

tion that there may be other patient groups in whom either short storage or long storage might have clinical effects, either beneficial or adverse. No significant between-group differences in acquired infections were noted in the three storage-duration trials cited. However, the hypothesis that transfusing red cells with a prolonged storage duration exacerbates established infection in humans would need to be tested.

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1. Steiner ME, Ness PM, Assmann SF, et al. Effects of red-cell storage duration on patients undergoing cardiac surgery. *N Engl J Med* 2015;372:1419-29.
2. Lacroix J, Hébert PC, Fergusson DA, et al. Age of transfused blood in critically ill adults. *N Engl J Med* 2015;372:1410-8.
3. Fergusson DA, Hébert P, Hogan DL, et al. Effect of fresh red blood cell transfusions on clinical outcomes in premature, very low-birth-weight infants: the ARIPI randomized trial. *JAMA* 2012;308:1443-51.

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Oral Propranolol for Infantile Hemangioma

TO THE EDITOR: The article by Léauté-Labrèze et al. (Feb. 19 issue)¹ emphasizes the therapeutic efficacy and the short-term safety of propranolol in the treatment of infantile hemangiomas. However, recent studies raise concerns about potential long-term neurodevelopmental or cognitive effects of the highly lipophilic propranolol.² Indeed, lipophilic beta-blockers cross the blood-brain barrier, leading to sleep and memory disturbances.³ For example, sleep disturbance, somnolence, and irritability have been observed in many infants treated with propranolol,⁴ and this drug has been shown to decrease specific memory functions in adults.⁵ A recent review suggested the possibility that blockage of neural pathways critical for learning and memory could be an unrecognized long-term side effect of propranolol in infants.⁶ Further long-term studies are thus needed before clinicians routinely suggest the use of propranolol in the treatment of infantile hemangiomas.

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1. Léauté-Labrèze C, Hoeger P, Mazereeuw-Hautier J, et al. A randomized, controlled trial of oral propranolol in infantile hemangioma. *N Engl J Med* 2015;372:735-46.
2. Langley A, Pope E. Propranolol and central nervous system function: potential implications for paediatric patients with infantile haemangiomas. *Br J Dermatol* 2015;172:13-23.

3. McAinsh J, Cruickshank JM. Beta-blockers and central nervous system side effects. *Pharmacol Ther* 1990;46:163-97.
4. Solman L, Murabit A, Gnarra M, Harper JI, Syed SB, Glover M. Propranolol for infantile haemangiomas: single centre experience of 250 cases and proposed therapeutic protocol. *Arch Dis Child* 2014;99:1132-6.
5. Kroes MC, Strange BA, Dolan RJ. Beta-adrenergic blockade during memory retrieval in humans evokes a sustained reduction of declarative emotional memory enhancement. *J Neurosci* 2010;30:3959-63.
6. Hoeger PH. Propranolol for infantile haemangiomas: certain chances, potential risks. *Br J Dermatol* 2015;172:3-4.

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THE AUTHORS AND A COLLEAGUE REPLY: Like Tozzi, we are very concerned about potential side effects of propranolol, as with any drug used in children. However, we found no evidence to indicate serious adverse effects of propranolol in our study.

The article by Langley and Pope that Tozzi cited is essentially theoretical, not evidence-driven. There are no data to suggest that the adverse events about which Tozzi is concerned are increased in children treated with propranolol. Moreover, it is uncertain how data from small studies involving healthy adults¹ relate to risks in developing children. Although historical comparisons are difficult and available studies of propranolol for infantile hemangioma (including ours) have not included formal neurocognitive evaluations, the rates of neurodevelopmental defect or delay observed among propranolol-treated patients^{2,3} seem to be within

the range observed in the general population.⁴ Thus far, data from more than 2000 propranolol-treated infants in clinical studies and a compassionate-use program in France have been reassuring, but we agree that there is a need for large studies assessing longer-term outcomes.

To date, propranolol is by far the best-studied beta-blocker in infants. We believe that any assessment of its benefits and potential risks should take into account that the efficacy and safety profiles of alternative drugs used for this condition are not as well documented.

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1. Button KS, Ioannidis JPA, Mokrysz C, et al. Power failure: why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci* 2013;14:365-76.
2. Phillips RJ, Penington AJ, Bekhor PS, Crock CM. Use of propranolol for treatment of infantile haemangiomas in an outpatient setting. *J Paediatr Child Health* 2012;48:902-6.
3. Gonski K, Wargon O. Retrospective follow up of gross motor development in children using propranolol for treatment of infantile haemangioma at Sydney Children's Hospital. *Australas J Dermatol* 2014;55:209-11.
4. Boyle CA, Boulet S, Schieve LA, et al. Trends in the prevalence of developmental disabilities in US children, 1997-2008. *Pediatrics* 2011;127:1034-42.

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Preoperative Testing in Patients Undergoing Cataract Surgery

TO THE EDITOR: I read the article by Chen et al. (April 16 issue)¹ with interest, because I have had several discussions with ophthalmologists at my institution about requests for unnecessary preoperative evaluations and testing (complete blood count, blood chemical profile, electrocardiography) before cataract extraction. The response has been, "Yes, I know they are not needed or recommended, but the hospital will not let me operate without them." At least in some situations, what looks like a provider-related practice pattern could be the result of institutional requirements that should be changed but so far have not been.

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1. Chen CL, Lin GA, Bardach NS, et al. Preoperative medical testing in Medicare patients undergoing cataract surgery. *N Engl J Med* 2015;372:1530-8.

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the practice patterns of individual providers. Other authors have reported that physicians order testing because of tradition, medicolegal concerns, or the belief that another physician expects testing before cataract surgery.^{1,2} Although it may be difficult to change institutional dogma and entrenched practice patterns, we believe that physicians should feel empowered to question and update policies and protocols that have not kept up with current evidence-based recommendations in order to provide better and higher-value care to their patients. In 2000, the American Academy of Ophthalmology issued a clinical statement recommending against the use of routine preoperative testing in patients undergoing cataract surgery, and the organization updated this statement in 2014.³ For low-risk elective ambulatory procedures such as cataract surgery, patients in their usual state of health should be allowed to proceed to the operating room without any further workup.³⁻⁵

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THE AUTHORS REPLY: We agree with Saver that the ongoing use of routine preoperative testing in patients undergoing cataract surgery may result from institutional requirements rather than