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- [Active surveillance for intussusception in a phase III efficacy trial of an oral monovalent rotavirus vaccine in India.](#)

John J.Vaccine. 2014.[1 comment](#)

[Jacob Puliyel2014 Aug 14 9:58 p.m.](#)

### **Licensing the vaccine for general use (in remote areas of India), seems impossible to justify**

I commend Dr John and colleagues for this report on the trial with the 116E Indian rotavirus vaccine. However the authors limit their discussion to comparisons with the trials of Rotarix and Rotateq which recruited some 60,000 patients each. It will be more useful to compare the 116E trial safety results with the RotaShield vaccine trials

[http://www.path.org/vaccineresources/files/RotaShield\\_Fact\\_Sheet\\_CDC.pdf](http://www.path.org/vaccineresources/files/RotaShield_Fact_Sheet_CDC.pdf).

### **RotaShield trial**

The RotaShield trial recruited double the numbers recruited in the present 116E study. RotaShield was licensed after the trial involving 14,687 patients (10,054 received the rotavirus vaccine and 4,633 received placebo). In the study there was one case of intussusceptions among the 4633 receiving placebo. This suggests that the 'normal rate of intussusception' was approximately 2/10,000, in that population. Five cases of intussusceptions occurred among 10,054 RotaShield vaccine recipients. Thus there were an excess of 3 cases of intussusceptions for each 10,000 children vaccinated. **All the intussusceptions were among infants who received a second or a third dose of vaccine.** The difference between the vaccinated and placebo recipients was not statistically significant

[http://www.path.org/vaccineresources/files/RotaShield\\_Fact\\_Sheet\\_CDC.pdf](http://www.path.org/vaccineresources/files/RotaShield_Fact_Sheet_CDC.pdf).

### **116E Trial**

With the 116E vaccine trial there were 6 cases of intussusceptions in 2267 controls which works out to be 2.6 cases per 1000 placebo recipients. The 'normal rate of intussusception' in this study was at least 10 times higher than the RotaShield trial (where it was 0.2 cases per 1000 placebo recipients). There were 17 cases of ultrasound confirmed intussusceptions among the 4532 given the 116E vaccine which is 3.75 cases per 1000 babies vaccinated. The comparative figure for the RotaShield study was 0.5 cases/1000. In the 116E trial there was an excess of 1 case of intussusceptions for every 1000 children vaccinated with the rotavirus vaccine (compared to the RotaShield trial where there were 3 excess intussusceptions per 10,000 vaccinated). RotaShield vaccine was withdrawn after licensing, on account of unacceptable risk of intussusception. The risk of intussusception in the 116E trial was three times higher than with the RotaShield trial. We are told that in the 116E trial, 50% intussusceptions diagnosed by ultrasound, resolved spontaneously [John J, 2014](#). In the remaining 50% there is need for urgent treatment by a radiologist or pediatric surgeon. In remote parts of India, without motorable roads, let alone radiologists and pediatric surgeons, mortality will be near 100%

<http://emedicine.medscape.com/article/930708-overview>. Such specialized care (radiological or

surgical reduction of intussusception) is not available in vast swathes of India and we can assume vaccinated babies would die at home passing blood and mucus in the stools and it will be presumed they had died of dysentery and sepsis rather than intussusception caused by the vaccine.

### **Intussusception risks compared to diarrhea deaths avoided**

Assuming only 50% ultrasound diagnosed intussusceptions need urgent treatment [John J, 2014](#) we can assume that one child in 2000 vaccinated babies will develop this life threatening condition. The possible harm in remote areas (deaths from intussusceptions 1/2000) is not offset by benefits (diarrhea deaths avoided using the 116E vaccine).

In the first two years after vaccination, there number of infants that needed to be immunized to prevent one episode of rotavirus diarrhea of any severity was 21 [Bhandari N, 2014](#). Assuming mortality from rotavirus diarrhea to be 1% in the first 2 years of life with community management [Lal S, 1994](#) [Kosek M, 2003](#) 2100 babies will have to be vaccinated to prevent one death from diarrhea in the first 2 years of life.

When 2100 babies are vaccinated to prevent that 1 death from rotavirus diarrhea - 1 child will have intussusceptions and die in remote areas of the country. This is why, given the limited evidence of this 116E trial, licensing the vaccine for general use (in remote areas of India), seems impossible to justify.