган изланишларга қарамай, ногиронликка сабаб бўлувчи патологик холатлар орасида бош мия инсульти дастлабки ўринлардан бирида эканлиги (Зыков В.П., 2006, Chalmers E.A., 2005),20- 30,7 % холатларда болалардаги инсуьлт бошқа диагнозлар остида қайд этилаётганлиги (Л.И.Краснова, 1980; Е.И.Гусев ва б.1990), клиник белгиларининг ўта хилма-хиллиги туфайли ташхислаш ва даволаш жараёнида муайян қийинчиликларга дуч келинмокда (Шамансуров Ш.Ш., 2010, Dudink J. et al, 2009). Болаларда ушбу хасталикни эрта аниқлаш ва самарали даволаш усулларини ишлаб чиқиш жамиятда ногиронлик ва касаллик туфайли ўлим сонининг камайишига замин яратади.

Тадқиқоднинг мақсади: Церебрал инсульт билан хасталанган болаларни аниқлаш, болаларда инсультга сабаб бўлувчи омилларни ўрганиш ҳамда касалликни эрта ташхислаш ва реабилитацион даволаш самарадорлигини ошириш.

Тадқиқоднинг вазифалари:

1. Вилоят болалар кўп тармоқли шифохонасининг неврология бўлимида 2014-2015 йиллар мобайнида церебрал инсульт билан хасталанган болаларнинг касаллик тарихини ўрганиш,тахлил қилиш ва бўлимдаги беморларни бевосита кузатиш.
2. Болаларда бош мияда ўткир қон айланишига сабаб бўлувчи омилларини ўрганиш.
3. Болалар церебрал инсультида МРТ ва ультра товушли дуплекс сканерлаш текширувида кузатиладиган ўзгаришларни ўрганиш.
4. Болаларда турли оғирликдаги церебрал инсультни комплекс реабилитацион даволашда нейропротекторларнинг самарадорлигини баҳолаш.

Тадқиқод объекти ва предмети:

Вилоят болалар кўп тармокли шифохонасидаги неврология бўлимида 2014-2015 йиллар мобайнида бош мияда қон айланишини ўткир бузилиши билан ётиб даволанган бемор болалар кузатилади.

Тадқиқод материаллари ва текширув усуллари:

1. Анамнестиква клиник-неврологиктекширув.
2. Параклиниктекширувусуллари (МРТ, ультра товушли дуплекс сканерлаш, лаборатория текширувлари).
3. Статистик маълумотлар.

Илмий янгилик:

Бош мияда қон айланишининг ўткир бузилиши кузатилган беморларнинг касаллик тарихи статистик тахлил қилиниб, мазкур йиллар учун хулоса берилади. Болаларда церебрал инсультга сабаб бўлувчи омиллар ўрганилиб, профилактик диагностика чоралари ишлаб чиқилади. МРТ, ультратовушли дуплекс сканерлаш каби ноинвазив усуллардан фойдаланиб, бош миядаги зарарланиш ўчоғини аниқлаш, қиёсий ташхислаш ва шу орқали даволаш самарадорлиги оширилишига эришилади.

Бош мия қон айланишининг ўткир бузилиши билан хасталанган болаларни комплекс даволаш ва асоратларнинг олдини олишда нейропротекторларнинг самарадорлиги баҳоланади.

Амалий аҳамияти:

Болалар церебрал инсультини босқичма босқич ташхислаш, даволаш алгоритми ва реабилитация чораларини ишлаб чиқиш даволашда максимал натижа олишга, ногиронликни олдини олиш ва полипрагмазиянинг салбий оқибатларини камайтиришга имкон беради.

Магистратура талабаси: Д. Э. Искандарова

Илмий раҳбар, т.ф.н., доцент: У.Т. Абдуқодиров

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List of provided destruction

AIS----------arterial ischemic stroke

ADBCB----------acute disorder blood circulation of the brain

ChS---------- children’s stroke

CT----------computed tomography

CTA----------computed tomography angiography

CVST----------cerebral venous sinus thrombosis

HS----------haemorrhagic stroke

IVH----------intraventricular hemorrhages

IPH----------intraparenchimal hemorrhage

IS----------ischemic stroke

MRI----------magnetic resonance imaging

MRA----------magnetic resonance angiography

P----------patients

SAH----------subarachnoid hemorrhage

TIA----------transient ischemic attack

Chapter 1. Early, modern way of diagnosis and treatment of children's stroke

Introduction

Despite growing appreciation by neurologists that cerebrovascular disorders occur more often in children than once suspected, the study of stroke in children and adolescents has remained largely descriptive. Child neurologists often encounter children with a cerebrovascular lesion, yet large scale clinical research is difficult because these disorders are less common than in adults and arise from diverse causes. Three fundamental problems hinder both clinical research and the routine clinical care of children with cerebrovascular disease:

1) The infrequency of cerebrovascular disorders in children makes it difficult to organize multicenter controlled clinical trials of the sort done in adults in recent years. The relative rarity of stroke in children also contributes to the still remaining reluctance of some clinicians to consider the diagnosis in individual children.

2) The causes of cerebrovascular disease in children are legion, and no one risk factor predominates. Thus, not only is stroke less common in children, but the diversity of risk factors creates a heterogeneous patient population which hinders clinical research.

3) Despite improved diagnostic techniques which make rapid, noninvasive diagnosis of cerebrovascular disease possible, many physicians still know very little about cerebrovascular disorders in children. This lack of awareness contributes to delayed diagnosis and in the near future will make it more difficult to use thrombolytic agents or other treatments which require early diagnosis and treatment.

Cerebrovascular disorders are defined as focal cerebral injury with an underlying vascular basis and can be divided in stroke resulting from arterial ischemic event, cerebral sinovenous thrombosis and hemorrhage. Stroke at young age (< age 18) is not common, but is an important cause of lifelong morbidity and is among the top ten causes of death in childhood [69-72]. It has incidence of approximately 1.3-13 per 100.000 per year in the developed countries. Causes, risk

factors and pathogenic mechanisms of pediatric stroke differ in the perinatal period or in childhood.

Types of stroke

There are 2 main types of stroke:

- **Ischaemic stroke** – an embolism (either a clot of blood or a piece of debris) blocks a blood vessel in the brain, interrupting blood flow.
- **Haemorrhagic stroke** – a ruptured blood vessel bleeds into the brain. In newborns, bleeding into the space surrounding the brain can occur and this is called a subarachnoid haemorrhage.

Arterial ischemic stroke (AIS) in childhood is usually non-atherosclerotic, which is different from the adult population. In half of the children with AIS, a pre-existing condition can be identified, such as congenital heart disease; in the order part it remains uncertain and may be due to an interplay of both genetic an environmental factors. AIS can occur for example in the presence of genetic prothrombotic disorders, but also in the text of a metabolic disease (Fabry disease, congenital disorders of glycosylation) or other underlying genetic cerebral artheriopathies.

Pediatric arterial ischemic stroke (AIS) is an important cause of long-term morbidity and is among 1 of the top 10 reasons for death in children [36, 37]. Although it occurs in 2 to 3 children per 100,000 children per year, with an increased incidence of about 1 in 4000 during the perinatal or neonatal period, accurate diagnosis is commonly delayed or missed [37]. As such, increasing recognition of the signs and symptoms of this significant cause of morbidity and mortality in children is critical to improving diagnosis and providing optimal treatment.

Important for pediatricians and other healthcare providers who care for children with AIS is the recognition that high-quality good evidence on treatment is largely lacking, and suggested recommendations by current guidelines are largely based on consensus only. The need to better treat childhood AIS is highlighted by data showing that many children will have lifelong neurological

residual symptoms, including hemiparesis and/or dysphasia, as well as neurocognitive and behavioral problems attributed to AIS [38].

Pediatric hemorrhagic stroke has an incidence of 1.1 per 100,000 person-years and encompasses subarachnoid hemorrhage and intracerebral (parenchymal) hemorrhage. Given the rarity of the condition and the under-recognition of cerebrovascular disease in children, it is not surprising that hemorrhagic stroke in children has not been well studied. This thesis will focus on information needed to move the field forward in terms of predicting hemorrhagic stroke etiology and outcome, as well as on improving treatment options [27]. With an incidence of 2–3/100,000 children, stroke is among the top ten causes of death in childhood [28, 29] and is as common as brain tumor in children [30]. A study of a California-wide hospital discharge database found an incidence rate of 1.1 per 100,000 person-years for hemorrhagic stroke and 1.2 per 100,000 person-years for ischemic stroke [31]. Thus, nearly half of pediatric strokes are hemorrhagic. Typically, the term "hemorrhagic stroke" (HS) includes spontaneous interparenchymal hemorrhage (IPH) and non-traumatic subarachnoid hemorrhage (SAH). Patients with traumatic IPH, primary subdural or epidural hematomas, or hemorrhagic transformation of ischemic stroke are usually not considered to have a hemorrhagic stroke [32, 33]. For the purposes of this article, we will focus on IPH, the most common type of HS. Non-traumatic SAH is most often due to intracranial aneurysm and is evaluated and treated differently, though like IPH, recommendations for childhood SAH are based on the adult literature. Two recent pediatric intracranial aneurysm case series and reviews of the literature are available [34, 35]. Children often experience different symptoms of stroke to adults. These can include seizures, headache and fever. However, many of the symptoms of stroke in children are similar to those experienced by adults. Strokes that occur in babies often show themselves as seizures, but they can be missed until parents notice later that the baby has difficulty moving a part of their body. Sometimes, strokes may affect the way a baby is developing.

Frequency of Pediatric Cerebrovascular Disease

Although cerebrovascular disorders occur less often in children than in adults, recognition of stroke in children has probably increased because of the widespread application of noninvasive diagnostic studies such as magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), computed tomography (CT) and, in the neonate, cranial ultrasound studies [36-38]. These studies allow confirmation of a diagnosis that in previous years would not have been suspected or at least not recognized as a vascular lesion. Also, the number of patients with cerebrovascular lesions from certain risk factors may have increased as more effective treatments for some causes of stroke have allowed patients to survive long enough to develop vascular complications. Patients with sickle cell disease or with leukemia, for example, now have a longer life-expectancy, and during this time they may have a stroke.

Most of the pediatric cerebrovascular literature consists of single case reports or small groups of children with a common etiology. These reports offer some insight into the relative frequency of various causes of stroke and draw attention to individual risk factors, but their usefulness is otherwise limited. Larger series of children selected for a common anatomic lesion or a single cause offer additional insight into the unique features of cerebrovascular lesions in children [39], but patients collected from large medical centers may not be representative of all children with stroke. None of these studies can accurately judge the incidence of cerebrovascular disease in children.

Schoenberg and colleagues studied cerebrovascular disease in children of Rochester, Minnesota from 1965 through 1974 [40]. Excluding strokes related to intracranial infection, trauma or birth, they found three hemorrhagic strokes and one ischemic stroke in an average at risk population of 15,834, for an estimated average annual incidence rate of 1.89/100,000/year and 0.63/100,000/year for hemorrhagic and ischemic strokes respectively. Their overall average annual incidence rate for children through fourteen years of age was 2.52/100,000/year. In this population, hemorrhagic strokes occurred more often than ischemic strokes,

while in the Mayo Clinic referral population, ischemic strokes were more common. The risk of childhood cerebrovascular disease in this study is about half the risk for neoplasms of the central nervous system of children, but neonates and children with traumatic lesions are excluded. Despite our impression that cerebrovascular disorders are recognized more often in children than in previous years, Broderick and colleagues[6]found an incidence of 2.7 cases/1 00,000/year, similar to the figure reported by Schoenberg and colleagues [40]. In the Canadian Pediatric Ischemic Stroke Registry incidence of arterial and venous occlusion is estimated to be 1.2/100,000 children/year.

The frequency of several individual risk factors for stroke in children is known, but in most instances, the occurrence of secondary cerebrovascular disease is so variable that it is difficult to assess the relative contribution of each risk factor to the problem of cerebrovascular disease as a whole. In one report which included both children and young adults, children were less likely than young adult stroke patients to have identifiable risk factors and more often fall victim to infectious or inflammatory disorders [42]. The implication is that children may have additional, as yet unknown, risk factors.

Etiology of stroke in children.

Probably the most fundamental difference between cerebrovascular diseases in children and adults is the wide array of risk factors seen in children versus adults (Table 1) [43].Congenital heart disease and sickle cell disease, for example, are common causes of stroke in children, while atherosclerosis is rare in children. No cause can be detected in about a fifth of the children with ischemic infarction, yet many of these children seem to do well. The recognized causes of cerebrovascular disorders in children are numerous (table1) and the probability of identifying the cause depends on the thoroughness of the evaluation. A probable cause of cerebral infarction was identified in 184 of 228 (79%) children in the Canadian Pediatric Ischemic Stroke Registry. The source of an intracranial hemorrhage is even more likely to be found [43]. The most common cause of stroke in children is probably congenital or acquired heart disease. In the Canadian Pediatric Ischemic Stroke

Registry, heart disease was found in 40 of 228 (19%) of the children with arterial thrombosis. Many of these children are already known to have heart disease prior to their stroke, but in other instances a less obvious cardiac lesion is discovered only after a stroke. Complex cardiac anomalies involving both the valves and chambers are collectively the biggest problem, but virtually any cardiac lesion can sometimes lead to a stroke. Of particular concern are cyanotic lesions with polycythemia, which increase the risk of both thrombosis and embolism.

Both the frequency and the cause of pediatric stroke may depend somewhat on both the geographic location and the specific hospital setting. The Canadian Pediatric Ischemic Stroke Registry, for example, lists only 5 children (2%) with cerebral infarction due to sickle cell anemia. A large metropolitan hospital in the United States might care for this many patients in a year, but early estimates [44] that cerebral infarction occurred in 17% of people with sickle cell disease proved far higher than the 4-5% figure derived from more representative samples in Jamaica and in Africa [45-46].

Causes of stroke in children.

It is currently thought that around a half of all strokes in children are due to blood vessel problems in the brain, while a quarter are due to clots travelling from the heart. In around one-quarter of children, no cause can be found. A number of medical conditions can increase the chance of your child having a stroke. These include:

- some types of heart disease or heart surgery
- abnormal or inflamed blood vessels in the brain
- blood clotting problems
- low blood count
- central venous catheters
- some types of cancer
- recent major infections around the ear sinuses or nose
- some viral infections (for example research has shown that chickenpox may cause ischemic stroke in children)

- head injury
- dehydration
- prolonged low blood pressure
- brain tumours
- Other conditions such as sickle cell disease and thalassaemia.

The majority of signs and symptoms of stroke are nonspecific, and can be easily attributed to other causes. One way to avoid delays or misdiagnoses would be to identify risk factors for stroke that would prompt more aggressive and timely investigation. Multiple risk factors are often present in as many as 25% of children with stroke, which means further investigations are warranted even when one risk factor has been identified [18,24].

Cardiac disease is the most common cause of stroke in childhood, accounting for up to a third of all AIS [4]. In children with a cardiac repair or catheterization, nearly 50% of strokes occur within 72 hours. Long-standing cyanotic lesions cause polycythemia and anemia, which both increase the risk of thromboembolism and cerebral infarction [2]. Embolic clots can arise in children with cardiomyopathies, rheumatic heart disease, prosthetic valves, or valvular vegetation from endocarditis [2, 24]. A patent foramen ovale (PFO) can occur in as many as 35% of people between ages 1 and 29 years, and may serve as a portal for venous embolic events to pass from the right to left side of the heart [40].

Hematologic facor.

Sickle cell disease (SCD) is a very common cause of pediatric stroke, occurring in 285 cases per 100,000 affected children [1]. Strokes may occur as early as 18 months of age, but most children present after five years of age [41]. AIS is more common in the younger age group whereas hemorrhagic strokes occurs more frequently in older children and adults [42]. Strokes may occur in the absence of pain or aplastic crises [43]. Two-thirds of children with SCD who have had previous strokes but remain untreated will have a recurrence [44]. The exact pathophysiology is not entirely clear, although it likely involves elements of

anemia, microvascular occlusion, stasis causing reperfusion injury physiology, and endothelial dysfunction [45].

Prothrombotic disorders have been identified in 30 to 76% of patients experiencing arterial or venous events, and should be suspected if there is a family history of early onset AIS (particularly if under 55 years old), heart disease, pulmonary embolism, or deep vein thrombosis events [24, 46–49]. Acquired prothrombotic disorders secondary to deficiencies in proteins C and S may occur in children with renal and liver disease, including nephrotic syndrome with loss of coagulation factors [2, 50]. Protein C deficiency has also been reported in children taking valproate [51]. Hemorrhagic strokes can arise from both Factor VII and factor VIII deficiency [52, 53]. Iron deficiency anemia has been reported in children with both AIS and venous thrombosis with no other apparent etiology [24, 54, 55].

Infection.

Varicella infection within the past year can result in basal ganglia infarction [56, 57]. HIV infection can cause stroke secondary to HIV-induced vasculitis, vasculopathy with subsequent aneurysms, or hemorrhage in the context of immune thrombocytopenia [58, 59]. More commonly associated organisms include mycoplasma and chlamydia, as well as enterovirus, parvovirus 19, influenza A, coxsackie, Rocky Mountain spotted fever, or cat scratch disease [58, 60]. Five to twelve percent of children with bacterial meningitis, TB meningitis, and viral encephalitis will have a stroke due to local vasculitis and thrombosis. A history of drinking raw milk or visiting a farm may point to a diagnosis of neurobrucellosis [61]. Head and neck infections, such as mastoiditis or periorbital infections, remain important causes of CVT [2, 31].

Vascular.

Arteriovenous malformations (AVM) are the most common cause of hemorrhagic stroke after infancy, but can also cause thrombotic stroke [8, 10, 62]. AVM may be associated with neurocutaneous syndromes such as Osler-Weber-Rendu syndrome (i.e., hereditary hemorrhagic telangiectasia), Sturge-Weber

disease, neurofibromatosis, or von Hippel-Lindau syndrome. Moyamoya is another important vascular cause of childhood stroke and is associated with conditions such as Down syndrome, neurofibromatosis, and sickle cell disease [24, 30].

Syndromic and Metabolic Disorders.

Although rare, children with Marfan syndrome are at risk of ischemic neurovascular complications [63]. Children with tuberous sclerosis have a higher risk of embolic events, and may also have hemorrhagic strokes secondary to hypertension, hemorrhage into a tumor, or rupture of an abnormal vessel [39]. Homocysteinuria can cause AIS and should be suspected in the presence of mental retardation associated with lens dislocation and occasionally pectus excavatum [64]. Nutritional deficiencies of folic acid or vitamin B12 may also cause hyperhomocysteinemia, leading to stroke [2]. There is an elevated risk for AIS secondary to thrombosis and premature arteriosclerosis [65], the latter of which is also caused by familial lipoprotein disorders [66–69].

Vasculitis.

Cerebral vasculitis is a less common cause of stroke in children, and is more common in children older than 14 years of age [8]. Although idiopathic vasculitis is most often diagnosed, signs and symptoms of systemic vasculitides with Kawasaki disease, Henoch-Scho¨nlein Purpura (HSP), polyarteritis nodosa, Takayasu's arteritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, sarcoidosis, Sjogren syndrome, or Behcet disease should be considered [37, 66, 70–74].

Oncologic.

Children with cancer are at increased risk for AIS as a result of their disease, subsequent treatment, and susceptibility to infection. Intracranial hemorrhage may complicate an intracranial tumor [2]. Leukemia and lymphoma create a hypercoagulable and hyperviscous state [75]. Treatment with L-asparaginase decreases antithrombin levels, and may trigger venous thrombosis in leukemic children concurrently receiving prednisone [73, 76]. Radiation therapy for optic chiasm gliomas or other sellar or suprasellar region tumours can cause

vasculopathies that result in strokes which may be preceded by transient ischemic attacks (TIAs) beginning months to years after treatment [60, 77–79].

Trauma.

Children who have experienced head and neck trauma are at risk of developing an ischemic event subsequent to dissection of the carotid or vertebral arteries. This can result from direct intraoral trauma delivered by a foreign object such as a pencil in the mouth or after tonsillectomy, and can also occur spontaneously [37, 66, 80–82]. Hyperextension or rotational injuries experienced during minor head trauma, motor vehicle collisions, sports such as wrestling, or even chiropractic manipulation can also result in strokes [60, 83, 84]. Symptoms of traumatic arterial dissection can be delayed by 24 hours, and the risk is greatest within a few days of the vascular injury [62, 83].

Drugs.

Drug use, both illicit and prescribed, are a concern in the adolescent population. Cerebral infarcts and hemorrhage have been reported in patients abusing drugs such as amphetamines, ecstasy, cocaine, phencyclidine (PCP), and glue sniffing [85]. Stimulants and heroin can also cause vasculopathies predisposing to infarction [83]. Adolescent girls using oral contraceptives are at higher risk of cerebral venous thrombosis [86]. Overuse of ergot alkaloids in the treatment of acute migraines, are also associated with increased risk of ischemic events [87].

About a quarter of all children who have had a stroke do not have any of these risk factors. It is unknown why these children have strokes. The cause of stroke in newborns is usually unknown. Risk factors include pregnancy complications, difficulties at birth, blood clotting disorders and heart problems. Discuss with your doctor your child’s risk factors and the potential causes of the stroke.

Prehospital Emergency Care

Children often experience different symptoms of stroke to adults. These can include seizures, headache and fever. However, many of the symptoms of stroke in children are similar to those experienced by adults. Strokes that occur in babies

often show themselves as seizures, but they can be missed until parents notice later that the baby has difficulty moving a part of their body. Sometimes, strokes may affect the way a baby is developing.

Toddlers or older children may develop sudden signs such as:

- weakness in an arm or leg, especially on one side. This can cause difficulty with walking, standing and/or using the affected arm. For older children this may also include numbness in the arm or leg.
- difficulty talking, understanding, reading, writing, or concentrating
- trouble seeing in one or both eyes
- dizziness, loss of balance or poor coordination
- difficulty swallowing including drooling
- severe or unusual headaches, nausea and/or vomiting
- occasionally, strokes can cause children to collapse, to change behavior or to have a seizure.

Lack of general awareness of cerebrovascular disorders in children probably delays medical attention for children with cerebrovascular disorders. It is not unusual, for example, for children with a cerebral infarction to be brought to a physician several days after the onset of symptoms. In contrast, family members are usually well aware of the significance of an acute neurological impairment in older individuals, and these patients are typically seen by a physician earlier than children with a similar lesion. Data from the Canadian Pediatric Ischemic Stroke Registry indicate that 48-72 hours often elapse between the onset of symptoms of arterial occlusion and a child's diagnosis [47]. Venous occlusion was discovered a bit more quickly than arterial occlusion, at least in younger children, perhaps because of the common occurrence of epileptic seizures in children with venous thrombosis. This seems to be fairly typical of the pattern seen in the United States as well. The typical adult with anew onset neurological deficit from cerebrovascular disease undoubtedly sees a physician much sooner. It is likely that this delay in the diagnosis of children reflects a lack of awareness by both physicians and families that cerebrovascular disease occurs in children. To the

extent that treatment might be improved by earlier evaluation and treatment, prompt recognition and treatment could improve management.

The Modified National Institutes of Health Stroke Scale (mNIHSS) was designed to eliminate the parts of the NIHSS that had poor interrater reliability while maintaining the original score's utility in assessing stroke severity.

- Lower is better; increasing mNIHSS scores are correlated with more severe strokes and worsened clinical outcomes.
- The mNIHSS performs as well as the original score in predicting patients at high risk of hemorrhage if given tPA and which patients are likely to have good clinical outcomes.
- The mNIHSS has superior interrater reliability (<90%) compared to the original NIHSS (~66%).
- The mNIHSS is more reliable in multiple settings, including calculating scores from medical records, when used via telemedicine, and when used in clinical trials.

Points to Keep in Mind.

- Currently, the mNIHSS is used much less frequently than the NIHSS in both the clinical setting and in trials.
- Many guidelines make reference to the NIHSS rather than the mNIHSS, including those making recommendations concerning tPA administration.
- The NIHSS only takes an average of 6 minutes to complete, so some who question the clinical utility of altering a well-validated and widely used scale.

Use cases.

The mNIHSS can help physicians quantify the severity of a stroke in the acute setting. (Why use it? There are nearly 800,000 cases of acute stroke in the United States every year, with 130,000 associated deaths (4th leading cause of death in Americans). The mNIHSS can help physicians determine the severity of a stroke, predict clinical outcomes and can help guide management.

The mNIHSS has the same correlation with clinical outcomes as the NIHSS but with better interrater reliability).

Modified NIH Stroke Scale/Score (mNIHSS)

Shortened, validated version of the NIHSS.

SI

US

The question numbers refer only to the original NIHSS question items; the mNIHSS contains 11 items total.

1B: Level of Consciousness/Orientation Questions

Ask Month and Age

Both Questions Correct

0

1 Question Correct

+1

0 Questions Correct

+2

1C: Level of Consciousness Commands

'Blink Eyes' & 'Squeeze Hands'

(Pantomime Commands if Communication Barrier)

Both Tasks Correct

0

1 Task Correct

+1

0 Tasks Correct

+2

2: Test Horizontal Extra-ocular Movements

Normal

0

Partial Gaze Palsy

+1

Total Gaze Palsy

+2

3: Test Visual Fields

No Visual Loss

0

Partial Hemianopia

+1

Complete Hemianopia

+2

Bilateral Hemianopia

+3

5A: Test Left Arm Motor Drift

No Drift

0

Drift before 10 seconds

+1

Falls before 10 seconds

+2

No Effort Against Gravity

+3

No Movement

+4

5B: Test Right Arm Motor Drift

No Drift

0

Drift before 10 seconds

+1

Falls before 10 seconds

+2

No Effort Against Gravity

+3

No Movement

+4

6A: Test Left Leg Motor Drift

No Drift

0

Drift before 10 seconds

+1

Falls before 10 seconds

+2

No Effort Against Gravity

+3

No Movement

+4

6B: Test Right Leg Motor Drift

No Drift

0

Drift before 10 seconds

+1

Falls before 10 seconds

+2

No Effort Against Gravity

+3

No Movement

+4

8: Test Sensation

Normal; No sensory loss

0

Abnormal; Sensory loss

+1

9: Test Language/Aphasia

Describe the scene; name the words; read the sentences.

Normal; No aphasia

0

Mild Aphasia

+1

Severe Aphasia

+2

Mute/Global Aphasia

+3

11: Test Extinction/Inattention/Neglect

Normal

0

Mild

+1

Severe

+2

Treatment and Rehabilitation.

No randomized controlled treatment trials have been completed in children with stroke; many of the procedures increasingly used in children with cerebrovascular disease have been adapted from studies in adults. Accumulating experience with antithrombotic and anticoagulant treatment in children suggests that these agents can be safely used in children, though their efficacy and proper dose still need to be established by controlled trials. Thrombolytic agents should be as effective in children as in adults, but the safety data are inadequate for children and the timing and dosage need to be determined for children and adolescents.

There are some drugs, which may use in the treatment:

- Aspirin

1) Background: There are no controlled trials on the use of aspirin or other antiplatelet agents in children with ischemic cerebral infarction. Nevertheless,

aspirin is being used more and more in the routine clinical care of children with cerebral ischemic disorders.

2) Safety: In addition to the potential complications of chronic aspirin use seen in adults, children taking daily aspirin could have an increased risk of developing Reye's syndrome. Evidently the risk of Reye's syndrome is fairly small, due perhaps to the low aspirin dose typically used in children. Despite the increasingly common use of aspirin in children with stroke, we were unable to find in the literature even one child who developed Reye's syndrome while taking prophylactic aspirin. One 65 year-olds, however, developed Reye's syndrome while taking aspirin for stroke prophylaxis, but he also took additional aspirin for influenza [48].

3) Efficacy: A daily aspirin dose of 2-3 mg/Kg/day causes an antiplatelet effect, though it remains to be seen whether this dose of aspirin is clinically effective in children.

- Heparin and Low Molecular Weight Heparins

1) Background: A decision to use heparin in a child rests on two questions: What is the likelihood of either extension of an infarction or of a second infarction from an embolus which might be prevented by treatment, and what is the risk of inducing a hemorrhage because of anticoagulation? Much like the situation in adults, heparin should be used in children thought to have a high risk of recurrence and a low risk of secondary hemorrhage.

2) Safety: There are no large scale trials of heparin in children with ischemic stroke, but increasing clinical experience suggests that children can be treated along the same lines as adult patients with reasonable safety [43,49,50]. Combined experience with over 100 pediatric patients treated for systemic clots with low molecular weight heparin indicates a good safety profile and dose finding feasibility [16]. No significant hemorrhagic complications occurred in these initial 100 children's [53].

3) Efficacy: The value of anticoagulation in children is difficult to assess without more information. Anticoagulation is commonly used in children with arterial

dissection, dural sinus thrombosis, coagulation disorders, or a high risk of embolism [43,50]. It also seems reasonable to anticoagulated a child with progressive deterioration or during the initial evaluation of a new cerebral infarction [43]. The loading dose of heparin is 75 units/Kg intravenously followed by 20 units/Kg/hour for children over one year of age (or 28 units/Kg/hour below one year of age). The target APTT to 60-85 is seconds [49]. Adult stroke patients who receive low molecular weight heparin for ten days starting within 48 hours of diagnosis have a better outcome [52] and it may be possible to adapt this approach for children. Low molecular weight heparin (Lovenex, Rhone-Poulenc) can be given to children subcutaneously in two divided doses of 1 mg/Kg/dose (or in neonates, 1.5 mg/Kg every 12 hours).

- Warfarin

1) Background: Experience in children with long term anticoagulation to prevent cerebral infarction is limited, and there is additional concern about anticoagulating an active child who may be prone to minor injuries through normal activities. Nevertheless, warfarin is the most effective means of prolonged anticoagulation in children.

2) Safety: Clinical experience suggests that warfarin can be used in children and adolescents with reasonable safety. The concern that active children could have an increased risk of hemorrhage due to trauma seems to be largely unfounded, though it is recommended that they avoid activities which carry an especially high risk of injury (e.g., contact sports).

3) Efficacy: The rationale for using warfarin in children with cerebrovascular disorders follows closely the approach used in adults. Thus, major uses of warfarin treatment in children include congenital or acquired heart disease, hypercoagulable states, arterial dissection, and dural sinus thrombosis. An INR of 2.0 to 3.0 is appropriate for most children on warfarin; for children with mechanical heart valves the INR should be 2.5 to 3.5.

- Thrombolytic Agents

1) Background: There is ample reason to seek new treatments for children with ischemic cerebralinfarction, because 75% of the children have serious sequelae including neurologic deficit, epilepsy, or death. While there is little information about the use of thrombolytic agents in children with stroke, enough work has been done with adult patients that the technique could possibly be adapted for selected children.

2) Safety: Urokinase and streptokinase are used infrequently in children with cerebrovascular disease, but no serious complications occurred in the few children treated for dural sinus thrombosis. Thrombolytic therapy for children with non-cerebral thrombotic complications has recently been evaluated. Pooled literature analysis of 203 children treated with thrombolytic agents (including 39 patients who received tPA) indicated that the thrombus was cleared in 80% of the children, but 54% had minor bleeding (not requiring transfusion) and one child suffered an intracranial hemorrhage. In 29 consecutive children treated with tPA (0.5 rng/`Kg) at Toronto's Hospital for Sick Children, the clot was dissolved in 79%, but almost a fourth of these children had bleeding which required transfusion [54,55]. Given this high rate of serious bleeding after systemic tPA and the lack of studies demonstrating improved outcome, we cannot recommend tPA except in the setting of a controlled clinical trial.

3) Efficacy: The delayed diagnosis which so often occurs in children with ischemic stroke reduces the likelihood that a child with an ischemic stroke will be seen early enough to benefit from thrombolytic agents. Intravascular urokinase or streptokinase have been used with apparent success in a few children with dural sinus thrombosis, 8,21-23 but there is even less experience with these agents in children with arterial thrombosis. The available data are insufficient to comment on the effectiveness of any of the thrombolytic agents in children with ischemic stroke. Certainly they would be expected to produce unacceptable roles of bleeding as seen in adults if given more than 4-6 hours after onset of stroke.

- Transfusion

1) Background: About half of the patients with a stroke due to sickle cell disease will have another stroke [46] and this increased risk can be reduced by repeated transfusions to suppress the level of circulating sickle hemoglobin to 30% or less. The risk of stroke increases again if the transfusions are discontinued even after a prolonged stroke-free interval, so most patients who begin transfusions must continue them.

Safety: Although the risk can be reduced by iron chelation, iron toxicity from repeated blood transfusions remains a major problem. Cohen and colleagues 24 proposed a less aggressive transfusion program to maintain the hemoglobin S near 50%; this regimen required an average of 31% less transfused blood and still no infarctions occurred. Miller and colleague had similar results, although their follow-up period was shorter. This new approach needs to be studied further.

Efficacy: Although no randomized clinical trials were ever done, years of clinical experience have produced general agreement that periodic transfusion greatly reduces the risk of ischemic cerebral infarction due to sickle cell disease. A patient who has had one stroke has about a 90% risk of having additional infarctions. The Stroke Prevention Trial in Sickle Cell Anemia (STOP) is now investigating the use of transcranial Doppler (TCD) to identify children at greatest risk for their first cerebral infarction due to sickle cell disease. This study could prove that periodic transfusions reduce the risk of ischemic infarction in children with sickle cell disease and that TCD can be used to identify those at greatest risk.

Treatment of AIS.

Treatment for pediatric AIS is aimed at acute treatment and secondary prevention. Because of the lack of good evidence-based studies in pediatric AIS, treatment has been variable with available guidelines offering only consensus-based recommendations [37,42-44]. In addition, because of the dearth of high-quality evidence on pediatric AIS, historic treatment has been based on extrapolating treatments from those used in adult AIS despite significant differences in the underlying etiology of disease [36]. Because of the complexity of AIS in children, acute management in most cases of stroke should involve a

multidisciplinary approach that includes pediatric subspecialties (i.e., intensive care, neurology, neuroradiology, thrombosis/hematology, and rehabilitation) as well as other specialties as needed per individual patient (i.e., cardiology, neurosurgery, infectious diseases, and rheumatology) [37]. The new emergence of pediatric acute stroke centers also can provide a useful resource for pediatricians to help in accurately diagnosing and acutely treating AIS in children [45].

Acute treatment.

The goal of acute treatment of AIS in children is to limit or reverse the effects of stroke on brain injury [36] as well as to look for etiology and risk factors that also may need treatment [37]. The cornerstone of acute treatment is supportive neuroprotective measures based on an assessment of airway, breathing, circulation, and disability [36,46].

Although data is scarce on whether controlling hyperthermia or hypertension/hypotension is beneficial to children with AIS, as it is in adults, the American Heart Association (AHA) guidelines suggest avoiding these conditions as well as hypovolemia/hypervolemia [37]. Overall, blood pressure management in children should be aimed at avoiding sudden acute changes in blood pressure by maintaining stable and adequate cerebral perfusion [36].

Prompt treatment of seizures is important to help maintain systemic homeostasis and prevent infarct expansion [36, 37] and aggressive management of raised intracranial pressure can be lifesaving [36]. For children with sickle cell disease, exchange transfusion to reduce levels of sickle cell hemoglobin to less than 30% is suggested for acute treatment of AIS, although this has not been tested in a clinical trial.

Although a large area of uncertainty and persistent lack of clear data is the role of antithrombotic therapy for neuroprotection in acute treatment [36] most stoke experts agree that some level of either antiplatelet or anticoagulation therapy is beneficial to prevent acute progression of thrombus [37]. Important for the effective use of antithrombotic therapy for acute management of AIS is to use it within a window of time from symptom onset (within 6 hours), which further

reinforces the need for prompt recognition and diagnosis [47]. Some pediatric stroke centers may consider other types of antithrombotic treatment as well, such as intravenous thrombolytic treatment for older adolescents or children with basilar artery thrombosis or endovascular hyperacute treatment in some cases [48, 51]. Caution is needed in using antithrombotic therapy in children, however, given the paucity of data on the safety and efficacy in this population. "When considering antithrombotic therapy in any child with arterial ischemic stroke, it is critical to continually balance the risk (hemorrhagic complication) of antithrombotic therapy with the risk of no treatment (extension of preexisting infarction and recurrence of stroke)," according to Mahendra Moharir, MD, Division of Neurology, The Hospital for Sick Children, Toronto, Ontario, Canada, in a review article of pediatric arterial ischemic stroke [37].

More: Using an electronic stethoscope for auscultation. Further understanding of the role of anticoagulant and antiplatelet therapy for acute treatment of pediatric AIS may come from the ongoing International Pediatric Stroke Study, the largest nonrandomized, multicenter, observational cohort to assess the safety and efficacy of these therapies in pediatric AIS. Current data show that subtypes of AIS treated with initial anticoagulant therapy were children with dissection and congenital heart disease, whereas children with sickle cell disease were associated with not using anticoagulation. For antiplatelet therapy, use was frequent in children with moyamoya disease but less frequent in children with dissection, altered consciousness, and bilateral ischemia [37, 52].

Secondary prevention.

Secondary prevention of AIS is aimed at identifying the underlying risk factors of AIS in individual children to help tailor treatment to prevent recurrence and estimate prognosis [36-38, 46, 53]. Secondary prevention of AIS remains challenging, with little evidence-based recommendations available to help guide physicians. The only clear guidance is for children with sickle cell disease for whom chronic transfusion is clearly established and for children with moyamoya disease for whom surgical revascularization is well accepted. Anticoagulation or

antiplatelets are both commonly used, and additional research is needed to determine best strategies for acute treatment and secondary stroke prevention [52, 53]. Table 6 provides an example of general recommendations on the role of antithrombotic therapy for secondary prevention based on expert consensus in the AHA guideline [42]. For more specific recommendations by the AHA and by the other 2 guidelines on the use of antithrombotic therapy for secondary prevention, see the specific guidelines [42-44]. Of note, secondary prevention of perinatal/neonatal AIS focuses on rehabilitation recommended for secondary prevention that includes physiotherapy, occupational therapy, and speech therapy. Observation is needed over time to watch for deficits that may emerge with maturation. Currently, there is no role for antithrombotic therapy in perinatal/neonatal AIS unless prothrombotic abnormalities or congenital heart disease are identified [37].

Directions for Research.

Until more information on childhood stroke is available, we must of necessity continue to adapt the knowledge obtained from adult stroke patients. It should not be necessary to repeat in children all the work already done in adults, but we do need to identify areas which are age specific. In some respects, our study of stroke in children recapitulates some of the early work in adult stroke patients. Databases such as the Canadian Pediatric Ischemic Stroke Registry will continue to provide data on the causes of childhood stroke as well as the patients' treatment and outcome. Under the best of circumstances, such databases are limited by the fact that the correct diagnosis may not be recognized or reported to the registry. Larger case series which concentrate on one cause of stroke or one anatomic lesion need to be published. Epidemiologic studies need to be reassessed to reflect better diagnostic techniques and the increased recognition of stroke in children by physicians. Several specific causes of cerebrovascular disease are relatively common in children and have a high enough risk of stroke to make collaborative trials feasible. There are several potentially productive areas to study. Research

should initially focus on the more common disorders or on children with risk factors which are usually identified before a stroke occurs:

- (a) The Stroke Prevention Trial in Sickle Cell Anemia (STOP) trial now underway could serve as a model for studies of childhood stroke from other causes. Sickle cell disease is common in some medical centers, and cerebral infarction frequent enough to make a study feasible. Early diagnosis and treatment probably improve the patient's outlook. Additional multicenter trials for patients with sickle cell disease could also address the use of hydroxyurea or other drugs in stroke prevention.

- (b) Sinovenous thrombosis seems to occur relatively more often in children than other cerebrovascular lesions and can now be identified quickly and noninvasively with MRI/MRA. Collaborative studies to evaluate systemic anticoagulation and/or thrombolysis should be feasible, particularly if similar trials in adults continue to show promise.Cardiac disease remains the most common cause of ischemic cerebral infarction in children. Most of these children have congenital heart lesions which are identified well before an infarction occurs, and ischemic infarction may occur frequently enough to warrant controlled trials of prophylactic agents or of neuro-protective agents during surgery when the risk of stroke is higher. Thrombolytic agents could play a greater role in children with heart disease because their families could be taught to recognize the significance of an acute neurologic deficit. Moyamoya is an uncommon condition but it could be studied via a collaborative approach. Most patients in the recent literature have had various surgical procedures designed to increase blood flow to the brain. But no controlled trials have ever been done to assess these operations, and there is some evidence that the natural history of untreated moyamoya may be less devastating than sometimes suggested. In one group of 27 children, 5 patients had no sequelae, 9 had only headache or transient ischemic symptoms, and 7 had mild intellectual or motor impairment. Only 6 of the 27 had a poor outcome: 1 death, 2 who required continuous care, and 3 who required special schooling or institutionalization. Only 11 of these 27 patients had surgery [61]. The fact that so many patients do well

without intervention makes it difficult to evaluate treatment in the absence of controlled trials. Several pediatric hospitals offer extracorporeal membrane oxygenation (ECMO), a technique which requires ligation of the right carotid artery. In some centers, the carotid artery is eventually reconstructed once ECMO is no longer needed [62]. These children provide an opportunity to study the long term effects of altered cerebral circulation and, for the children whose carotid is reopened, to explore the effects of carotid artery trauma on the development of atherosclerosis.

A quick diagnosis is important to minimize risk for brain damage. Doctors rely on imaging machines and other tests to see what has happened in a child's brain.

Computed Tomography (CT) scan uses X-rays to take a detailed picture of the affected area of the brain. A CT scan will confirm whether or not the child has had a stroke, what kind of stroke it is and where in the brain it occurred.

Magnetic Resonance Imaging (MRI) uses magnetic radio waves to create an image of the brain. It provides greater visual details than a CT scan.

Cerebral Arteriogram uses a special dye injected into the arteries of the brain and an X-ray is then taken.

Echocardiogram uses sound waves to take pictures of the heart to see whether there are problems with the heart valves or other heart functions that may be creating blood clots.

Blood tests may also be ordered to find out whether your child has a blood-clotting disorder.

Lumbar puncture (also known as a spinal tap) to find out if there are signs of infection or inflammation in the nervous system.

Making the differential diagnosis of AIS in children is challenging and contributes to its often delayed or missed diagnosis. Among the diseases that AIS can mimic include focalseizures, demyelination, and tumor with hemorrhage, hemiplegic migraine, hypoglycemia, andconversion [37]. Some data show a mean of 7 days between initial assessment and final accurate diagnosis, with a change in

diagnoses often leading to changes in therapy [38]. Because AIS may present differently in children than adults (Table 1) [36,37,39], the first step in diagnosis is recognizing the particular clinical signs and symptoms of pediatric AIS, as well as risk factors. The most important differences of AIS in children compared with adults is that about 30% of children will present with headache or seizure, and symptoms of AIS may wax and wane (unlike in adults who usually have a sudden onset) [40,41]. Table 1 lists other things to look for that differentiate AIS in children from adults [36, 37, 40, 41]. About 50% of children with AIS will have a preexisting medical condition relevant to AIS, including congenital heart disease, sickle cell disease, trisomy 21, iron deficiency, prothrombotic states, and infection [36].An immediate workup to identify or rule out AIS is critical. Once AIS is suspected, neuroimaging with magnetic resonance imaging (MRI) of the brain and magnetic resonance angiography (MRA) of the intracranial arteries is indicated to confirm a diagnosis [37]. Other imaging studies that may be useful include computed tomography (CT) or CT angiography (CTA) when MRI is difficult to undergo for a child, and invasive catheter cerebral angiography if CTA and MRA findings are unremarkable or detect vascular abnormality of unclear etiology.

There are many other diseases that may mimic a stroke. Complicated migraines can cause focal neurologic symptoms that typically resolve within 24 hours, and should be considered if there is a family history of migraine or hemiplegic migraine [10]. Focal seizures can result in subsequent transient postictal hemiparesis (Todd's Paresis), but stroke should be considered if the duration of the deficit is prolonged relative to the duration of the preceding seizure. Intracranial neoplasms should be considered, as well as intracranial infections such as meningitis, brain abscess, and herpes simplex encephalitis [4, 37]. Although rare, alternating hemiplegia is a possibility, especially if there is a distinct history of episodes of hemiplegia that last rarely longer than a day, alternate between sides, and present in a child with progressive developmental regression [23]. Common metabolic abnormalities like hypoglycemia can cause focal, stroke-like

Table 1. Risk factors for pediatric cerebrovascular disease.

Congenital Heart Disease	**Hematologic Disorders and Coagulopathies**
Ventricular septal defect Atrial septal defect Patent ductus arteriosus Aortic stenosis Mitral stenosis Coarctation Cardiac rhabdomyoma Complex congenital heart defects **Acquired Heart Disease** Rheumatic heart disease Prosthetic heart valve Libman-Sacks endocarditis Bacterial endocarditis Cardiomyopathy Myocarditis Atrial myxoma Arrhythmia **Systemic Vascular Disease** Systemic hypertension Volume depletion or systemic hypotension Hypernatremia Superior vena cava syndrome Diabetes **Vasculitis** Meningitis	Hemoglobinopathies (sickle cell anemia, sickle cell-hemoglobin C) Immune thrombocytopenic purpura Thrombotic thrombocytopenic purpura Thrombocytosis Polycythemia Disseminated intravascular coagulation (DIC) Leukemia or other neoplasm Congenital coagulation defects Oral contraceptive use Pregnancy and the postpartum period Antithrombin IR deficiency Protein S deficiency Protein **C** deficiency Congenital serum C2 deficiency Liver dysfunction with coagulation defect Vitamin K deficiency Lupus anticoagulant Anticardiolipin antibodies

Systemic infection	**Structural Anomalies of the Cerebrovascular System**
Systemic lupus erythematosus	Arterial fibromuscular dysplasia
Polyarteritis nodosa	Agenesis or hypoplasia of the internal carotid or
Granulomatous angiitis	vertebral arteries
Takayasu's arteritis	Arteriovenous malformation
Rheumatoid arthritis	Hereditary hemorrhagic telangiectasia
Dermatomyositis	Sturge-Weber syndrome
Inflammatory bowel disease	Intracranial aneurysm
Drug abuse (cocaine, amphetamines)	**Trauma**
Hemolytic-uremic syndrome	Child abuse
Vasculopathies	Fat or air embolism
Ehlers-Danlos syndrome	Foreign body embolism
Homocystinuria	Carotid ligation (e.g., ECMO)
Moyamoya syndrome	Vertebral occlusion following abrupt cervical rotation
Fabry's disease	Posttraumatic arterial dissection
Malignant atrophic papulosis	Blunt cervical arterial trauma
Pseudoxanthoma elasticurn	Arteriography
NADH-CoQ reductase deficiency	Posttraumatic carotid cavernous fistula
Vasospastic Disorders	Coagulation defect with minor trauma
Migraine	Amniotic fluid/placental embolism
Ergot poisoning	Penetrating intracranial trauma
Vasospasm with subarachnoid hemorrhage	

deficits [38]. Uncommon metabolic disorders such as MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke), which is inherited, can also cause stroke-like symptoms, without an actual ischemic or hemorrhagic event [2, 39].

Summary.

Stroke is rare among children and babies, but it can occur. The causes of childhood stroke are not well understood, but are thought to include blood vessel problems in the brain and clots travelling from the heart. In around one in a child include seizures, fever, speech impairment and paralysis.

In childhood, arterial ischemic stroke has emerged as an important cause of neurological disability. The clinical observation that recovery can vary greatly within the pediatric stroke population, despite similar infarcts, led to investigations beyond traditional radiographic measures (ie. lesion characteristics), and pursuit of the current study proposal. Motor recovery following stroke has been attributed to a number of factors, including the extent of damage to the brain regions supporting motor function, and the ability of the brain reorganize motor function.

Increased awareness of these disorders by the public, and by medical personnel will potentially improve accessibility of pediatric stroke patients to newer forms of thrombolytic and neuroprotective agents. Increased awareness by research teams and research funding agencies will provide the means for the intervention trials critically necessary to realize that potential.

The primary hypothesis was that the extent of motor recovery in the affected hand would be associated with two factors: 1) the extent of anatomical damdge to the affected corticospinal tract and 2) the extent and pattern of "functional reorganization" within the motor system. Specifically, the degree of damage to the corticospinal tract in the injured hemisphere will be less in patients with good recovery compared to patients with poor recovery. Accordingly, the degree of damage to the corticospinal tract would also be associated with the pattern and extend of cortical reorganization: i.e. less damage to the tract would be associated with activation in the stroke affected (ipsilesional) hemisphere and good recovery, and greater damage within the corticospinal tract would be associated with activation in the unaffected (contralesional) hemisphere, and poor recovery [88].

Chapter 2. Materials and methods of research

Scientific research had been done in neurological department inmulti-disciplinary medical center of Andijan region. According to tasks of research and conform to requirement of WHO had been checked children's 46 cases and 20 patients that diseased with acute disorder blood circulation in the brain in regional children's medical center during January in 2014 – may in 2015.Outer to this, to define the early way of prophylactics of children's stroke had been examined 80 children with ultrasound duplerograph.

Methods of research:

-Anamnesis

-To examine clinic-neurological status.

-Population statistic method

-Modified Ashworth Scale Grading Spas tidy

-Gross Motor Function Classification System-GMFCS

-To estimate physical and emotional function of patients.

-Glazco scale

-Stroke scale.

Results of dividing of disease according to gender, age, and type of stroke had been described on table №1. It was being 3,4 % stroke of common hospitalized patients. Patients were divided in 3 groups according age: 1) early childhood- from 1 year to 3 years, 2) until school age – from 3 years to 7 years old, 3) school years old – from 7 years to 17 years old. It was nominated on the table № 2, that 27 (58,7%) patients were carried out HS and 19 (41,3%) IS. Often P(patients) address to hospital with outcomes of stroke in winter and spring times (32-34%) and thinly on summer, autumn times (16-18%). According to anamnesis, symptoms of HS were progressing acutely. Symptoms of IS was progressing at 6 patients acutely, at 13 children (68,4%) bellow acutely.

In this table has been shoved some results, according to dividing of disease depending to gender, age and type of stroke.

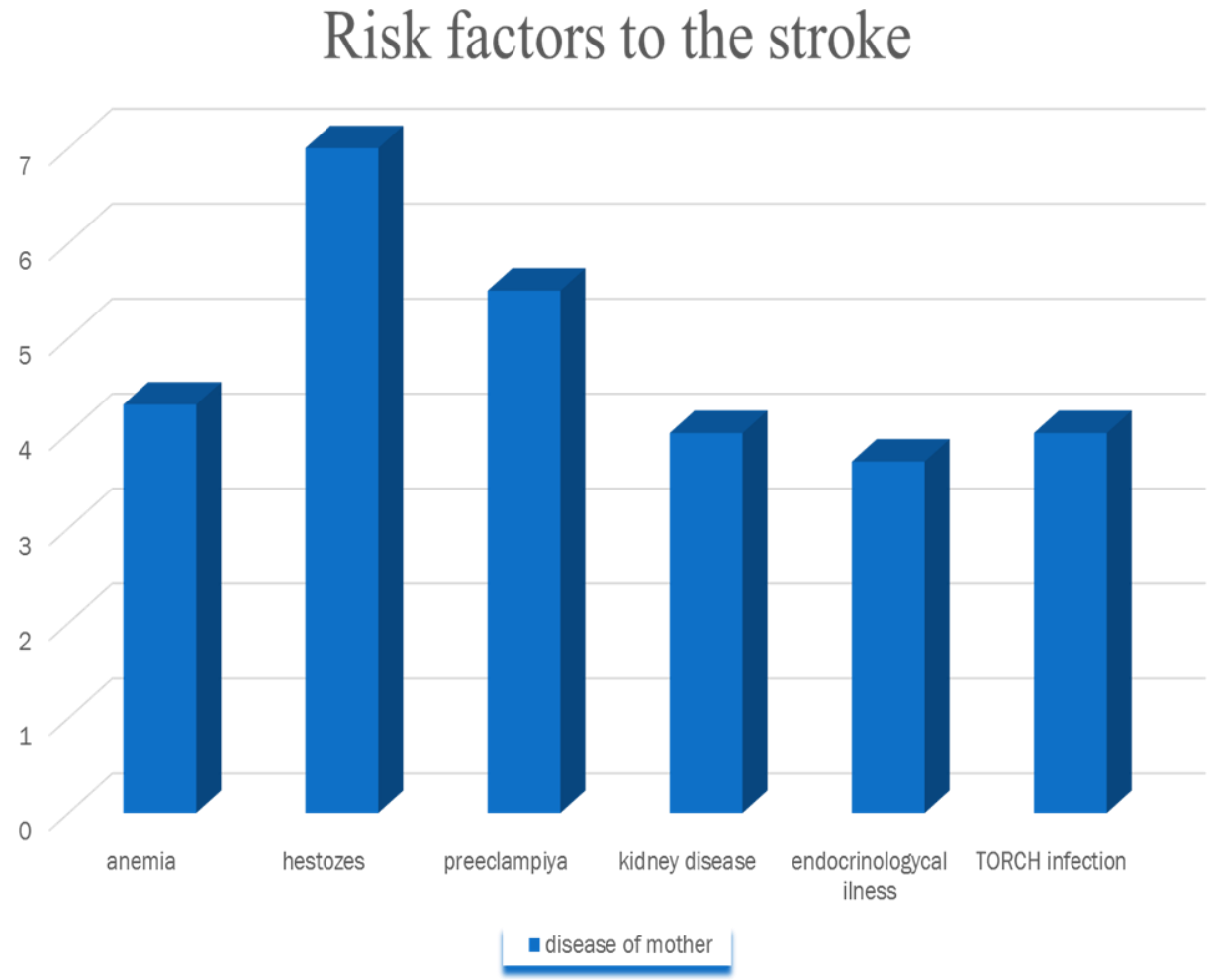
Table 2. Dividing of disease according to gender, age, and type of stroke

№	Type of stroke	Age (years old)						Total
		1-3		3-7		7-17		
		M	F	M	F	M	F	
1.	Haemmorragyc	10	3	4	5	1	4	27
2.	Ischemic	9	2	2	5	-	1	19
Total		19	5	6	10	1	5	46

Etiological factors of this disease in that patients were inborn traumas,DIS syndrome, blood disease of mother and child. Cause of stoke at adolescence period were blood-vessel dystonia, inborn heart defect, adolescence hypertonia, vasculitis. In time of rehabilitation complains were to limiting of motion: on left – at 8, on right – at 10 P, tetrpaurez – at 5 P, epileptic syndrome – at 4 P. In this case localization of pathological place is did not matter. Mental developing reared at 6 P, microcephaly at 1.At neurostatus were defined central injuring of nerves facialis and nerves hypoglossus, hemiparesis with hypotenuses, hyperreflexia, pathological reflexes such as Babinsky, Rossolimo e.t. Elements of motor aphasia observed at 8 P.To define structure and etiological factors of HS, had been examined 18 children, who endured haemmorragyc stroke. It had been learning anamnesis vita and anamnesis morbi, age of debut, form and burden of S. It had been carried out blood examination to inside infection with IFA, common clinical analyses, to learn results of MRI and neurological examination. There were 11 (61,1%) boys and 7 (38,9%) girls of common 18 P with HS. Subarachnoid haemorrhage were 8 (44,4%), subdural haemorrhage were 1 (5,6%), hematoma in the brain were in 4 (22.2%) cases. In 5 cases (27,8 %) had been observed several forms of S in one time, including in 2 (11,1%) P with subarachnoidal haemorrhage and haemorrhage

in the ventricles, in 2 (11,1%) cases with subarachnoidal haemorrhage and hematoma in the brain, subarachnoidal haemorrhage and subdural haematoma observed in 1 (5,6%) cases.Analyses age of debut get witness about in 11 (61,1%) cases S started at early ages, namely they were 4 (22,2%)in the 1-st month of life and 3 (16,7%) cases till 3 months of life.Among the etiological factors 100 % were perinatal defeat of central nervous system, antenatal infection (Herpes and cytomegalovirus) recognized in 11 (61,1%) cases. Vessel anomaly detected in 3 (16.7%) events, vasculitis in 1 (5,5%) cases. In 3 (16,7%) occasions etiology of S ley down uncertain.To define structure and etiological factors of IS, it had been explored 16 children, who brought ischemic S. It had been investigated anamnesis vita and anamnesis morbi, mode and heaviness of S. We had conducted docimasia of blood infection with method of immunoferment analyses, general clinical analyses of blood, coagulogramm, searching results of MRT and neurological checkup.From 16 Ch, who endured ischemic S, boys were 9 (56,25%), girls 7 (43,75%). At 5 P had been registered hart pathology (on 1 innate defect of hart, at 1 idiopathic aritmiya, at 1 P syndrome of lengthen interval QT, at 1 reumocardit, at 1 bacterial endocarditis). At 4 P noted blood disease (at 1 P deficit cofactor of heparin III and deficit protein C; at 1 deficit antitobmin III; at 2 one mow cellular anemias). At 2 P we registered infection on the face, ear and paranasal sinuses; at 1 Herpes simplex and Herpes zoster (alternatively hemiplegia). At 3 P observed blood vessel disease (on 2 Ch pathological bend, stenosis slumber artery, at 1 inborn aplasia of vertebral arteries). Analyses age of debut get witness about till 3 years old in 11 (68,75%) cases S started at early ages, namely they were 4 (25%) in the 1-st month of life.

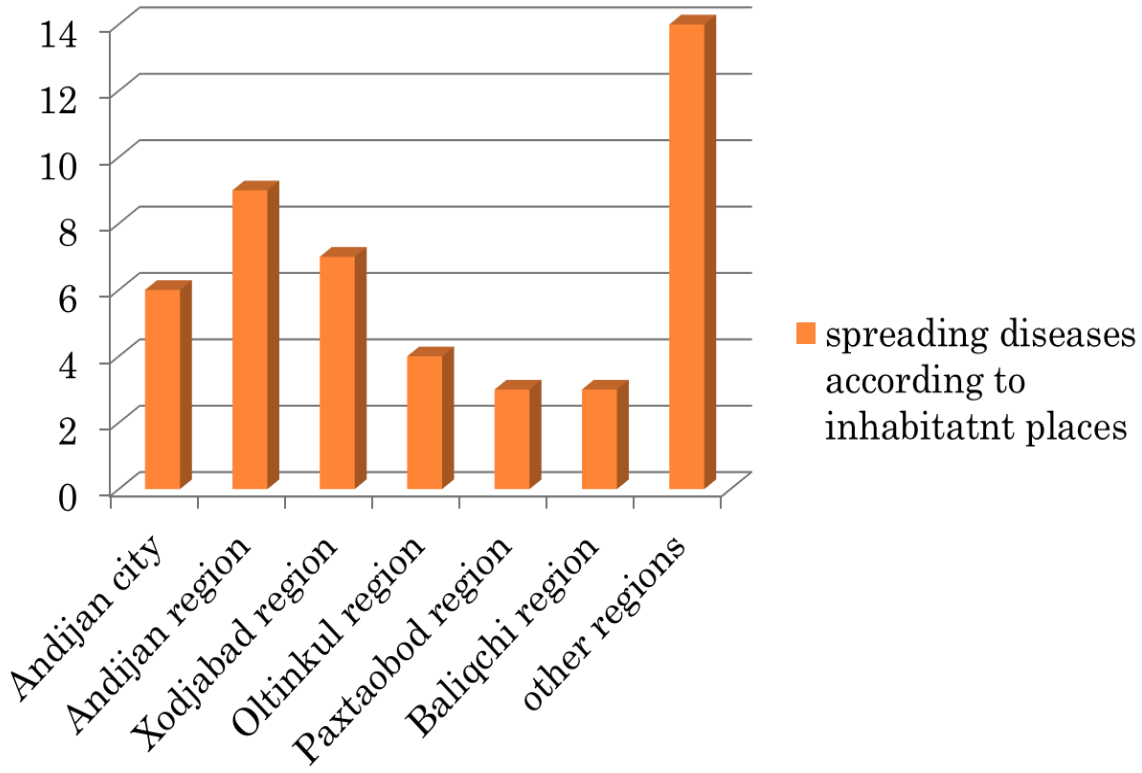
Among the etiological factors 100 % were perinatal defeat of central nervous system, antenatal infection (Herpes and cytomegalovirus) recognized in 11 (68,75%) cases. In 1 (6,25%) occasions etiology of S lay down uncertain. Anamnesis of P showed, that on every mother of that P noted anemia of several burden degrees.



To estimate, role of TORCH infection in developing ABDBC, we checked out 16 P on ages from 2 month of life till 5 years old, who treated at stationary with ABDBC (acute blood disorder of the brain). At all P noted secondary immunnodeficient condition. At 3 P till 1 years old in the blood had been registered Anti-CMV-IgG antitella in the class IgG to CMV, Anti-HSV-IgG antitella class IgG to Herpes simplex 1-2 types (HSV-1,2). On the clinic were noted ABDBC on hemorrhagic form. At 5 P till 3 years old in the blood had been registered Anti-CMV-IgG antitella in the class IgG to CMV, On the clinic were noted ABDBC on ischemic form. At 8 P till 5 years old in the blood had been registered Anti-CMV-IgG, Anti-Toxo-IgG (antitella class IgG to Toxoplasma gondi). On the clinic were noted at 4 P subarachnoid hemorrhage, at 2 P intraventricular hemorrhage, at 2 P ABDBC on ischemic form. At all P' blood noted decreasing concentration CD4 cells.

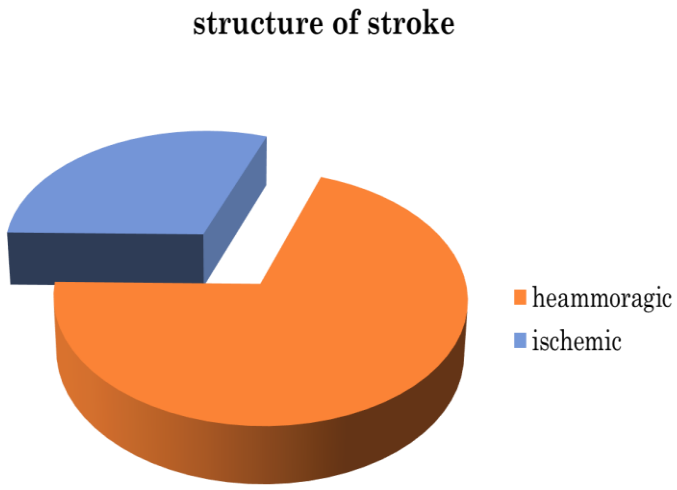
For define spreading of stroke in children and do statistical analysis, 1369 cases of P during 2014 in neurological department were had been analyzed. 46 (3,4%) cases were of P with ADCBC from number of common cases. Climate-geographic peculiarities of cities and districts of Andijan region is not principal differences. According to statistical analyses of cases, 21 (45,6 %) P were from cities and 25 (54,4%) P were from villages. Due to observing structure of strokes, hemorrhagic strokes diagnosed more than ischemic and comparing hemorrhagic and ischemic strokes in cities were 2,3:1; in villages it the same indicates.

Dividing P according to place inhabitant was described this diagram:

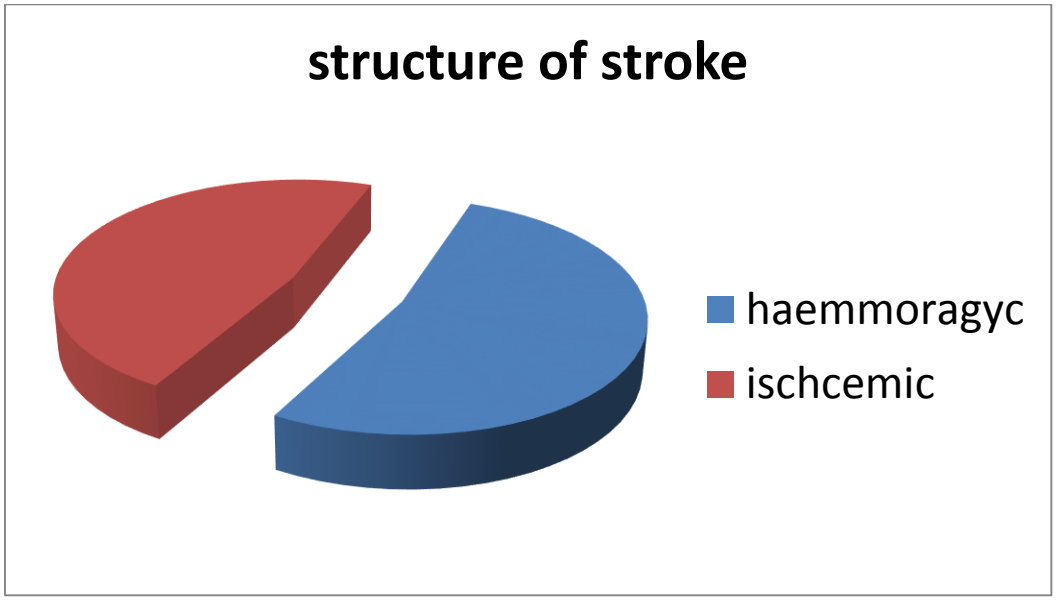


In this diagram we can see, more than frequency of acute disorders blood circulation in the brain observed in Andijan region and Xojabad region (there are mainly rural places). Other regions mean, rural areas and there particularly villages. The second places of spreading of acute disorders blood circulation in the brain observed in Andijan city (there are many structures of modern city).

In the city



In villages



We can do conclusion, rare and structure of stroke in children would influence sum ecological and social peculiarities of this region. There are much of transports, more using computer technologies, mobile phones and e.t. in cities. In villages this factors may be using chemical materials overhead. Every factor in cities and villages may influence to health of adults and children. There is sum of social-economic factors: less of account of children in a family, most of parents of this children busy with intellectual job (teachers, doctors, economics and others) in

the cities. Most of in the such families risked to hard-vessel pathologies, hypertonia. In rural areas more of account of children and their parents busy with physical works. In these families could observed more methaboligical encephalopathy, chronic anemia.

Due to, to define modern way of protection CHS in early stages, we did some experiments. The 1st group of our research composes of children of 20 patients till 43 years old admitted to the 1st department of neurology of Andizhan State Medical Institute's clinic with stroke diagnostics. Altogether there are 40 children: 24 of them are boys, others are girls. Children of 20 families whose parents are till 43 years old and have not ever had stroke are chosen by random sample to the 2nd group. Altogether there are 40 children: 25 of them are boys, 15 are girls. Extra and intracranial blood vessels of both group members have been examined with ultra sound duplex scanner. According to the results of the research: in the 1st group there have been determined at 7 children C type, at 5 children S type, at 3 ones kayling, at 4 ones kay-kay, at 6 ones mix, at 3 ones aneurism and at 12 ones without pathology blood vessels types. In the 2nd group at 2 children C type, at 3 child S type, at 4 - mixed, at 1 – aneurism and at 30 without pathology blood vessels types have been determined. There have not been found out cranial pathologic blood vessels such as kayling and kay-kay.

It is obviously by the results that in most of cases there have been determined the cranial blood vessels pathology at children of patients till 43 years old with stroke diagnostics.

Likewise, we examined P on MRI methods. There are 2 pictures with results of research.

Making the differential diagnosis of AIS in children is challenging and contributes to its often delayed or missed diagnosis. Among the diseases that AIS can mimic include focal seizures, demyelination, tumor with hemorrhage, hemiplegic migraine, hypoglycemia, and conversion disorder. Some data show a mean of 7 days between initial assessment and final accurate diagnosis, with a change in diagnoses often leading to changes in therapy.

Picture № 1

Comparatively diagnostic aspects of ischemic and hemorrhagic strokes on newborns

	hemorrhagic	ischemic
Algorithm	simultaneousness	unsimultaneousness
Dense of hearth	Hyperechogen, homogeneity hearth	Changeable homogeneity hearth
Border	clear	Not clear
Localization	Not typical localization	Parenchyma of the brain, basic blood vessel's basin
Mass-effect	Suitable to the hyperechogen zone	Not suitable to the hyperechogen zone
Symmetry	Only one side	differently

Because AIS may present differently in children than adults,1,2,4 the first step in diagnosis is recognizing the particular clinical signs and symptoms of pediatric AIS, as well as risk factors. The most important differences of AIS in children compared with adults is that about 30% of children will present with headache or seizure, and symptoms of AIS may wax and wane (unlike in adults who usually have a sudden onset).

About 50% of children with AIS will have a preexisting medical condition relevant to AIS, including congenital heart disease, sickle cell disease, trisomy 21, iron deficiency, prothrombotic states, and infection.

An immediate workup to identify or rule out AIS is critical. Once AIS is suspected, neuroimaging with magnetic resonance imaging (MRI) of the brain and magnetic resonance angiography (MRA) of the intracranial arteries is indicated to confirm a diagnosis. Other imaging studies that may be useful include computed

tomography (CT) or CT angiography (CTA) when MRI is difficult to undergo for a child, and invasive catheter cerebral angiography if CTA and MRA findings are unremarkable or detect vascular abnormality of unclear etiology.

Picture№2

Comparatively diagnostic aspects of ischemic and hemorrhagic strokes on newborns

examination	hemorrhagic	ischemic
Neurosonography	Homogeny hyper echogenic hearths on different places	hyper echogenic hearths on the brain parenchyma
MRT	T1- izointensive signal T2-hypointensive signal	T1- hypo intensive hearths on parenchyma T2-hyperintensive

Treatment of ChS.

For estimate effect of citocholins, we checked up 20 P with S treating in set up period at children's neurology department at regional multidisciplinary center. P was divided in 2 groups: in the 1-stgroup was 11 children until 3 years old, in the 2-nd group 9 children at 7- 14 years old. It used anamnestic, clinic-neurological and neurovizual methods. Complex rehabilitation was included special physiotherapeutic methods which adapted for these children: massage, treatable physical training, orthopedic correction with preparation Encephabol. The aim of rehabilitation were set up motion damages and to prevent progress of pathological process. There was taken into consideration motor developing with spastic's degree in calm period and in doing exercises, common muscle gipotonia and

degree of mental-speech developing. Encephabol (piritinol) increases decreasing pathological methobalism due to augmentation catch, increases metabolism nuclein acids and existing acetylcholine to synapses of neurons, improves cholinergic impulses among neurons. Antigipocsantal pyiritinol is stimulator of tissue's regeneration. Its effect starts after 30 minutes from addition. Methoboligical and blood vessels disorders of encephalon are indications for using encephabol (including IS). Pyiritinol admitted to children by 2,5-10 ml suspense 1-3 times in 1 day (50-300 mg/day) due to ages every day after meal during 3-4 weeks (after 7 years old admitted tabulate form). At 60 % P with influence of S were observed positive neurological dynamic. Effect among 7-14 years old had observed better than until 3 years old. It could be explore following, cerebral nerve system of children at these years old more grown and they had been pass from many rehabilitation course. P's muscle's tonus had been normalized and capacity of motion had been widening in paralyzed hand or leg, decreased assimetriya on face and dissension of swallow, coordination was set up. Cognitive disorders were visible on psycoemotional and speech violable at P till 3 years old. Cognitive disorders at P till 3 years old visible on psycoemotional and speeches violable. Improvement visible after treatment: P contacted more actively than before, concentration of attend increased, interested to toys and speech speeded. Non lifting and impro -per effects of pyiritinol was not observed. Also, we had been observed comparing research group of children with S. Researches had been done in children' multidisciplinary hospital of Andijan region in children' neuorology department. For thus research 20 Ch (children) from 6 to 12 years old have been selected with sunedly choosing method on the acute disorders cranial blood circulation diagnosis. In the 1-st group have been 10 ch (5 girls and 5 boys). Their done basis differential therapy and drug Cereton. The second group had been organized from 10 ch too (5 girls and 5 boys). In this group we did basis differential therapy without praparate Cereton. At the first using preperate Cereton on injection by 1000 mg per a day by drop during 10 days, later threating did admit preparete on a capsule by 400 mg 2 times a day before 30 min from meal during 3

months. In the time of we considered condition of injures of brain and individual peculiarities of child. It had been observed decrease neurological complications. There are main symptoms of acute disorder blood circulation of the brain on children:

1. Hemorrhagic stroke: cerebral depression, cerebral elevation, epileptically crises, distention of liquors-blood.
2. Ischemic stroke: epileptically crises, symptoms of changing muscles tonus.

Table №3. Indications of results of improving neurological disorders on 11 P at until 3 years old.

Damages	Until treating	After treating	
		After 3 months	After 6 months
Injuries of n.facialis	2 (9%)	1	-
Bulbar disorders	4(36%)	3	1
Limiting of movements	10(91%)	7	2
Tonus of muscle	11(100%)	9	4
Hypertonia	9(64%)	6	3
Hypotonia	2(9%)	3	1
Disorders of motion coordination	5(45%)	3	-
PR, BR	11(100%)	6	1
Increasing	8(73%)	5	1
Decreased	3(27%)	1	-
Pathological reflexes	9(%)	4	1

Table №4. Indications of cognitive sphere at P on period of treating.

Disorders	Until treating	After treatment	
		After 3 month	After 6 months
Down reaction to voice	9 (82%)	6	3
Looking voice components	7(64%)	4	2
to make a speech subsequently	10(91%)	7	4
Being later pronouncing simple words	9(82%)	6	3
To be late on visional attention			
To face	9(82%)	6	4
To toys	9(82%)	6	4
to be late on to know relatives and strangers	8(73%)	5	2
Emotional lability	10(91%)	6	2
Motion brake	11(100%)	8	4

According to results of research, we get 80 % positive effect of treating in the 1-st group and the 2-nd group it was 50 %. Neurostatus was more improving in the 1-st group, which used differential therapy with choline alfoscirate than the 2-nd group, which without alfoscerate. Also, we did supplementary method of research-brain's MRT: according to research, icshemisation in the brain got less after 3 monthly treating (at the acute period preparate get injection by 1000 mg by drop, further it admitted on capsule by 400 mg 2 times a day during 3 months) in the 1-st group, but in the 2-nd group hearth of ischemization get some wider.

Conclusion: we get result, that admission Cereton decreased neurological complications in that group.

Table №5. Indicates of improvement of neurological disorders on 7 P at from 7 till 14 years old with influence of acute disorders cranial blood circulation.

Disorders	Until treating	After treatment	
		After 3 month	After 6 months
Injuriesofn.facialis	2(22%)	1	-
Bulbar disorders	3(33%)	2	1
Limiting of movements	9(100%)	7	3
Tonus of muscle	9(100%)	5	1
Hypertonia	7(78%)	4	1
Hypotonia	2(22%)	1	-
Disorders of motion coordination	4(44%)	2	-
PR, BR	9(100%)	4	1
Increasing	7(78%)	3	1
Decreased	2(22%)	1	-
Pathological reflexes	7(78%)	4	1
Defers in mental and speech developing	8(89%)	5	2

CHAPTER 3

According to results of research, we can do following conclusion:

1. It had been recommend to plan observation of P with ADBCB with risk of pregnancy anamnesis, to test titer of antitella to TORCH-infection and to define immune status of P to rational therapy.
2. During the year, number of P with stoke and its influences were 3,4 % of whole number of hospitalized P in department “children’neurology”.
3. Among the P high rate was at early childhood ages (from 1year to 3 years old) and relatives of gender were 4:1 (boys more than girls).
4. 58,7 % children hurt with HS, 41,3% with IS and localization of process at right or left hemispheres was at the same rate.
5. According to reserve seasoning disease, high rate of stroke in spring and winter periods.
6. Etiological factors of this disease in that patients were inborn traumas, dissemination inravessel syndrome, blood disease of mother and child. Cause of stoke at adolescence period were blood-vessel dystonia, inborn heart defect, adolescence hypertonia, vasculitis.
7. Pyiritinol affected positively to cranial blood circulation and metabolism. It apparent as decreasing symptoms of neurological deficient.
8. Neuroprotection is important in an acute and influence period of disease in children at every year old.
9. Absent of unaccepting and rare improper effects of pyritinol are shows safety this preparate in longer courses.
10. Peculiarities vessel deficit and risk factors to this condition of children depends their parents health. The first and secondary protection of S must be done depending of this information.
11. Ultra sound duplex scanner examination takes an important place in determining the cranial blood vessels pathology on the early stages and in the modern way of its prophylactics at children of patients till 43 years old, with stroke diagnostics. With this method we can diagnose cranial blood vessels pathology at

children on the early stages and enable to develop our society by protecting of invalidity.

12. HS were observed in early years old and supervised development several form diseases. In etiology of illness larger meaning owns perinatal pathology, antenatal infection, vascular malformation. Conclusion: thus, HS were observed in early years old and supervised development several form diseases. Among etiological factors, hart vessel disease and blood illness were more considerable. Mother's anemia, autoimmune and hypercoagulacion disease were more important to progressing infarct brain.

In summary we get following conclusions: some disease of pregnant (anemia (70,6%), hestozes (56,5%), preeclampsia (32,9%), pathological pregnant act (51,7% and others) may be cause of stroke in children. We can note frequently cerebral depression, cerebral arising, epileptically syndrome, distention of liquors-blood on neurostatuse of HS. In ischemic stroke we can note epileptically crises, symptoms of changing muscles tonus.According to results of neurovisual research, it had been noted hemmorrhagic stoke: homogeny hyper echogenic hearths on different places on neurosonography, T1- izointensively signal, T2-hypointensive signals on MRI. On ischemic stroke: hyper echogenic hearths on the brain parenchyma on NSG and T1- hypo intensive hearths on parenchyma
T2-hyperintensive on MRI. In children with influence of ADBCB characterized with injuries of CBN, pyramidal systems and late on psychomotor and intellectual developing. Blood disorders of the brain in children characterized with acute decreasing blood circulation's speed in the injuring vessel.To use cytocholins gave us positive effects on treatment of childhood stroke and its influence at early childhood period.We may use it on complex rehabilitation measure of stroke with treatment physical training, massage, paraphyne and others.

Our primary goal was to improve the diagnostics in this group of children, in order to provide better counselling of families too. Since little was known, we wanted to gain insight in the contribution of genetic factors in this group of

patients. In addition, when known causes of cerebral hemorrhage were excluded, we wanted to identify novel genetic causes for childhood cerebral hemorrhage.

The clinical and molecular finding of some families with pseudo- TORCH syndrome and in addition severe cerebral hemorrhage and early demise, who harbor autosomal recessive mutatiin in USP18. Usp18 mouse knockout models have already shoved cerebral hemorrhage and hydrocephalus with ependymal necrosis. Immunohistochemistry on patient brain tissue shows a very abnormal brain ependyme.

Brain MRI findings included periventricular and subcortical white matter disease, hemorrhagic changes, corpus collosum hypoplasia, cerebral atrophy and cerebral hypoplasia. Most findings may reflect changes following brain injury. Both ischemic vascular and inflammatory componenets may play a role in the cerebral and ocular phenotype. However, a role of disturbed apoptosis during development may also be a contributing factors [88].

Practical recommendations:

1. Main risk factors of children's stroke are hard chronical disease of mother and some pathologies in the pregnancy period and their perinatal and antenatal influences. There for, neonatologists, pediatricians and children's neurologists must pay attention to these conditions.
2. Early diagnostically methods (such as, NSG, MRI, and CT) gave us possibility to prevent of invalidism among injured children.
3. To use cytocholins at early childhood period with stroke gave us effect on treatment. It had been recommended from 2 month of life to 1 years old by 100 mg (1 ml suspension) 2 times a day, at 1-3 years old 100 mg (1 ml suspension) 3 times a day in the morning and afternoon. Course of treatment are 1,5 months.

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