Reviewer's report

Title: Comparative estimation of chikungunya prevalence in Reunion Island

Version: 1 Date: 3 October 2007

Reviewer: Jean-Paul Chretien

Reviewer's report:

General:
Overall, this manuscript describes a well-conducted study that provides a useful addition to the growing literature on the chikungunya fever epidemic in La Reunion during 2005-2006. Previous population-based studies estimating the extent of the epidemic in La Reunion have used clinical diagnostic criteria alone. Guernier et al. provide the first population-based study using laboratory diagnosis. Their prevalence estimate following the epidemic (38%) is similar to that obtained previously using clinical criteria (34%), but the apparent validation of the surveillance program based on clinical criteria is an important result. Their analysis of serum from pregnant women at the peak of the epidemic also agrees with general-population results from the clinical surveillance program.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached):

PATIENTS AND METHODS - PREGNANT WOMEN
1) Were these outpatients or inpatients, or both?

2) In participating laboratories, were all sera collected from pregnant women during 15 Jan-15 Feb 2006 included in the study? If not, how were sera selected?

PATIENTS AND METHODS - GENERAL POPULATION
3) How was the stratification on “population size and type of habitat performed”? What does “type of habitat” mean?

4) A reference should be provided for the “Kich method” and it should described in simple terms.

5) How many potential subjects were lost to each of the reasons for exclusion?

6) What does “redressed by INSEE…” mean?

7) What was included in the questionnaire? What timeframe were subjects asked to consider in answering the questions?

RESULTS:
8) Several prevalence estimates are given in the text that could be assessed more efficiently in a table. For example, a table of test result (+, -) by antibody (IgG, IgM, IgG &/or IgM), stratified by study (pregnant women, general population), would convey the key results of the manuscript.

9) A point estimate should be provided to accompany the range of possible number of infections based on results in pregnant women (154,000 to 190,000), and the type of range used should be identified (is it a 95% CI?).

10) Table 1 would be easier to interpret if either the row or column margins totaled to 100%. For example, if the row margins totaled to 100%, one could read directly from the table the % seropositive among those who answered “No” and those who answered “Yes”. In its current form, the Table does not allow comparison of seropositivity by questionnaire response, or of questionnaire response by seropositivity, without calculation. Also, I suggest dropping the 95% CIs from the table, and adding sample size for each cell (e.g., each cell could have the cell sample size and, in parentheses, the %, based either on the row or column total sample size). Footnotes “a” and “b” could be dropped.

11) The data presented near the end of the second-to-last paragraph of the Results section (following “Moreover, considering responses…”) would not need to be presented in the text if Table 1 were revised as suggested above, with cell percentages based on row totals.

12) The data presented in the last paragraph of the Results section are a bit confusing. Since 88.5% of people who self-reported chikungunya fever also reported fever and arthralgia, there must have been separate questions on whether subjects had chikungunya and more specifically on what symptoms subjects had. These data would be easier to assess in a table, showing questionnaire answers on symptomatology by serological results.

13) In fact, Table 1 could be expanded to include both the question it currently has as well as questions on symptoms. Demographic and other questionnaire data also may be helpful to see by serology, either in the same table or separately.

DISCUSSION:

14) The possibility that some of the “asymptomatic” or “atypical” cases might have been infected before the current epidemic should be discussed, especially since only IgG was tested in this general population.

15) I’m not sure how the Positive Predictive Value for clinical diagnosis “at the peak of the outbreak”, given as > 95%, was calculated. The data in this paper from the peak of the outbreak comes from pregnant women, for whom clinical information is not provided. The general-population study did include self-reported clinical information, but 1) it is not clear that patients were asked to report whether they had received a diagnosis of chikungunya fever, or whether they were asked to report symptoms and their own assessment of whether they had chikungunya fever; 2) this study occurred after the epidemic, not at its peak;
and 3) PPV for self-report of chikungunya fever based on Table 1 would be
31.4%/35.9% = 87.5%.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

TITLE:
1) The title is ambiguous – it suggests that prevalence estimates based on different methods, or in different populations, have been compared, but does not identify those methods or populations. It may be more helpful to identify the study as a seroprevalence study – e.g., “Seroprevalence of Chikungunya virus infection in Reunion Island”, or something like that.

ABSTRACT:
2) Background: The meaning of the sentence, “However, it was not known…” is unclear. This sentence could probably be omitted, and the following sentence revised to introduce the present study as a serological assessment that complements previous clinical diagnosis-based prevalence estimates.

3) Methods: The questionnaire should be mentioned and key questions identified.

4) Results: Prevalence should be given separately for IgM+, IgG+, and IgM+/IgG+. If space permits, comparison of ELISA results to questionnaire results also should be included. A range of number of cases in Reunion based on results in pregnant women is provided (154,000 to 190,000), but a point estimate based on general-population results is provided (300,000). These results should be communicated consistently – e.g., point estimate alone for both.

5) Conclusions: The seroprevalence estimates should be compared to previous estimates by CIRE using clinical diagnosis alone.

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Discretionary Revisions (which the author can choose to ignore)

RESULTS:
1) The sentence, “The rate of asymptomatic cases combined to atypical cases…” might be clearer if rephrased as “The prevalence of seropositivity with negative self-report of chikungunya fever diagnosis was 5.0% (95% CI 3.9-6.3%)”, or something like that.

DISCUSSION:
2) The authors mention that their results “allow evaluating the order of magnitude of seroprevalence and herd immunity”. Their estimate of seroprevalence certainly is much better than an order-of-magnitude estimate. But there’s no direct assessment of herd immunity, so I suggest dropping reference to it here.
3) I don’t see that references 13 and 15 provide the figures given in parentheses for asymptomatic infection rate in West Nile and dengue, respectively. It’s possible that calculation is required or that I’ve missed where these papers provided those numbers, but the authors may wish to verify.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests