3. Poon R. T. P. Current techniques of liver transection. HPB : *The Official Journal of the International Hepato Pancreato Biliary Association.* 2007:9(3):166-173.
4. Schmidbauer S., Hallfeldt K. K., Sitzmann G., Kantelhardt T., Trupka A. Experience with ultrasound scissors and blades (UltraCision) in open and laparoscopic liver resection. *Ann Surg.* 2002;235:27-30.
5. Kim J., Ahmad S. A., Lowy A. M., Buell J. F., Pennington L. J. Increased biliary fistulas after liver resection with the harmonic scalpel. *Am Surg.* 2003;69:815-819.
6. Sugo H., Mikami Y., Matsumoto F., Tsumura H., Watanabe Y. Hepatic resection using the harmonic scalpel. Surg Today. 2000;30:959-962.
7. Rau H. G., Wichmann M. W., Schinkel S., Buttler E., Pickelmann S. Surgical techniques in hepatic resections: Ultrasonic aspirator versus Jet-Cutter. A prospective randomized clinical trial. *Zentralbl Chir.* 2001;126:586-590.
8. Smith J. A. Possible venous air embolism with a new water jet dissector. *Br J Anaesth.* 1993;70:466-467.
9. Koo B. N., Kil H. K., Choi J. S., Kim J. Y., Chun D. H. Hepatic resection by the Cavitron Ultrasonic Surgical Aspirator increases the incidence and severity of venous air embolism. *Anesth Analg.* 2005;101:966-970.
10. Sakamoto Y., Yamamoto J., Kokudo N., Seki M., Kosuge T. Bloodless liver resection using the monopolar floating ball plus ligasure diathermy: preliminary results of 16 liver resections. *World J Surg.* 2004;28:166-172.
11. Czauderna P., Otte J. B., Aronson D. C. Guidelines for surgical treatment of hepatoblastoma in the modern era--recommendations from the Childhood Liver Tumour Strategy Group of the International Society of Paediatric Oncology (SIOP). *Eur J Cancer.* 2005;41:1031-1036.
12. Spinelli C., Strambi S., Rossi L. Surgical management of papillary thyroid carcinoma in childhood and adolescence: an Italian multicenter study on 250 patients. *J Endocrinol Invest.* 2016:1-5. doi:10.1007/s40618-016-0474-0
13. Skinner M. A., DeBenedetti M. K., Moley J. F., Norton J. A., Wells S. A. Medullary thyroid carcinoma in children with multiple endocrine neoplasia types 2A and 2B. J Pediatr Surg. 1996 ;31:177-181; discussion 181-182.
14. Cost N. G., Stock J. A. Current and Future Issues in Pediatric and Adolescent Urologic Oncology. *Urology.* 2016:91:174.
15. Lorenzo A. J., Romao R. L. The Evolving Role of Minimally Invasive Surgery in Pediatric and Adolescent Urologic Oncology. *Urology.* 2016:91:180-189.
16. Clarke M. J., Price D. L., Cloft H. J. En bloc resection of a C-1 lateral mass osteosarcoma: technical note. *J Neurosurg Pediatr.* 2016:11:1-7.
17. Markiewicz M. R., Ruiz R. L., Pirgousis P., Bryan B. R., Dierks E. J. Microvascular Free Tissue Transfer for Head and Neck Reconstruction in Children: Part I. *J Craniofac Surg.* 2016;27(4):846-856.

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NEUROTOXICITY CAUSED BY ANESTHETICS IN PEDIATRIC ANESTHESIA

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НЕЙРОТОКСИЧНОСТЬ, ВЫЗЫВАЕМАЯ ОБЩИМИ АНЕСТЕТИКАМИ У ДЕТЕЙ

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In a review of the current literature assesses the recently discovered phenomenon and the toxicity of anesthetics in the developing child brain. The ways of diagnostics of morphological and functional abnormalities of brain activity in children. Provides indisputable data on the possibility of this type of interactions taking into account the mechanism of action of anesthetics. Comparative characteristics of strength toxic effects on children's brain different types of inhalation and non-inhalation anesthetics. There is a comparison of the degree of toxic impact on the brain at single and repeated exposure of anaesthesia. Emphasizes the lack of information and especially objective data visualization of degenerative changes in children's brain due to ethical constraints and the impossibility of obtaining samples for biopsy. The conclusion about the appropriateness of expectant surgical tactics in the absence of urgent indications for surgical intervention to 4 years of a child's life. Also, our patients need more researches in this direction.

Key words: anesthesia, newborns, children, pediatric surgery, neurotoxicity, neurodegeneration, cognitive disorders

В обзоре дается оценка недавно обнаруженному феномену токсичности анестетиков для развивающегося детского мозга. Определяются способы диагностики морфофункциональных нарушений мозговой активности у детей. Приводятся неоспоримые данные о возможности такого вида взаимодействий с учетом механизма действия анестетиков. Дается сравнительная характеристика силы токсического воздействия на детский

мозг различных видов ингаляционных и неингаляционных анестетиков. Происходит сравнение степени токсического воздействия на головной мозг при однократном и неоднократном воздействии анестезии. Подчеркивается недостаточность информации и особенно объективных данных визуализации дегенеративных изменений в детском мозге вследствие этических ограничений, а также невозможности получения образцов для биопсии. Делается вывод о целесообразности выжидательной хирургической тактики при отсутствии экстренных показаний к оперативному вмешательству до 4 лет жизни ребенка. Кроме того, подчеркивается необходимость проведения дальнейших исследований в этом направлении.

Ключевые слова: анестезия, новорожденные, детская хирургия, нейротоксичность, нейродегенерация, когнитивные расстройства

For a long time has it been thought that properly administered anesthesia with modern clean drugs, delivered by properly trained anesthesiologists, does not harm the patient. In elderly patients an effect on memory was accounted to occurring hypoxia and cholinergic side-effects of too deep anesthesia. In children were until recently no deleterious effects of anesthesia detected, although the effects of maternal exposure to alcohol and other consciousness altering medications on the developing fetus are already well recognized [1]. Similar to alcohol, most anesthetic agents act via NMDA and GABA-A receptor mechanisms. Up till today have more than 2000 studies on possible neurotoxic effects of anesthetics and sedatives been published. Almost all are animal studies, only few involve patients. Nevertheless, there is now growing concern that exposure to general anesthetics can lead to subsequent learning impairment, memory deficits and behavioral abnormalities in young subjects.

Short review of the recent literature

It was already in 1953 suggested by Eckenhoff that anesthesia may have adverse effects resulting in personality changes in children [2]. There was no further follow-up to this suggestion. However, since approximately three decades has increasing experimental evidence suggested an association between exposure to anesthesia in early life and subsequent poor neurodevelopmental outcome in animal species. In 1999 published Ikonomidou et al. that ketamine in 7 days old rats caused widespread apoptotic brain cell death [3]. Jevtovic-Todorovic et al. showed in 2003 that a combined anesthetic of midazolam, nitrous oxide, and isoflurane administered to a 7-day-old rat for 6 hours had both an immediate and long-term neurodevelopmental abnormalities [4]. Thereafter have numerous animal studies demonstrated morphological and histological changes as well as long-term cognitive impairment in several animal models, including non-human primates. Multiple studies using non-human primates, have demonstrated neuroapoptosis, as well as degeneration of oligodendrocytes, neuroinflammation, and impairment of both synaptogenesis and neurogenesis, these studies have alarmingly demonstrated long-term neurocognitive dysfunction i.e. learning and behavior disturbances [5].

These observations have raised substantial concerns for human pediatric anesthesia practice [6, 7]. Despite the overwhelming study outcome in the same direction are many physicians reluctant to accept the conclusions. In a number of editorials, letters to the editor and commentaries has it, with all sorts of arguments been stated that the observed outcome does not apply to human. Differences in methodology between the various studies, prolonged administration of anesthesia (hours in rats supposedly equal weeks or months in man), concentrations of anesthetic drugs beyond clinical used doses, and many other arguments were used. Discussions have arisen about the differences in vulnerability windows between animals and man. Fear that patients and parents become afraid of anesthesia and surgery, and probably loss of income, appears to be the reasons for denial of the outcome of the various animal studies.

That so far conclusive studies on anesthesia exposed children have not been published does in my opinion not mean that learning and behavior disturbances are not present. It merely indicates that such studies in human are extremely difficult, need large numbers, while for example morphological changes cannot be proven because the impossibility of taking brain biopsies. Furthermore, it is impossible to separate the effects of the anesthetic drugs from the effects of the operation, the procedure, or the illness. Besides are most existing human studies retrospective studies, and to be conclusive need a long follow-up.

However, is it not surprising that the neurotoxic effects did occur in all animal species tested, even in non-human primates? Is it not surprising that also short duration administration at low dosages caused similar effects? Is it not surprising that not only inhalation anesthetics but also intravenous agents have similar neurotoxic effects? Studies with NMDA receptor antagonists such as nitrous oxide and ketamine and with γ-aminobutyric acid receptor (GABA) agonists, including isoflurane, propofol, etomidate, halothane, benzodiazepines, and barbiturates all had similar effects. Is it not surprising that the receptors (GABA and NMDA) on which anesthetics have their action, are also involved in the development of the nervous system? Is it justifiable to suggest that the biological development and function of the human brain is different from the animal brain, and thus animal results cannot be extrapolated to man?

Adverse neurologic effects of most currently clinically used anesthetic agents were seen in species studied ranging from worms and zebrafish to rodents, pigs, and monkeys. Long duration, multiple agents, and repeated exposures increased neurotoxicity. The histologic evidence of brain cell death during development is associated with long-term adverse effects on cognitive function and behavior. Several reviews on the results of animal studies have appeared.

In a metanalyses of the existing preclinical literature concluded Disma et al. in 2015 that that anesthesia exposure at early stages of life may impair normal neurological development [8]. They suggested that different mechanisms are associated with anesthesia toxicity at different stages of brain development. Neuroapoptosis, especially during the peak of synaptogenesis (which appears to be the most vulnerable period for anesthetic toxicity), has been related to adverse cognitive outcomes. Anesthetic agents have also been shown to be potent neuromodulators able to affect the production of neurotrophic factors, and to influence neuroplasticity; and this has led to proposals that the paradigm of neurotoxicity should be shifted into the concept of neuromodulation or neuroplasticity.

Anesthetic agents are also known to influence immunological factors, such as the production of pro- and anti-inflammatory cytokines. Dose-dependency in the toxic effect was demonstrated and differences in effect between the inhalation anesthetics exist. Desflurane is more detrimental than isoflurane which has more effect than sevoflurane. Also with intravenous anesthetics exists dose-dependency, but subclinical doses of ketamine proved have a deleterious effect. Multiple anesthetics enhance the toxicity, as do administration of mixtures of anesthetics.

From the animal studies is it clear that brain susceptibility of neurotoxicity is largest during drain developmental. This would, since human brain development continues from the third trimester through the first several years of life, mean that children during pregnancy and until approximately 4 years are vulnerable. The human infant brain has growth peaks at postnatal week 1–2 and declines to 25 % of peak at age 6 months.

A small number of clinical observational studies have appeared in the literature. Although these observational studies offer conflicting results and are confounded by multiple factors, they suggest that some such children may have deficits in learning and school performance [9]. For example, Ing et al. found in 2012 in a clinical study that children exposed to anesthesia before age 3 had a higher relative risk of language and abstract reasoning deficits at age 10 than unexposed children [10]. Wilder et al in a 2009 retrospective study found that in children under the age of 4 years, exposure to 2 or more anesthetics or more than 120 minutes of anesthesia was associated with a significant increased risk in learning disability [11]. Kalkman et al. could not demonstrate neurobehavioral disturbances in a retrospective study of urology patients under 6 year of age [12]. Bartels et al. in a study in monozygotic twins found that overall, children exposed to general anesthesia before 3 years of age had significantly lower educational achievement scores and higher incidences of cognitive problems than children not exposed to anesthesia. However twin pairs discordant for anesthesia exposure revealed no differences in cognitive development. DiMaggio et al. found in 2009 that children treated with inguinal hernia repair before age 3 years were more than twice as likely as controls to have a subsequent behavioral or developmental diagnosis [13]. In a publication of 2011 DiMaggio et al. described children who received general anesthesia before age 3 years were approximately 1.9 times as likely as controls to show subsequent language disability and approximately 1.7 times as likely to show subsequent cognitive disability even after a single anesthetic [14]. Hansen et al. found that children who underwent inguinal hernia repair in the first year of life showed no significant difference in subsequent mean test scores compared to controls but they were slightly more likely not to achieve normal scores [15]. Children with a history of multiple exposures to general anesthesia before age 4 years were in a study by Sprung et al. at significantly increased risk for subsequent learning disability compared to those with a history of single or no exposure [16]. Children with a history of multiple exposures to general anesthesia before age 2 years were at significantly increased risk for subsequent learning disability [17]. The same investigators found that the risk of subsequent learning disability was significantly decreased in children born by cesarean delivery using regional anesthesia but not in those born by cesarean delivery using general anesthesia or those born vaginally [18]. These retrospective studies thus indicate associations between early exposure to anesthesia and subsequent neurodevelopmental deficits in children. Ing et al. studied in 2014 the effect of anesthesia on children between 3 and 10 years of age [19]. They concluded that children initially exposed to anesthesia over age 3 did not have an increased risk of neurodevelopmental deficits in language and abstract reasoning at age 10. But an increased risk of motor deficit was found in these children. The authors suggested that there may be distinct windows of vulnerability for different neurodevelopmental domains in children. Ing et al. found in 2012 that there is an association between anesthesia and neuropsychological outcome which may be confined to specific domains. When exposed to anesthesia before age 3 had an increased long-term risk of clinical deficit in receptive and expressive language, as well as abstract reasoning. Children who only had a single exposure to anesthesia also had an increased risk of deficit in receptive language and abstract reasoning. In another publication in 2016 did Ing et al. state that children exposed to anesthesia and surgery before age 3 will show deficits primarily in language and cognition, but that behavioral deficits are not associated with exposure [20]. In 2014 reviewed Davis et al. the published literature on possible differences between general anesthesia and regional anesthesia in the development of cognitive disorders when administered at young age [21]. They concluded that the available studies did not allow to decide that such a difference exists nor that either techniques result in cognitive dysfunctions. However, Wagner et al. in the same journal issue stated that because of its overwhelming complexity, brain development has many possible points of vulnerability to toxic exposures, and that it appears that anesthetic agents could disrupt circuit formation through several discrete mechanisms, none of which are mutually exclusive [22]. Lei et al. concluded from reviewing the existing literature and summarizing the presentations at the Fourth Pediatric Anesthesia Neuro Developmental Assessment (PANDA) symposium in 2014) that general anesthetics in children cause serious concern regarding their deleterious long-term effects on brain development and neuronal plasticity [23]. Sun et al. found in 2016 that children exposed one time to general anesthesia at age of 3 years did not show neurodevelopmental deficits at age 4–5 years [24]. Diaz et al found in 2016 that cumulative exposure to volatile anesthetics in children below age 5 was associated with poor neurodevelopment in children with hypo plastic left heart syndrome [25]. Green et al. published in 2015 a study on histopathological changes in brains of children was died after exposure to inhalation anesthetics [26]. They found histological changes that were not observed in the brains of children died without exposure to anesthesia. In summary, the human literature is controversial as to whether anesthesia in infancy causes cognitive problems later in life. Furthermore, it is unclear what the period of vulnerability to anesthetic neurotoxicity is.

Some other factors involved in neurotoxic phenomena in neonates

Data from animal studies has also shown that untreated painful experiences early in life are associated with neuroplastic changes in the central nervous system that result in hyperalgesic responses to noxious stimuli later in life. Unattended pain can also provoke apoptosis in the developing rat brain, particularly in the thalamus, hypothalamus and amygdala, with subsequent impairment in neurodevelopment and memory. Such reactions have proven to be mitigated by administration of anesthetics [27]. Therefore could surgical stimulation theoretically balance the anesthetic injury or surgery could exacerbate the neural injury. Such effects are not involved in most animal studies where only anesthesia, but nor sur-

gical stimulation was applied. Neuroinflammation can result from surgery and can lead to cognitive changes [28]. It has been demonstrated that it can cause persistent changes in affective behavior in rats. Neonatal anaesthesia is also complicated by physiological and pathological derangements that can contribute to neurological injury. Possible factors involved are cerebral hypoperfusion, hypotension, hypoxia/hyperoxia, hypercarbia/hypocarbia, metabolic derangements (glucose), hypothermia, and coexisting disease.

One of the confounders that is difficult to include in the studies is the severity and development of the original disease and the fact of hospitalization. It might well be that the disorder that needs to be operated is a major factor, however, such disorders does not exist in the animal studies.

Conclusions. From the consistency in outcome of animal studies must it be concluded that even single exposure to general anesthetics during periods of brain development is harmful in animals. This not only occurs at long duration and high dosing exposures but also at clinically relevant duration and dosing. In my opinion are the facts from the numerous animal studies a strong suggestion that neurotoxicity will also occur in children which are anesthetized during the vulnerable period of development of the nervous system. That clinical studies so far only have rather weak indications for neurotoxic effects can be accounted to the difficulty in testing, insufficient consistency in testing methods and the existing many possible confounders. However, possibility of neurotoxicity should, in the opinion of the various investigators be taken into consideration when deciding for surgery. The mechanism of neurotoxicity can be found in the fact that the GABA and NMDA receptors on which the anesthetics act, are also involved in regulation synaptogenesis and neural plasticity. The fact that anesthetics may be neurotoxic, will not make anesthesia in children impossible, but only indicates that administration of anesthesia in children below the age of 34 years should be limited to cases where a serious and strict indication for surgery exist. It also is not ethically proper to withheld anesthesia to children that need to be operated. The chance for the development of neurotoxicity also applies to pregnant women where not only the mother, but also the fetus is exposed to anesthetics during this vulnerable period of development of the child. Parents and care providers should be made aware of the potential risks that anesthetics pose to the developing brain. These opinions are supported by many other physicians [29, 30]. Most of them feel that besides shortening of the duration of anesthesia the number of exposures should be decreased as much as possible [31, 32]. Surgery should, when possible, be postponed till the age of four years of life.

References

1. Behnke M., Smith V. C. Prenatal substance abuse: short- and long-term effects on the exposed fetus. *Pediatrics.* 2013;131:1009-1024.
2. Eckenhoff J. E. Relationship of anesthesia to postoperative personality changes in children. *AMA Am J Dis Child.* 1953;86:587-591.
3. Ikonomidou C., Bosch F., Miksa M. et al. Blockade of NMDA receptors and apoptotic neurodegeneration in the developing brain. *Science.* 1999;283(5398):70-74.
4. Jevtovic-Todorovic V., Hartman R. E., Izumi Y. Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. *J. Neurosci*. 2003;23:876-882.
5. Paule M. G., Li M., Allen R.R. Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys. *Neurotoxicol. Teratol*. 2011;33:220-230.
6. Rappaport B. A., Suresh S., Hertz S. Anesthetic neurotoxicity-clinical implications of animal models. *N. Engl. J. Med.* 2015;372:796-797.
7. Psaty B.M., Platt R., Altman R.B. Neurotoxicity of generic anesthesia agents in infants and children: an orphan research question in search of a sponsor. *JAMA.* 2015;313:1515-1516.
8. Disma N., Mondardini M. C., Terrando N,. Absalom A. R., Bilotta F. A systematic review of methodology applied during preclinical anesthetic neurotoxicity studies: important issues and lessons relevant to the design of future clinical research. *Paediatr. Anaesth.* 2016;26:6-36.
9. Flick R. P., Katusic S. K., Colligan R. C. Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. *Pediatrics.* 2011;128:1053-1061.
10. Ing C., DiMaggio C., Whitehouse A. Long-term differences in language and cognitive function after childhood exposure to anesthesia. *Pediatrics.* 2012;130:476-485.
11. Wilder R., Flick R., Sprung J. Early exposure to anesthesia and learning disabilities in a population based birth cohort. *Anesthesiology.* 2009;110;796-804.
12. Kalkman C. J., Peelen L., Moons K. G. Behavior and development in children and age at the time of first anesthetic exposure. *Anesthesiology.* 2009;110:805-812.
13. DiMaggio C., Sun L. S., Kakavouli A. A retrospective cohort study of the association of anesthesia and hernia repair surgery with behavioral and developmental disorders in young children. *J. Neurosurg. Anesthesiol.* 2009;21:286-291.
14. DiMaggio C., Sun L. S. and Li G. Early childhood exposure to anesthesia and risk of developmental and behavioral disorders in a sibling birth cohort. *Anesth. Analg.* 2011;113:1143-1151.
15. Hansen T. G., Pedersen J. K., Henneberg S. W. Academic performance in adolescence after inguinal hernia repair in infancy: a nationwide cohort study. *Anesthesiology.* 2011;114:1076.
16. Flick R. P., Katusic S. K., Colligan R. C. Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. *Pediatrics.* 2011;128:1053-1061.
17. Sprung J., Flick R. P., Katusic S. K. Attention deficit/hyperactivity disorder after early exposure to procedures requiring general anesthesia. *Mayo Clin. Proc.* 2012;87:120-129.
18. Sprung J., Flick R. P., Wilder R. T. Anesthesia for cesarean delivery and learning disabilities in a population-based birth cohort. *Anesthesiology.* 2009;111:302-310.
19. Ing C. H., DiMaggio C. J., Whitehouse A. J. Neurodevelopmental outcomes after initial childhood anesthetic exposure between ages 3 and 10 years. *J. Neurosurg. Anesthesiol.* 2014;26:377-386.
20. Ing C., Wall M. M., DiMaggio C. J. Latent Class Analysis of Neurodevelopmental Deficit After Exposure to Anesthesia in Early Childhood. *J. Neurosurg. Anesthesiol.* 2016 in press. doi: 10.1097/ANA.0000000000000303
21. Davis N., Lee M., Lin A. Y. Postoperative cognitive function following general versus regional anesthesia: a systematic review. *J Neurosurg Anesthesiol.* 2014;26:369-376.
22. Wagner M., Ryu Y. K., Smith S. C. Review: effects of anesthetics on brain circuit formation. *J. Neurosurg. Anesthesiol.* 2014;26:358-362.
23. Lei S. Y., Hache M., Loepke A. W. Clinical research into anesthetic neurotoxicity: does anesthesia cause neurological abnormalities in humans? *J. Neurosurg. Anesthesiol.* 2014;26:349-357.
24. Sun L. S., Li G., Miller T. L. Association Between a Single General Anesthesia Exposure Before Age 36 Months and Neurocognitive Outcomes in Later Childhood. *JAMA.* 2016;315:2312-2320.
25. Diaz L. K., Gaynor J. W., Koh S. J. Increasing cumulative exposure to volatile anesthetic agents is associated with poorer neurodevelopmental outcomes in children with hypoplastic left heart syndrome. *J. Thorac. Cardiovasc. Surg.* 2016:e46-e121. doi: 10.1016/j.jtcvs.2016.03.095
26. Green M. S., Aman M. M., Stevens L. Histopathological observations in the brains of children exposed to inhalational anesthetic agents: a retrospective autopsy-based study. *Minerva Anestesiol.* 2015;81:1329-1337.

27. Anand K. J., Garg S., Rovnaghi C. R. Ketamine reduces the cell death following inflammatory pain in newborn rat brain. *Pediatr. Res.* 2007;62(3):283–290.
28. Lotrich F. E., El-Gabalawy H., Guenther L. C., Ware C. F. The role of inflammation in the pathophysiology of depression: different treatments and their effects. *J. Rheumatol. Suppl.* 2011;88:48-54.
29. Monteleone M., Khandji A., Cappell J. Anesthesia in children: perspectives from nonsurgical pediatric specialists. *J. Neurosurg. Anesthesiol.* 2014;26:396-398.
30. Rappaport B. A., Suresh S., Hertz S. Anesthetic neurotoxicity--clinical implications of animal models. *N. Engl. J. Med*. 2015;372:796-797.
31. Byrne M. W., Casale P., Garzon M. Pediatric surgeons and anesthesiologists expand the dialogue on the neurotoxicity question, rationale for early and delayed surgeries, and practice changes while awaiting definitive evidence. J. *Neurosurg. Anesthesiol.* 2014;26:391-395.
32. Hays S. R., Deshpande J. K. Newly postulated neurodevelopmental risks of pediatric anesthesia: theories that could rock our world. *J. Urol.* 2013;189:1222-1228.

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ПРОБЛЕМЫ АВТОРСТВА В НАУЧНОЙ РАБОТЕ

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In the review consider of questions about research activities, including publications of clinical research in pediatric surgery and pediatric urology. In most cases requires a multidisciplinary cooperation, which results in dramatic increase in the number of authors in an article. The International Committee of Medical Journal Editors (ICMJE) includes suggestions and recommendations for co-author. Also in the article bring to conformity with collective-authorship as possibility to getting of the result of the multinational and interdisciplinary medical care.

Key words: clinical research, ICMJE, pediatric surgery, multidisciplinary cooperation

В обзоре рассматриваются вопросы научно-исследовательской деятельности, в том числе публикации результатов клинических исследований в области детской хирургии и урологии. В работе отмечается, что использование мультидисциплинарного сотрудничества ведет к резкому увеличению числа соавторов в научных статьях. Приводятся рекомендации Международного комитета редакторов медицинских журналов (ICMJE) по количеству соавторов и написанию научных статей, которые соответствуют мировым требованиям. Кроме того, указаны данные по междисциплинарному соавторству в исследованиях как возможность публикации научных результатов в рейтинговых медицинских журналах.

Ключевые слова: клинические исследования, ICMJE, детская хирургия, многопрофильное сотрудничество

Objective

To determine how many authors should be included in a medical article and to attempt to find an answer to this widely disputed debate.

Background

The medical community is no exception to the world of financial interest and success-oriented professions. The professional progress, the resulting material and moral benefit depend on a number of factors, all of which are easily measurable in the publishing activity (1).

After graduating from the medical school, those young doctors have great advantages who were involved in undergraduate scientific works, attending student conferences, giving presentations and achieving awards, or joined a research groups of an institute and featured as a co-author in an article. These doctors continue to remain ahead of contemporary colleagues whom have shorter scientific CV. After graduating, colleagues with publications are more likely to receive scholarships, academic grant, more often take part in national and international congresses, acquire a PhD degree and faster progress through the professional ladder.

In the USA the candidates entered paediatric surgery residency programme had twice as much publications as those who were not recruited [2]. Doctors must have general (adult) surgery specialty before entering paediatric surgery programme.

In addition, the employer (academic institutions, national institutions, clinics, hospitals) expects its employees to have more publications and achieve higher academic qualifications. For the employ this is not only a prestige matter, but also a financial issue, as the institution budget is based on its scientific achievements. The aforementioned