

Title: Colposcopy: Still Useful in Microbicide Safety Trials?

Authors: Christine Mauck*¹, Debra Weiner², Jaim Jou-Lai²

¹CONRAD, Arlington, VA, USA; ²Family Health International, Research Triangle Park, NC, USA

Background: Colposcopy has been standardized for vaginal microbicide research. It is assumed that epithelial disruption is of most concern, since grossly observed disruption was associated with HIV in one trial. However, colposcopically observed disruption has not been correlated in a Phase III trial with risk of HIV infection, nor has any other colposcopic finding. The justification for continuing colposcopy has recently been questioned. This meta-analysis was performed to determine what would have been missed in nine microbicide safety trials if colposcopy had not been done.

Methods: Nine Phase I trials conducted between 2002 and 2008 were selected on the basis of having data on whether findings were seen by both naked eye exam and colposcopy or by colposcopy alone.

Results: A total of 694 colposcopic findings were observed. Of these, 319 (45.8%) were seen by colposcopy alone and would have been missed if colposcopy had not been done. Twenty-six findings of deep epithelial disruption were observed, seven (26.9%) of which were seen by colposcopy alone. Analogous figures for peeling, petechiae/ecchymoses and erythema were 50/95 (52.6%), 112/194 (57.7%), 98/255 (38.4%), respectively. The seven deep findings were < 5mm and involved one woman in each of four studies. Six were lacerations and one was an abrasion. Six were on the cervix and one was on the vaginal wall. 333/694 findings were small (<0.5cm): of these, 200 (60.1%) were seen only by colposcopy. 210 large (>1 cm) findings were seen, 51 (24.3%) of which were seen only by colposcopy. The anatomical site with the greatest proportion of findings that would have been missed was the cervix: 196/378 (51.9%).

Conclusions: Almost half of findings observed in these nine trials would have been missed without colposcopy. A quarter of the deep disruptions would not have been seen, which is consistent with an earlier small study designed to look at this question, although such findings are rare. The clinical significance of other findings (e.g., erythema) is unknown. Somewhat surprisingly, about a quarter of large findings would have been missed, as would about half of findings on the relatively visible cervix. While colposcopic findings have not been validated as an indicator of HIV risk, neither has any other safety marker. Colposcopy is subjective and dependent on examiner effort, but discontinuing colposcopy in safety trials would be premature until we have a more objective, validated replacement. Efforts are underway to identify such a marker.