

Format for ANSWERING REVIEWERS



October 25, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 21500-review.doc).

Title: Amniocentesis: A contemporary review

Author: Katherine Ann Connolly, Keith Arnold Eddleman

Name of Journal: *World Journal of Obstetrics and Gynecology*

ESPS Manuscript NO: 21500

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer #742373

- “The abstract provided little contemporary information, reviewer suggest rewrite”
 - Lines 25-32 discuss role of amniocentesis when compared to cell-free fetal DNA testing
 - Lines 49-51 readdress the risk of fetal loss and give a new contemporary assessment of risk
- “It should included the most recent studies results, especially why this technique cannot replaced by other new techniques”
 - Lines 368-383 address the reason why cell free fetal DNA cannot replace amniocentesis
- “Conception argument: In abstract: For genetic diagnosis, amniocenteses is offered for those patients require to do gene or chromosome diagnosis. Not every patient need have it done”
 - ACOG still recommends that all women be offered amniocentesis and we agree with this recommendation and support it in our review article
- The language need improvements in multiple places. For example: Indications, paragraph 1: ‘This mosaicism is usually confined to the placenta, however can be also seen in the fetus in 10% of cases’ Rewrite this sentence”
 - Line 135-136
- “Suggest to use the standard medical term as keywords. “
 - We do feel that we have used standard medical terms as keywords. Please let us know if we are incorrect.
- “Please give detail for abbreviations for the first time in the manuscript. For example MCA.”
 - Thank you. We have now edited each instance where we had not done this.
- “Some important issue is not touched in this manuscript. For example: amniocenteses procedure in patients with blood transmitted disease (HIV, HBV, etc), amniotic fluid embolism, stem cells from amniotic fluid, etc. Hope this can also be discussed in the manuscript”

- New section was added under “indications” outlining potential use of amniotic cells as stem cells (lines 204-216)
- New section was added under “ other considerations” addressing amniocentesis in the setting of HIV/HBV/HCV. (Lines 327-362)

Reviewer #742121

- Comment [u1]: It is not clear if “this” refers to amniocentesis or cell free fetal DNA testing – please rephrase
 - Edited line 26 and changed “this” to “amniocentesis”
- Comment [u2]: The authors should also discuss viral intrauterine infections (see also p.8)
 - See new lines 197-203
- Comment [u3]: The NICHD and ACOG recommendation should be added (see also p. 6 and 7) – please re-phrase
 - Lines 37-43
- Comment [u4]:What about other multiple gestations?
 - Lines 304-305
- Comment [u5]: The NICHD and ACOG recommendation should be added (see also p. 6 and 7) – please re-phrase
 - Lines 59-62
- Comment [u6]: The authors should provide more information on this study, including number of participants, study design etc.
 - Lines 103-106
- Comment [u7]: The authors should provide more information on this study, including number of participants, study design etc.
 - Lines 106-109
- Comment [u8]: Is reference 12 indeed a randomized trial or just a prospective comparative study? Were there any other clinically relevant findings in this particular study?
 - This was truly a randomized trial, with participants randomized in a 1:1 fashion to either a 20 or 22 gauge needle. The major findings of the study are detailed in our text. Lines 113-124
- Comment [u9]: The authors should provide more information on this study, including number of participants, study design etc.
 - Lines 118-120

- Comment [u10]: The authors should however mention the advantages of CVS as compared with amniocentesis.
 - Lines 313-315
- Comment [u11]: The authors should mention this in the Abstract and core tip
 - Lines 37-43
- Comment [u12]: The authors should also discuss viral intrauterine infections, which can be detected with molecular tests in the amniotic fluid following amniocentesis.
 - Added lines 195-201
- Comment [u13]: This should be mentioned in brief in the Abstract
 - Lines 45-47
- Comment [u14]: What about higher order multiple pregnancies?
 - Lines 304-305
- Comment [u15]: What does really 15.5 mean?
 - Line 325

Reviewer #742054

- “I believe that the article would benefit more of a critical review, focusing on one aspect of the amniocentesis and critically explore the literature, It would also be great if the authors could address the shortcomings of the research on the amniocentesis and provide direction for future research.”
 - We highlighted the shortcomings on the research regarding loss rates and explained why further RCTs are not feasible. New sections added on the limited data in the setting of maternal HIV, hepatitis B, hepatitis C and the limited data in the setting of higher order multiples highlights directions for future research.

Reviewer #742268

- Minor comments: Titel page ‘Cononlly KA et al’ should read as ‘Connolly KA and Eddleman KA’
 - Corrected Line 6
- Abbreviation list is missing
 - All abbreviations are in parentheses following the first time they are used in the text
- Historical considerations: ‘Fuchs’ should read as ‘Fuchs and Riis’
 - Corrected line 75
- Sentence not complete: ‘Diagnostic testing with amniocentesis or CVS remains the only way to definitively perform karyotype and offer microarray’
 - Corrected lines 381-383

- First section: a missing period: comparison Similarly
 - Corrected line 318
- Repetitively used sentence: ‘We counsel patients that technology has changed since the original studies in the 1970s and feel comfortable quoting a loss rate of 1/500-1/1,000 based on contemporary data’
 - We felt that this is a rate we would like to emphasize by repeating it in several sections.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Obstetrics and Gynecology*

Sincerely yours,

Katherine Ann Connolly, MD

Division of Maternal-Fetal Medicine, Department of Obstetrics

Gynecology and Reproductive Sciences, Mount Sinai Hospital

5 East 98th Street, Room 256, New York, NY 10029, United States

E-mail: katherine.connolly@mssm.edu

Telephone: +1-212-2415681

Fax: +1-212-3487438

Revision has been made according to the suggestions of the journal Editor-in-Chief:

Thank you very much. Here is the revised version. The editor had asked for one new reference to be incorporated and I have highlighted the area where I added this into the manuscript.

All the best,

Katherine Connolly