Rocky Mountain spotted fever in Sonora, Mexico

Gerardo Álvarez PhD
Session: Vector-Borne/Zoonotic Disease
**Background**

- Sonora, Mexico borders the U.S. state of Arizona
- Population: 2,925,366
- Considered as a well-developed state within Mexico (UN Program, 2012)
- After 5 decades with no cases of RMSF, reemerged early 2000’s (Álvarez G. Salud Publica Mex 2013; 55 (2): 151-52)
  - Endemic from 1900-1950. Known as “Fiebre Pinta”
- RMSF incidence coincides with the presence of the tick *Rhipicephalus sanguineus* on dogs (Tinoco L. Vet Rec 2009;164:59-61; Eremeeva ME. J Med Entomol. 2011;48:418–21)
Background

• April 2015, Mexican MOH issued a declaration of epidemiologic emergency on Rocky Mountain spotted fever (RMSF)
• Public health concerns in several states, mostly in northern Mexico
• Significant impact in underserved populations
  • Particularly children < 10 years old
Incidence of RMSF by state. Mexico, 2009-2014

States with positive samples
States with documented incidence
From 2000

Epi Bulletin DGE/SSA
Registered cases 2009-2014: 3978
2009: 3/32 States notified cases
2014: 21/32 States documented cases

3 States with highest incidence
1. Baja California
2. Baja California Sur
3. Sonora (331) → 1034 cases in state

RMSF incidence by State, Mexico, 2014

RMSF (A77.0) incidence by State. México, 2014

Coahuila: 2.97
Baja California: 2.71
Sonora: 2.56
Nuevo León: 0.62
Baja...: 0.40
Morelos: 0.26
Nacional: 0.26
Sinaloa: 0.17
Chihuahua: 0.16
Quintana Roo: 0.13
Guanajuato: 0.03

RMSF Annual incidence. Mexico, 2003-2016

RMSF cases by year of occurrence, Mexico 2003-2016*

* Up to May 31, 2016
RMSF Annual incidence. Sonora, 2003-2016*

RMSF incidence by year of occurrence. Sonora, 2004-2016*

Source: Sonora Secretariat of Health * Up to July 22, 2016
RMSF incidence and CFR, Sonora. 2003-2016*

USA CFR <0.5%. Sonora CFR >25%
Epidemiology

• RMSF in Sonora spreads from the southern to the northern areas of the state

• 2004-2016: 1200 cases; 211 deaths. CFR = 17.6%

• 497 cases in <19 years old; 108 deaths. 51% of RMSF total mortality. CFR=22%
  • 225 cases in a pediatric hospital; 75 deaths. CFR=33.3%
Rocky Mountain spotted fever. Case-fatality ratio by age group.
Sonora, Mexico. 2004-2015*
(n=1030)

Source: Epidemiological Surveillance System. UIEES/DE/DGSSC/SSP
*Up to 10/22/2015
Epidemiology

- RMSF in children from Sonora
- Mostly urban (75% patients live in urban localities)
- Socioenvironmental factors may play a role in the epidemic → 90% live in poverty
  - 85% has temporary medical insurance (seguro popular)
- 90% had a documented history of tick contact

RMSF cases by medical care insurance. Mexico, 2009-2013
Epidemiology

• “Where you live makes a difference to your health, over and above who you are” (S.V. Subramanian, 2000)

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Fatal (63)</th>
<th>Nonfatal (147)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>100</td>
<td>99.3</td>
</tr>
<tr>
<td>Rash (palms and soles)</td>
<td>92.1</td>
<td>86.4</td>
</tr>
<tr>
<td>Headache/Irritability</td>
<td>85.7</td>
<td>80.2</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>77.8</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;50,000µL)</td>
<td></td>
<td>82.5</td>
</tr>
<tr>
<td>Hyponatremia (&lt;135 meq/L)</td>
<td></td>
<td>69.8</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td></td>
<td>62.3</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td></td>
<td>52.4</td>
</tr>
</tbody>
</table>

* 01/01/2004-06/18/2015
RMSF. Clinical features

RMSF rash may involve palms and soles. Sign of delay in clinical suspicion

[Buckingham, 2007; Graham, 2011; Alvarez, 2015]
RMSF. Clinical features

Other significant clinical signs include periorbital edema and swelling of ankles and hands. [Buckingham, 2005; Graham, 2011; SSA-Mexico, 2013]
RMSF. Clinical features

“With progression the rash becomes more petechial and individual lesions often enlarge and coalesce to form ecchymoses” (Paddock, C. In press, 2015)
RMSF. Clinical features

RMSF. Female 4 years old. 2014
RMSF. Male 3 years old. 2013
RMSF. Female 16 years old. 2013

Petechial component is very frequent, 82% of our patients had severe petechiae
RMSF. Clinical features

RMSF. Male 6 years old. 2006

RMSF. Male 1 year old. 2015
RMSF. Clinical features
### Predictors of mortality in hospitalized children with Rocky Mountain Spotted Fever, Sonora 2004-2015

**Results of logistic multivariate analysis***

<table>
<thead>
<tr>
<th>Predictor</th>
<th>β coefficient</th>
<th>Standard error</th>
<th>OR&lt;sub&gt;adj&lt;/sub&gt;</th>
<th>95% IC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-2.33</td>
<td>0.28</td>
<td>0.10</td>
<td>(0.02, 0.42)</td>
</tr>
<tr>
<td><strong>Delay in specific treatment with doxycycline (&gt; 5&lt;sup&gt;th&lt;/sup&gt; day) [1=Yes]</strong></td>
<td>1.08</td>
<td>0.51</td>
<td><strong>2.95</strong></td>
<td>(1.10, 7.95)*</td>
</tr>
<tr>
<td><strong>Acute kidney injury (1=Yes)</strong></td>
<td>2.17</td>
<td>0.48</td>
<td><strong>8.79</strong></td>
<td>(3.46, 22.33)*</td>
</tr>
<tr>
<td><strong>Severe sepsis (1=Yes)</strong></td>
<td>1.31</td>
<td>0.48</td>
<td><strong>3.71</strong></td>
<td>(1.44, 9.58)*</td>
</tr>
<tr>
<td>Age (1= Less than 10 years old)</td>
<td>1.07</td>
<td>0.57</td>
<td>2.93</td>
<td>(0.97, 8.87)</td>
</tr>
<tr>
<td>Hypoproteinemia [&lt;6.4 g/dL] (1=Yes)</td>
<td>0.70</td>
<td>0.92</td>
<td>2.02</td>
<td>(0.33, 12.32)</td>
</tr>
<tr>
<td>Ecchymosis (1=Yes)</td>
<td>0.46</td>
<td>0.46</td>
<td>1.58</td>
<td>(0.64, 3.91)</td>
</tr>
<tr>
<td>Petechiae (1=Yes)</td>
<td>-0.88</td>
<td>0.70</td>
<td>0.42</td>
<td>(0.11, 1.64)</td>
</tr>
<tr>
<td>Thrombocytopenia &lt;50,000 μL (1=Yes)</td>
<td>1.08</td>
<td>0.64</td>
<td>2.95</td>
<td>(0.84, 10.35)</td>
</tr>
</tbody>
</table>

* The significance of the final model was assessed by Log Likelihood [-66.36229]. Model R<sup>2</sup> = 0.50224.

1/ Adjusted odds ratio accounting for all the variables included in the final model. *Statistically significant

Multiple risk factors for RMSF

- **Social deprivation** (poverty, marginalization)
- **Risk perception** (daily contact with ticks; the role of dogs)
- **Knowledge of disease** (i.e. meaning of fever)
- **Thoughts on prevention**

**Social context**
- Policies, programs and allocated resources
- The role of science
- Risk communication
- **Knowledge of disease** (clinical signs and symptoms, and risk factors)
- **Poor knowledge on prevention** (timely diagnosis, reluctance to treatment, care of medical complications)

(Suárez, 2006; Süss, 2008; Labruna, 2011)
• What factors are associated with morbidity and mortality of people infected by *R. rickettsii* in Sonora?
Aware of RMSF case-fatality rate, by age of medical provider. Sonora, Mexico. 2015 (n=343)

- Physicians do know very little about fatality of RMSF

P = 0.023

Alvarez G et al. Knowledge, attitudes and practices of physicians on Rocky Mountain spotted fever. Sonora, 2015
Manuscript in preparation. Do not cite
• 30-40% of physicians are reluctant to initiate doxycycline in children

Use of doxycycline in children with RMSF, by age of medical provider. Sonora, México. 2015 (n=343)

Alvarez G et al. Knowledge, attitudes and practices of physicians on Rocky Mountain spotted fever. Sonora, 2015 Manuscript in preparation. Do not cite
• <50% of physicians initiate timely specific treatment

Alvarez G et al. Knowledge, attitudes and practices of physicians on Rocky Mountain spotted fever. Sonora, 2015
Manuscript in preparation. Do not cite
Diagnosis at initial presentation for medical care in children with RMSF. Sonora, Mexico, 2004-2015*

* 01/01/2004-06/18/2015

No statistically significant differences were observed
Community knowledge about RMSF. Sonora, 2015

If you or someone of your family got fever, where would you go?

- There is a low perception in community about early manifestations of RMSF

Alvarez G et al. Knowledge at community level on Rocky Mountain spotted fever. Sonora, 2015
Manuscript in preparation. Do not cite
• In areas highly epidemic, 40% of those responsible for family health care do not know about RMSF

Community knowledge about RMSF. Sonora, 2015
Have you heard about a disease called RMSF or “rickettsia”? (n=400)

P < 0.001
• Almost 50% of subjects do not know how to prevent RMSF.
• Poor knowledge about RMSF in both physicians and community
• We know very little about diagnosis, treatment, prevention
• “…I allude to a blindness of reason. We are blind to reason and behave as blind” (José Saramago, 1995)
Final remarks

1. RMSF is reemerging in Sonora
2. Highly lethal but preventable. Deaths can be avoided
3. Shows an unacceptable burden in pediatric population
4. Participation of pharmaceutical industry and international agencies of health and social welfare is required
Final question

• Is RMSF in Mexico just a health-related problem ... or is an ethical neglect?
• It is not only a health problem, it is an expression of social injustice
  • Because it is associated with social backwardness, does affect individuals and vulnerable populations and is not addressed as a priority
Conclusion

• In Mexico, to properly address RMSF political will and moral commitment is needed, in addition to technical and scientific approach.
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