








Complexity of Treating New World Cutaneous Leishmaniasis

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Factors causing variation in response to antileishmanial chemotherapy

- *Leishmania* species 
- Clinical factors 
- *Leishmania* intrinsic variability 
- Clinical response to treatment 
- Is there a need of doing specie specific diagnosis for treatment? 

Leishmania species causing NW-CL

| <i>Leishmania</i> Species | Country |
|----------------------------------|-------------------------------------|
| <i>L. (viannia) braziliensis</i> | Central and South America |
| <i>L. (v) guyanensis</i> | South America |
| <i>L. (v) panamensis</i> | Nicaragua, Panamá and South America |
| <i>L. (v) peruviana</i> | Perú and Argentina |
| <i>L. (v) lainsoni</i> | Bolivia and Brazil |
| <i>L. mexicana</i> | México, Central and South America |
| <i>L. amazonensis</i> | South America |
| <i>L. venezuelensis</i> | Venezuela |
| <i>L. chagasi</i> | Central and South America |

Clinical factors causing variation to antileishmanial chemotherapy

- Clinical forms
 - Single non ulcerated lesion
 - Single ulcerated lesion
 - Multiple lesions
 - DCL
- Lesion localization
 - Joints
 - Ears
- Time of evolution
 - Recent vrs old lesions
- Manipulation (home made remedies)
- Over infections
- Host immune status

Leishmania intrinsic variation

- There is sufficient information supporting the intrinsic differences in *Leishmania* species sensitivity to different antileishmania drugs.
 - Studies using the amastigote-macrophage model
 - Sensitivity of promastigotes and amastigotes in vitro assays
 - Murine macrophage –amastigote model

| | |
|-----------------------|---|
| Sodium Stibogluconate | <i>L. braziliensis</i> and <i>L. donovani</i> more sensitive than <i>L. mexicana</i> , <i>L. amazonensis</i> and <i>L. guyanensis</i> |
| Amphotericin B | <i>L. mexicana</i> is less sensitive than <i>L. donovani</i> |
| Miltefosine | <i>L. donovani</i> more sensitive than <i>L. braziliensis</i> , <i>L. guyanensis</i> and <i>L. mexicana</i> |
| Paromomycin | <i>L. major</i> and <i>L. tropica</i> more sensitive than <i>L. braziliensis</i> and <i>L. mexicana</i> |
| Azoles | Contradictory information |



Clinical response to treatment

| Drug | Country / <i>Leishmania</i> specie | Cure rate | Reference |
|-----------------------|---|-------------------|---|
| Sb^v | Brazil (Rio Janeiro): <i>L. braziliensis</i> | 84% | Oliveira-Neto, 1993 |
| | Brazil (Bahia): <i>L. braziliensis</i> | 51% | Romero, 2001 |
| | Guatemala: <i>L. braziliensis</i> | 90% | Arana, 1994 |
| | Perú: <i>L. braziliensis</i> | 70% | Arévalo, 2007 |
| | Colombia: <i>L. braziliensis</i> <i>L. panamensis</i> | 67% 93% 81% | Palacios, 2001 Velez, 1997 Soto, 2005 |
| | Ecuador: <i>L. panamensis</i> (+++) <i>L. guyanensis</i> (+) | 91% | Guderian, 1991 |
| | Brazil: <i>L. guyanensis</i> | 26% | Romero, 2001 |
| | Perú: <i>L. guyanensis</i> | 92% | Arévalo, 2007 |

Clinical response to treatment

| Drug | Country / <i>Leishmania</i> specie | Cure rate | Reference |
|--------------|------------------------------------|-----------|-------------|
| Miltefosine | Guatemala: <i>L. braziliensis</i> | 33% | Soto, 2004 |
| | Guatemala: <i>L. mexicana</i> | 64% | Soto, 2004 |
| | Colombia: <i>L. panamensis</i> | 91% | Soto, 2004 |
| Ketoconazole | Panamá: <i>L. panamensis</i> | 76% | Saenz, 1990 |
| | Guatemala: <i>L. braziliensis</i> | 30% | Navin, 1992 |
| | Guatemala: <i>L. mexicana</i> | 89% | Navin, 1992 |
| Itraconazole | Colombia: <i>L. panamensis</i> | 05% | Soto, 1993 |
| | Guatemala: <i>L. braziliensis</i> | 31% | Arana, UR |
| | Guatemala: <i>L. mexicana</i> | 77% | Arana, UR |

Clinical response to treatment

| Drug | Country / <i>Leishmania</i> specie | Cure rate | Reference |
|-------------|--|-----------|-----------------|
| Paromomycin | Ecuador: <i>L. panamensis</i> | 85% | Krause, 1994 |
| | Belize: <i>L. mexicana</i> and <i>L. braziliensis</i> | 68% | Weinrauch, 1993 |
| | Honduras: <i>L. chagasi</i> | 1.8% | Neva, 1997 |
| | Guatemala: <i>L. braziliensis</i> and <i>L. mexicana</i> | 91% | Arana, 2001 |
| | Ecuador: <i>L. panamensis</i> and <i>L. braziliensis</i> | 79% | Armijos, 2004 |

Difficulties to generalize these results:

- No randomized studies
- Few patients
- Different treatment schemes
- Lack of standardized cure definitions

Do we need to do specie specific diagnosis for treatment?

Everyday there is more and more evidence supporting the link between *Leishmania* species and treatment outcome

- Ideal vrs reality
 - Difficulties to establish parasitological diagnosis in rural areas (personnel, equipment and costs)
- Research
- Travel medicine

Treatment by species

| Species | Drug | Dose |
|------------------------|-------------------------------------|---|
| <i>L. mexicana</i> | Local: PMC+MBCI | Twice daily for 20 days |
| | Ketoconazole | 600 mgs PO for 28 day |
| <i>L. braziliensis</i> | Pentavalent antimonials | 20 mgs/kg/day for 20 days |
| | Local: PMC+MBCI | Twice daily for 20 days |
| | Local infiltration with antimonials | ~5 ml per infiltration, once or twice weekly |
| <i>L. panamensis</i> | Pentavalent antimonials | 20 mgs/kg/day for 20 days |
| | Miltefosine | 2 mg/Kg/day for 28 days |
| | Ketoconazole | 600 mgs PO for 28 days |
| <i>L. guyanensis</i> | Pentavalent antimonials | 20 mgs/kg/day for 20 days |
| | Pentamidine isethionate | Four injections, 3 mgs/kg/day every other day |
| <i>L. donovani</i> | Local infiltration with antimonials | ~5 ml per infiltration, once or twice weekly |



Thank you very much for your attention

