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(Accepted for publication July 27, 2010.)

In Reply:

We thank you for Dr. Mohammadhosseini's comments to our article on predictive risk factors for persistent postherniotomy pain.[1] We will emphasize that the main purpose of the study was to identify relevant preoperative risk factors together with detailed neurophysiological data from open *versus* laparoscopic groin hernia surgery. We used high ligation and cutting of the hernia sac in indirect hernia, which was the case in 60% of patients. We believe that the literature on the role of sack ligation is not conclusive and at least not quantitatively important for persistent pain. Regarding type of mesh, this was reported in our article, and we agree that the heavyweight mesh used in the Lichtenstein repair may—although the literature again is not conclusive—result in more postoperative discomfort ant potentially persistent pain problems.[2] However, this again does not invalidate our study, where the methodology otherwise is well explained. The point on nerve identification is well taken—although again the literature is not finally conclusive. The ilioinguinal and iliohypogastric nerves were identified in about 95% of cases, but in only about 20% could the genitofemoral nerve be identified; 2.2% of nerves were cut on purpose to allow sufficient position in suturing of the mesh. We do not agree that the quoted study by Caliskan *et al.*[3] is conclusive on prophylactic neurectomy compared with other studies in the literature, also because the study included only 54 patients, which in our opinion is insufficient to provide useful answers on persistent pain problems.

Since our large two-center study was planned, a better understanding of some surgical risk factors has become available, such as those raised by Dr. Mohammadhosseini. However, although such modifications of surgical technique may alter the risk of persistent pain, we believe that our well described study, including preoperative characterization as well as 6 months follow-up with neurophysiological assessment, provides unique information and better understanding of the mechanisms of persistent postherniotomy pain and the potential to reduce this burden.

Eske K. Aasvang, M.D.,* Henrik Kehlet, M.D., Ph.D.
*The Juliane Marie Centre, Rigshospitalet, Copenhagen University, Copenhagen, Denmark. eskeaasvang@yahoo.dk

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(Accepted for publication July 27, 2010.)

Neurotoxicity of Anesthetic Agents and the Developing Brain in Rodents and Primates: The Time Has Come to Focus on Human Beings

To the Editor:

In a recent experimental animal study, Bambrink *et al.*[1] have shown that 5 h of isoflurane anesthesia (0.7–1.5 vol%) in 6-day old primates (Rhesus macaque) caused a large increase in neuronal apoptosis in several brain regions 3 h later. This study adds to a plethora of studies published the last decade showing that exposure of infant animals—primarily rodents—to anesthetic agents, whether *N*-methyl-D-aspartate receptor antagonist or γ-aminobutyric acid receptor agonist, triggers widespread apoptotic death of neuronal cells in the developing brain. Background information about these studies can be found in a recent review article.[2] Indeed, these studies have been a subject of intense speculation and debate in the pediatric anesthetic community.[3] Unfortunately, although human studies are being mounted, they are still scarce, and the results of animal studies and laboratory investigations cannot easily be translated into the human clinical environment because of, for example, pharmacokinetic and pharmacodynamic differences.[3]

However, at this point, there is solid animal evidence that anesthetic drugs induce acute apoptotic neurodegeneration in the developing animal brain. In our opinion, there is no need for any more animal studies of this kind. These will only add to the current confusion rather than contribute to a move forward. From now on, experimental animal research on this topic should be focused on the long-term morphological and, in particular, the neurocognitive consequences of these findings (if any), as well as a safer use of our anesthetic drugs, including possibly protective strategies. For instance, why did the authors not wait several months or even years before harvesting the brains of the monkeys used in the present study? Apoptosis can be elicited by physiologic and pathologic stimuli. The number of supernumerary neurons disappearing due to physiologic apoptosis during normal brain development has been estimated in human beings and rodents to be 50–70% of the entire neuronal cell population. Therefore, one could expect significant recovery of function because the pathologic process occurs at a time of great neuroplasticity.

Researchers should now focus on human beings and neurocognitive function after exposure to anesthetic agents in infancy and early childhood in various clinical situations; there is no need or reason to sacrifice more animals.