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REPLY

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Thank you for your interest in our article. Our studies in $ATP7b^{-/-}$ mice indicate that the genetic program regulating lipid metabolism is down-regulated at 6 weeks of age. At this age, the mice have evidence of elevated hepatic copper, but liver disease has not yet developed.⁽¹⁾ We were able to prevent the development of liver disease using the liver X receptor (LXR)/retinoid X receptor agonist, yet we did not affect hepatic copper (which remained high). We have not yet been able to definitively show how copper disrupts LXR-mediated lipid metabolism in animals, but *in vitro* experiments have shown that copper can alter nuclear receptor signaling.⁽²⁾

The results you have presented are interesting. We certainly agree that patients with severe liver disease will have low cholesterol. There are many factors affecting serum lipid levels in children, which may account for the lack of correlation reported between copper levels and serum cholesterol. There are several published reports indicating that there is deranged lipid metabolism and low serum lipids in Wilson's disease (WD).^(3–5) We encourage you to submit your data for peer review so the WD community can learn from your experiences.

We also agree that animal data must be scrutinized rigorously before applying the findings to humans. Even in mice, lipid metabolism is dependent upon multiple factors, such as age, sex, and disease stage. Nonetheless, we believe our research has shed new light onto the evolving paradigm for the pathogenesis of WD and may open new avenues for potential therapies.

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