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Chromoblastomycosis versus Phaeohyphomycosis

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CHROMOBLASTOMYCOSIS

- Cutaneous and subcutaneous chronic infection caused by the traumatic inoculation of a dematiaceous fungus.
- No death, incapacitating and deforming
- Described at five continents (tropicals and subtropicals), is comun in Venezuela, Brasil, Mexico and Central-America

Diagnosis

- Direct examination (warty nodules)

Clinical characteristics as: development of nodular lesions which can progress over years to irregular verrucose hyperkeratotic forms, scaly plaques or cicatricial atrophic skin lesions


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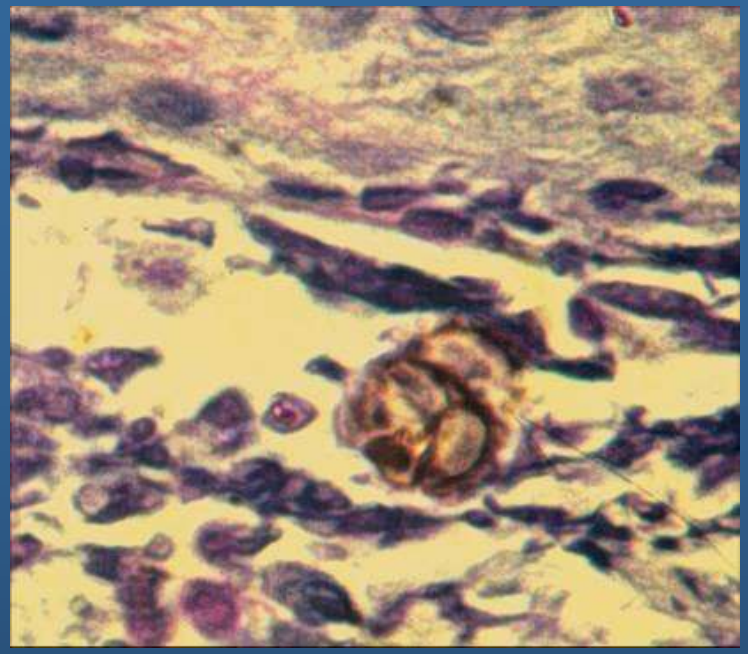
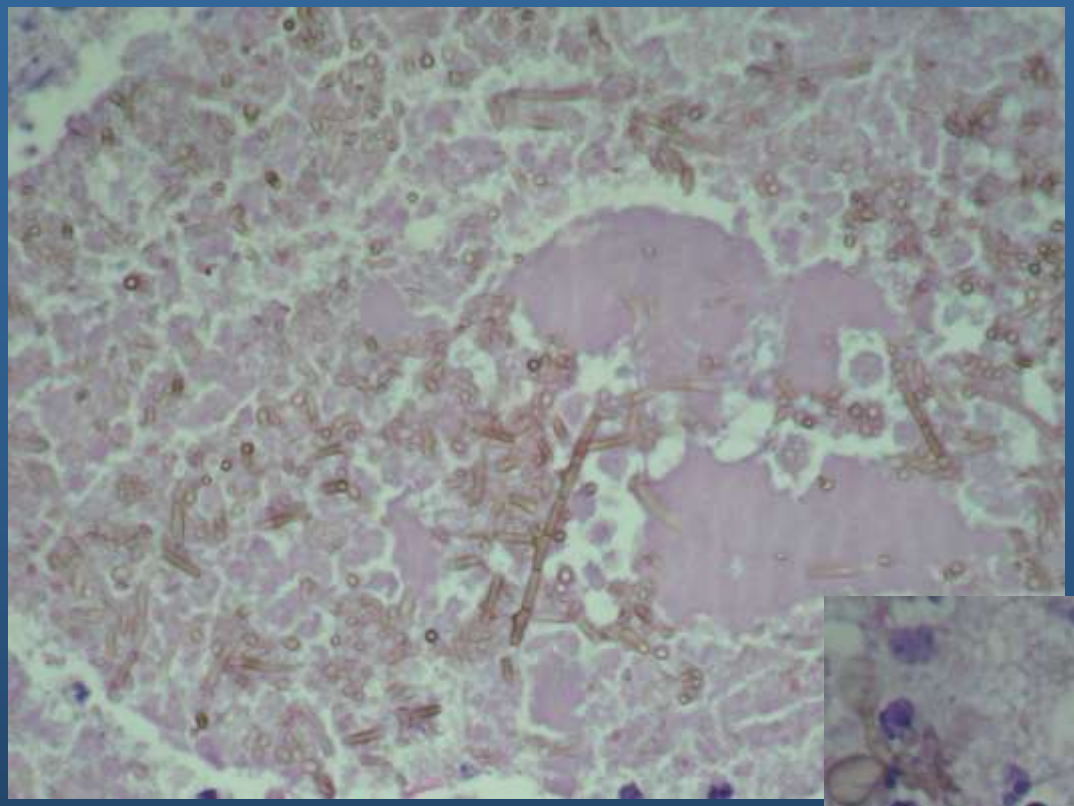
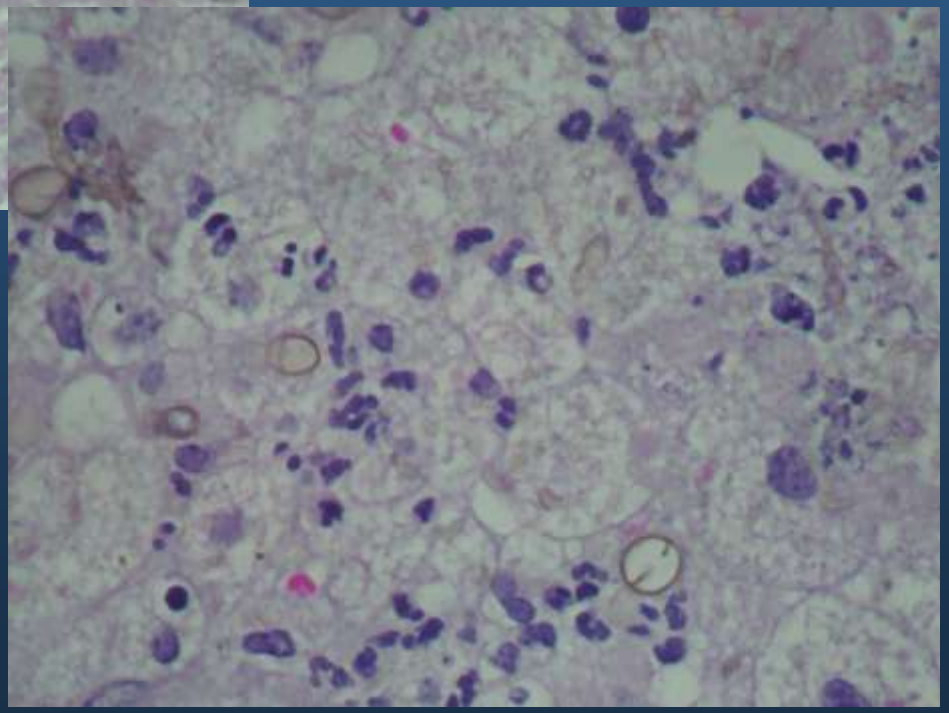






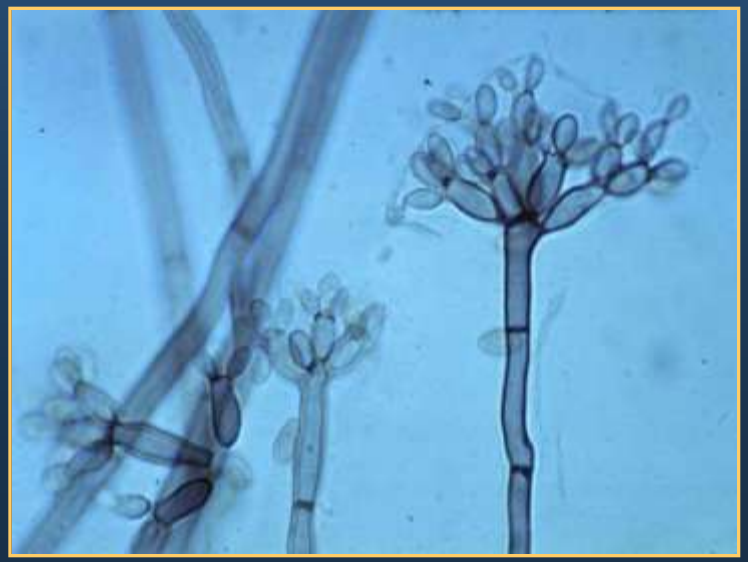
Diagnosis

- Culture
- Histology (presence of muriform cells or Medlar bodies)

Main fungi causing the disease

- *Fonsecaea pedrosoi*, *Cladophialophora carrionii*, *Phialophora verrucosa*, *Rhinocladiella aquaspersa*

- *Exophiala jeanselmei*, *Exophiala spinifera*, *Exophiala dermatitidis*
- *Cladophialophora bopii*



Objetives:

- To establish a chronic murine model of chromoblastomycosis
- To observe the cyto-histological patterns and response on tissue
- To compare the evolution of the infection after the administration of new generation treatments (posaconazole and voriconazole) in front of the recommended therapies (itraconazole and terbinafine)

Model establishment

Mice	Inf. route	Response
• **IMMUNOCOMP.**	**IV**	**ACUTE INFECTION**
• **IMMUNOSUP. (CORTISONE)**	**IV**	**ACUTE INFECTION**
• **INMUNOCOMP.**	**SC**	**ACUTE INFECTION**
• **IMMUNOSUP. (ATHIMICS)**	**SC**	**CHRONIC INFECTION**
• **INMUNOCOMP. (LACTANTES)**	**IP**	**ACUTE INFECTION**
• **INMUNOCOMP.**	**IP**	**CHRONIC INFECTION**

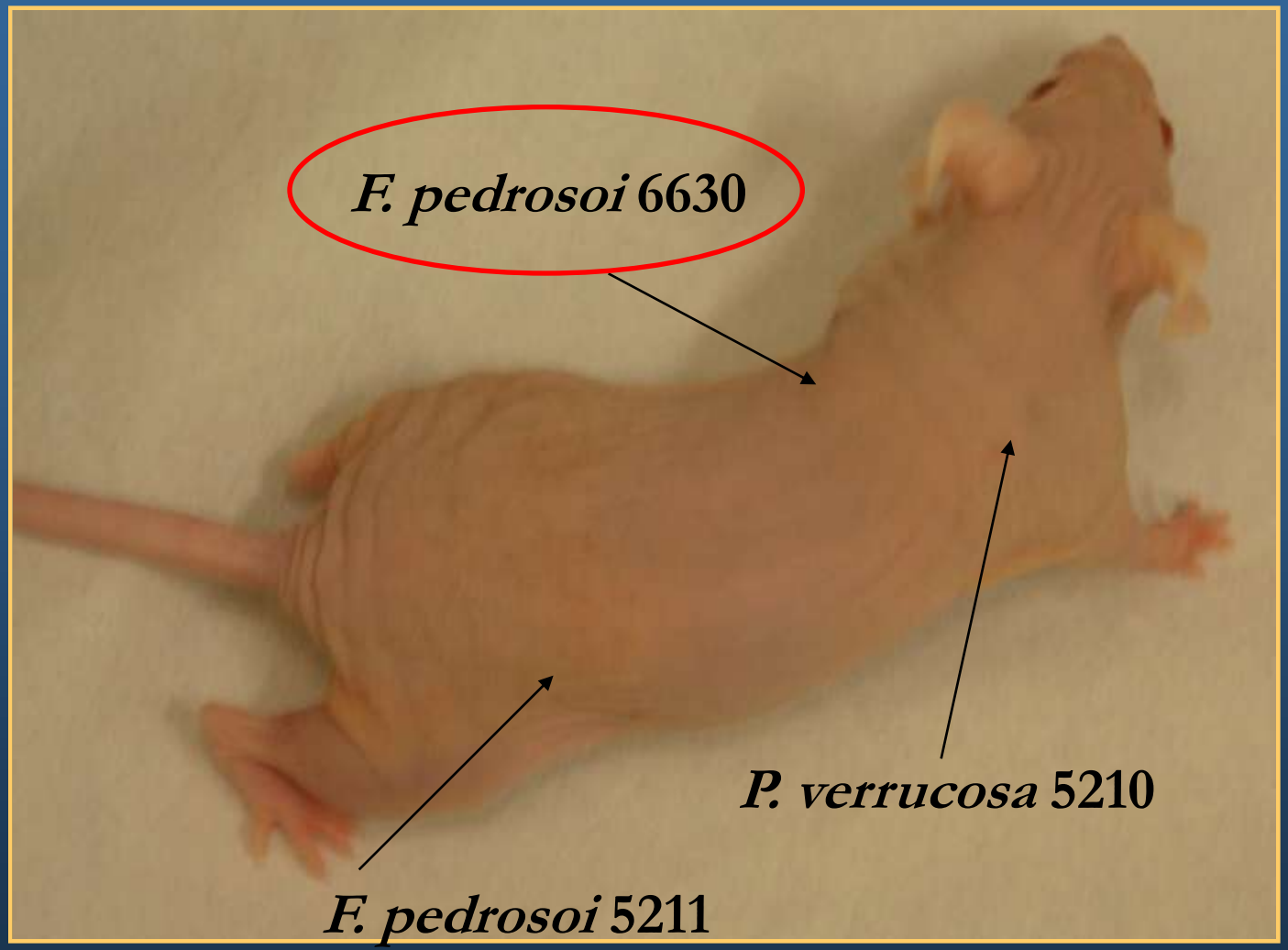
INOCULA $1x10^5$-$1x10^8$ cfu/mL

Cardona-Castro et al. 1999. Med. Mycol. 37:81-83

Materials & Methods

- Strains: *F. pedrosoi*: FMR 5211, FMR 6630
  P. verrucosa FMR 5210
- Mice: Cd1/nude (athimics)
- Ceftazidime: 0.05 mL (150mg/kg) s.c.
- Anesthetic: isoflurane
- Infection: 0.1 ml s.c. ~$3x10^7$ cfu/ml

Subcutaneous infection in nude mice


F. pedrosoi 6630
P. verrucosa 5210
F. pedrosoi 5211

12 weeks post-infection strain FMR 6630

Materials & methods

- Treatments: (3 weeks after the infection)
  - Posaconazol 10, 20 mg/kg/day (orally)
  - Voriconazol 10, 20 mg/kg/day (orally)
  - Itraconazol 25, 50 mg/kg/day (orally)
  - Terbinafine 150, 250 mg/kg/day (orally)

In vitro activities of antifungal drugs against the isolate *F.pedrosoi* FMR 6630

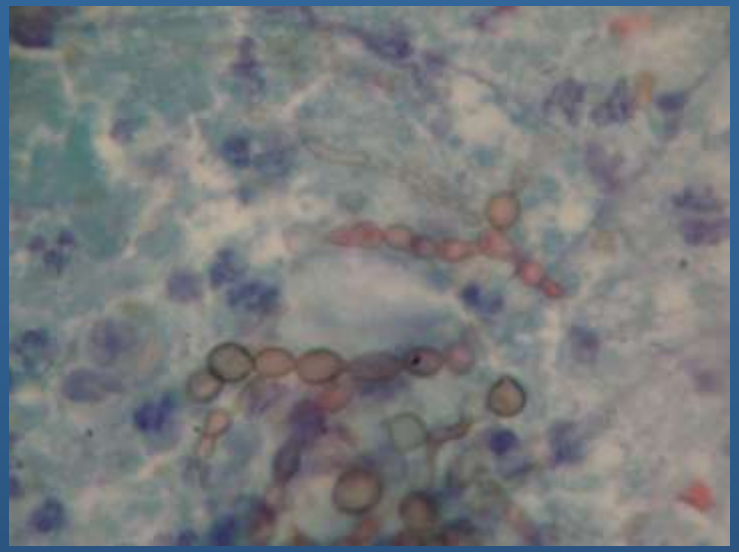
MICs (μg/ml)				
	PSC	**VRC**	**ITZ**	**TRB**
6630	0.12	0.12	0.5	0.12

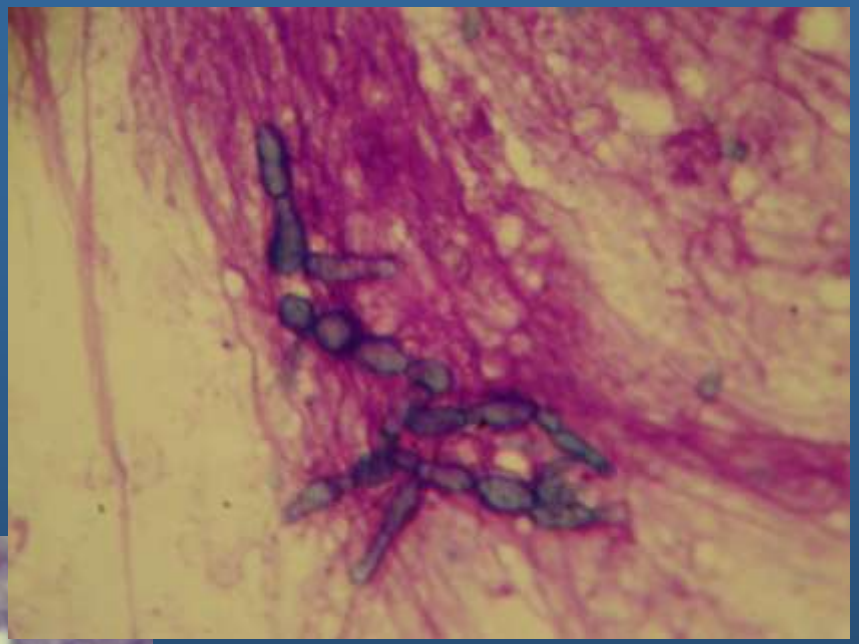
Materials & methods

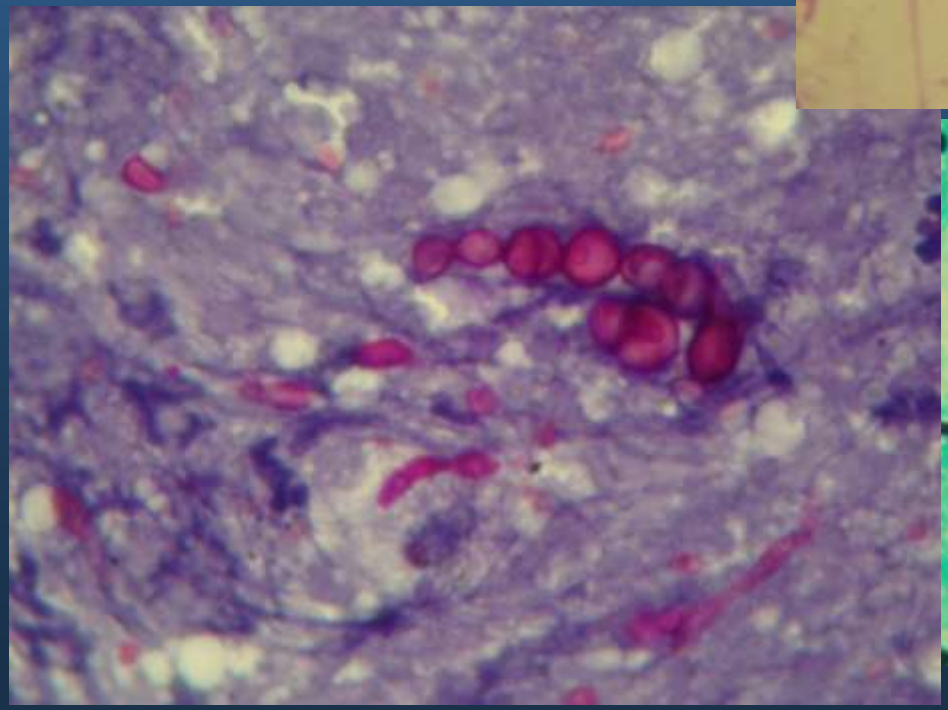
- Lesions were measured at 3 weeks intervals

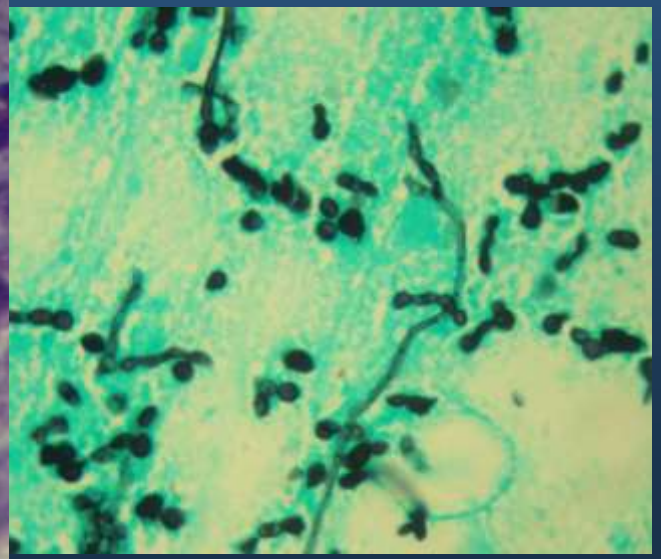
Culture

At the end of the therapy skin lesions were cultured

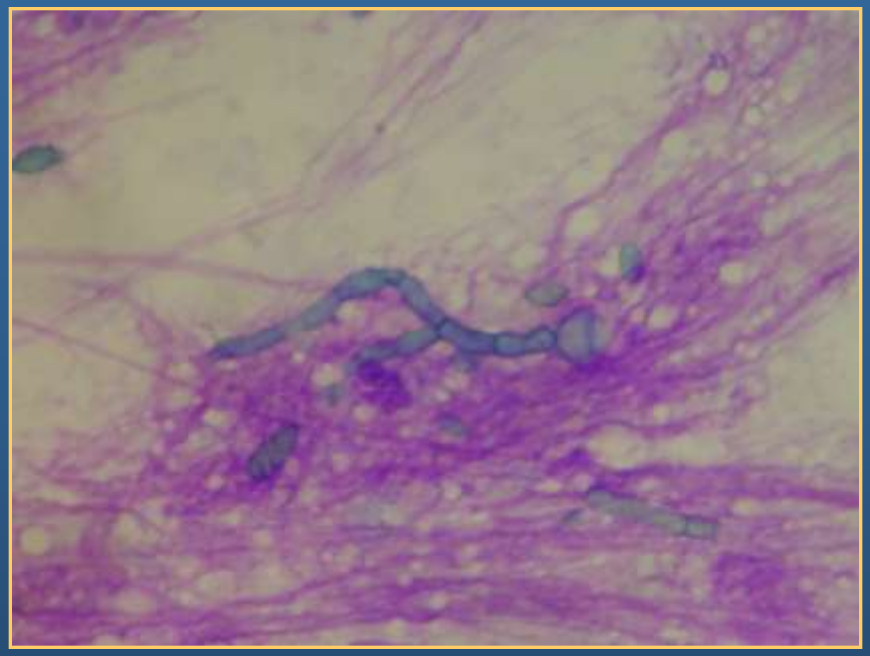


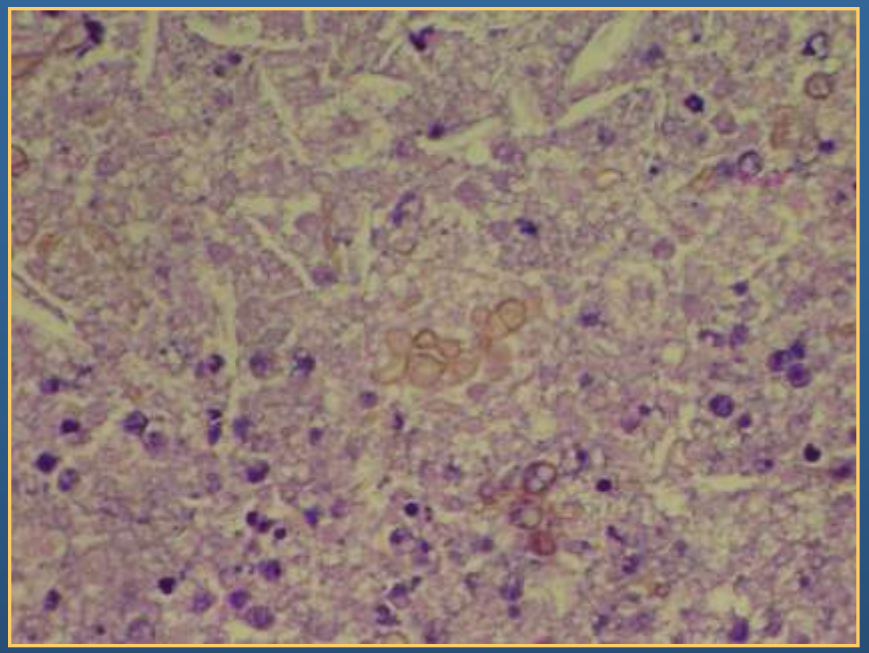


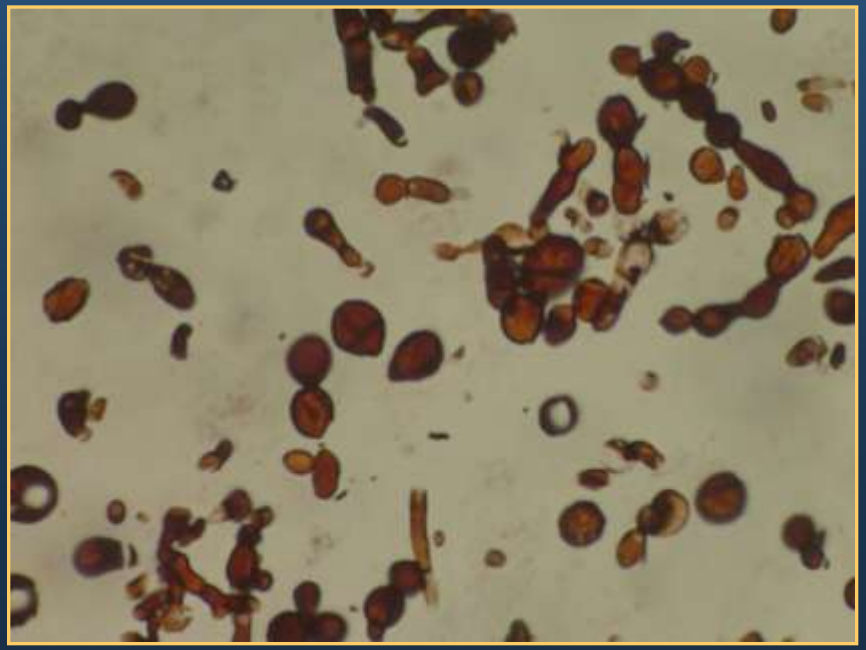


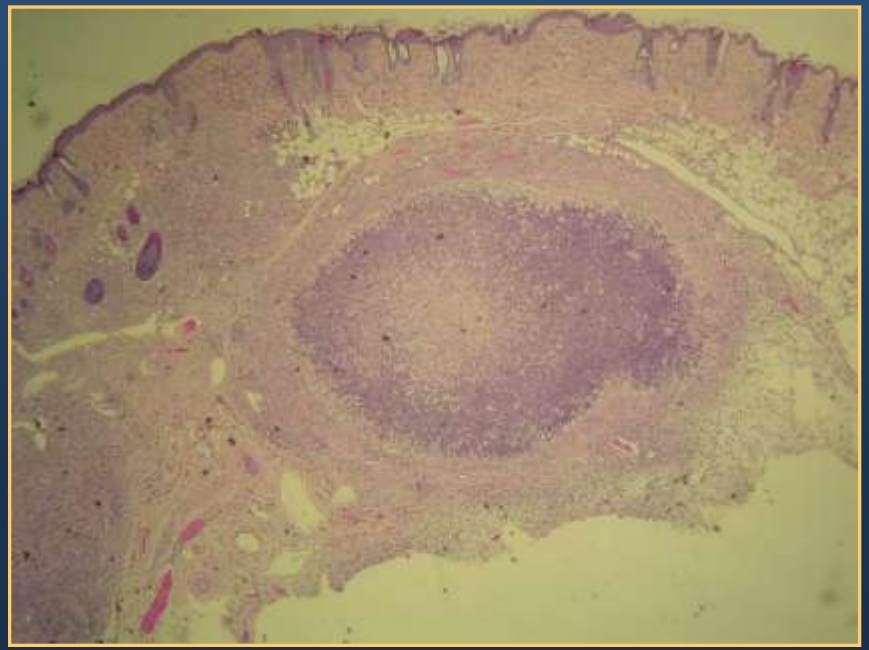


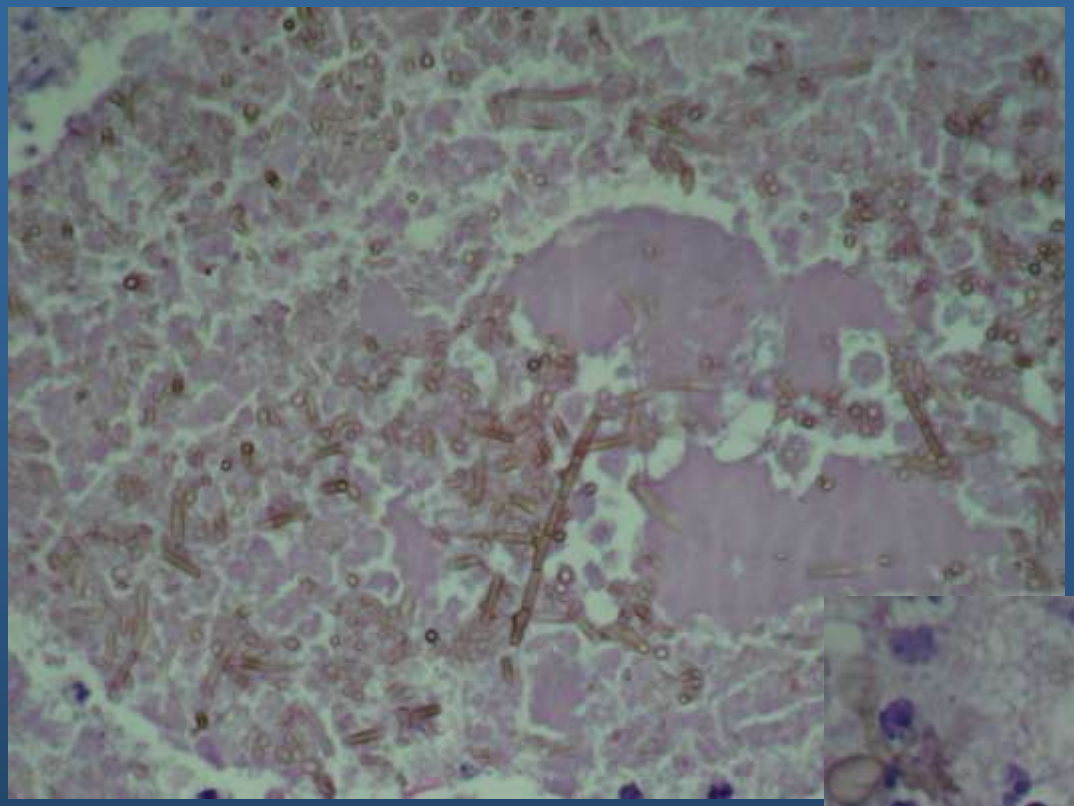
Histology

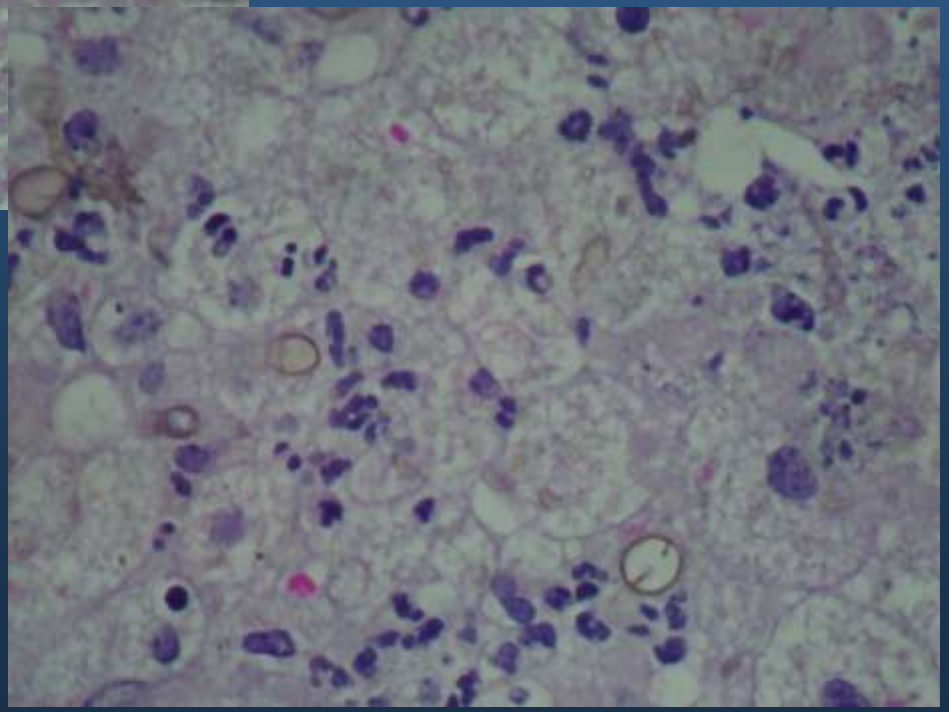






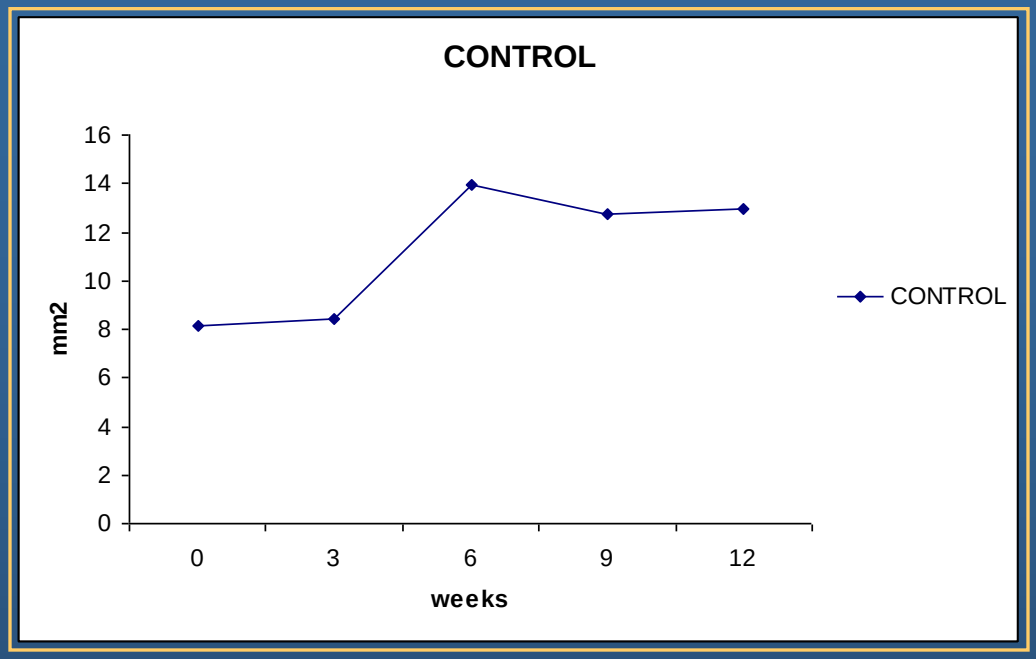


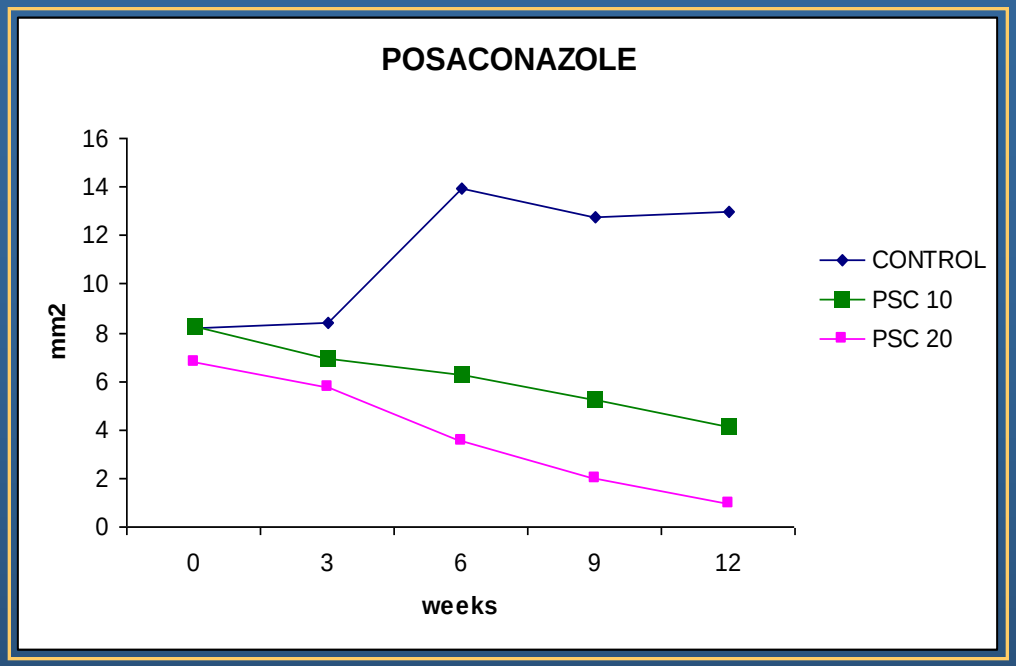


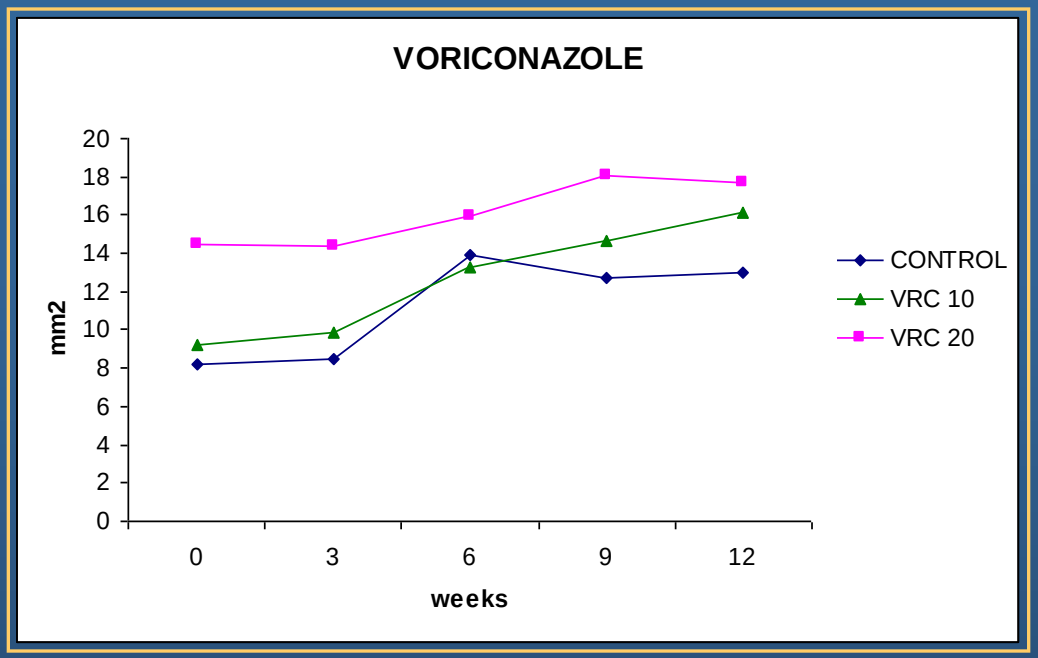


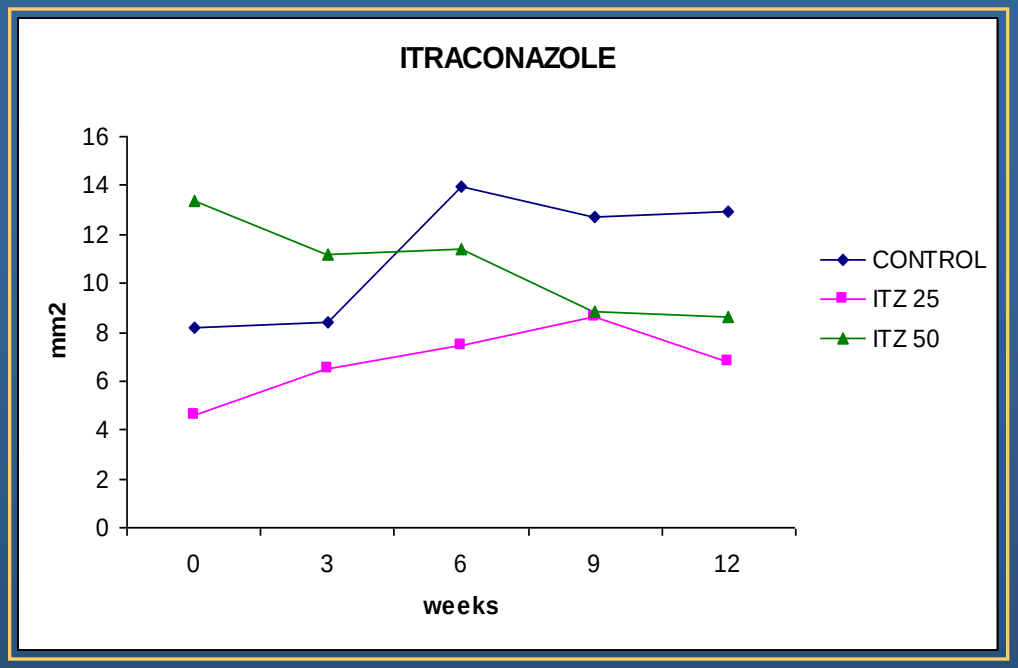
Results:

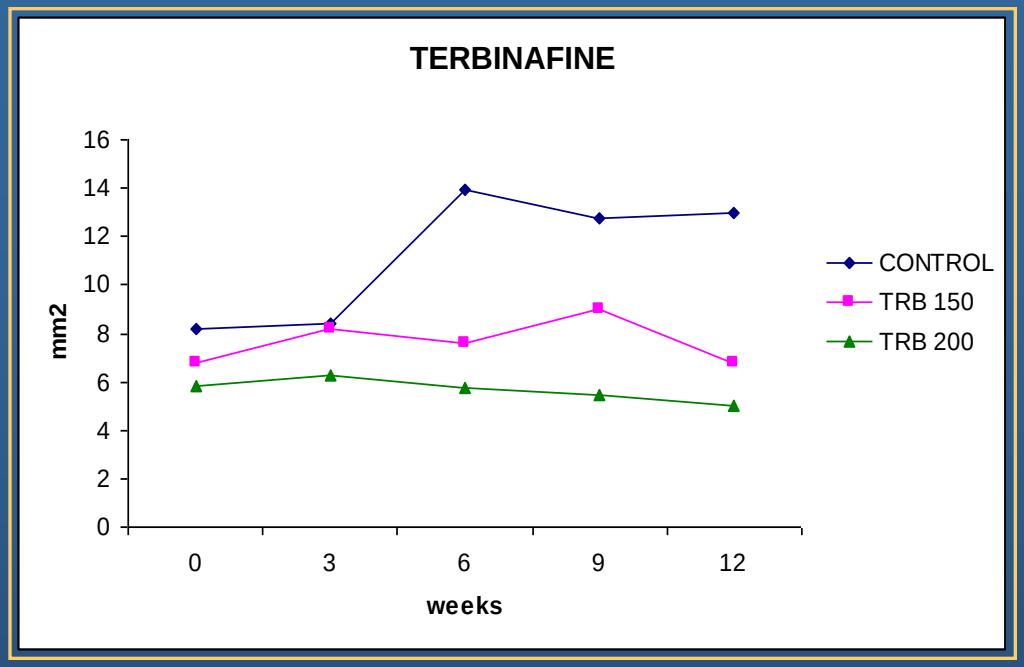
Control group




POSACONAZOLE
16
14
12
10
8
6
4
2
0
mm2
0
3
6
9
12
weeks
CONTROL
PSC 10
PSC 20


VORICONAZOLE
20
18
16
14
12
10
8
6
4
2
0
mm2
0
3
6
9
12
weeks
CONTROL
VRC 10
VRC 20


ITRACONAZOLE
16
14
12
10
8
6
4
2
0
mm2
0
3
6
9
12
weeks
CONTROL
ITZ 25
ITZ 50


TERBINAFINE
16
14
12
10
8
6
4
2
0
mm2
0
3
6
9
12
weeks
CONTROL
TRB 150
TRB 200

Group 1	Group 2	Mann Whitney p-value **
Control	ITZ 25	0.222
Control	ITZ 50	0.009
Control	PSC 10	*0.076*
Control	PSC 20	0.009
Control	TRB 150	0.117
Control	TRB 250	0.047
Control	VRC 10	0.917
Control	VRC 20	0.222
ITZ 25	ITZ 50	0.347
PSC 10	PSC 20	0.028
TRB 150	TRB 250	0.602
VRC 10	VRC 20	0.302

* K muestras independientes
** 2 muestras independientes

Kruskal-Wallis p-value * = 0.016

Groups	Increase in the lesions after 12 weeks (%)	Positive cultures (%)
CONTROL	+82.6	100
ITZ 25	+23.9	100
ITZ 50	-24.3	80
PSC 10	-23.8	60
PSC 20	-69.6	40
TRB 150	+13.7	100
TRB 250	-0.6	100
VRC 10	+84.2	100
VRC 20	+10.5	100

Conclusions

- Cytopathological studies are neccesary.
- The results confirm PSC as an alternative in the treatment of chromoblastomycosis. However, its elevate cost would limit its use to cases in which therapies with ITZ and TRB were not completely successful.
- VRC showed modest results and its efficacy in this kind of infections seems to be poor.

¡MUCHAS GRACIAS!

THANK YOU!