Reviewer's report

Title: Establishment of a leptospirosis model in guinea pigs using an epicutaneous inoculations route

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Reviewer: Daniel athanazio

Reviewer's report:

1. Background. Second paragraph. The authors adequately state that “intraperitoneal inoculation route is the most commonly used in these models of leptospirosis”. However, if the main point of the study is to search for alternative ways to establish experimental infection, some references are lacking on:

- Conjunctival infusion, mainly in dogs

- Subcutaneous route in hamsters

  Attempts to reproduce natural conditions, such as inoculation of rat urine or exposure to rat bites (in guinea pig model).

  Thus, a more detailed discussion of alternative methods of inoculation is warranted to clearly introduce what is the background of the issue addressed by the authors.

2. Results. “Tissue distribution...”. “A pronounced acute inflammatory response were induced in site inoculation”. Please note that this is not usually described in clinical settings. No local response seems to follow human infection after penetration of leptospires in superficial tissues. Since this observation is of more
interest than histopathology of classical lesions in target organs, the reader would benefit of having a more detailed description of such findings with the correlation of skin lesions and the presence of leptospires.

3. Discussion. The main concern on the whole article is that it describes a clever way to reproduce skin abrasions that could better reproduce a natural way to acquire leptospirosis, however, this new model was not compared to established ones. Since intraperitoneal inoculation is much easier to handle than this new abrasion route, intraperitoneal infection would be still the route of choice except if the authors can show that intraperitoneal infection result in artificial outcomes such as different patterns of dissemination of leptospires in tissues, different immune responses or different clinical outcomes. If all of these are the same, intraperitoneal infection will still be the route of choice. If intraperitoneal and abrasion routes are different in those results they provide, than that would be a strong point favoring the new method.

Only establishing infection resulting in acute lethal disease is not sufficient to support a new route of infection to the scientific community devoted to study leptospirosis. Please note that there is already a study comparing different routes of infection and the dissemination of leptospires in tissues.


All these concerns have not been discussed in the manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests