ABSTRACT
Limited effective treatments are emerging for treatment of scabies. There was an impression that ivermectin would be always (or almost always) effective, but as it should be expected, resistant strains are being found. Molecular studies are defining better targets in the mites and we begin to understand mechanisms of resistance on them. However, we are in need of more information on the biology of those parasites.

Keywords: Mite infestations; Scabies; Ivermectin

RESUMO
Tratamentos efetivos limitados para a sarna estão surgindo. Tinha-se a impressão de que a ivermectina seria sempre (ou quase sempre) efetiva. Mas, como era de se esperar, espécies resistentes à medicação estão sendo encontradas. Estudos moleculares estão definindo alvos melhores nos ácaros e nós começamos a entender os seus mecanismos de resistência. Entretanto, necessitamos mais informações sobre a biologia desses parasitas.

Descritores: Infestações por ácaros; Escabiose; Ivermectina

A recent article published by Mounsey et al.\(^1\) analyzes the unexpected emergence of resistance in a multicellular parasite that is theoretically less competent than bacteria and other less complex infectious agents to be resistant. Scabies represents a serious problem among infectious disease for causing outbreaks in closed communities and for being difficult to control. The clinical symptoms may appear only six weeks after the infestation and it is transmitted much before the individual manifests symptoms. Some immunodepressed patients suffer from the famous Norwegian scabies or hyperinfestation. They have huge populations of parasites and are much more contaminant than other individuals. In such conditions, scabies does not present the characteristic lesions observed in ordinary patients and may be confused with other skin diseases, even by experienced dermatologists. When it occurs in patients who would be considered ‘above any suspicion’ for having good socioeconomic conditions, the diagnosis may be delayed and, when finally made, many other individuals and healthcare professionals will already be contaminated. A consensus among all professionals dealing with scabies is the need to treat all those who had contact with the patient, presenting or not the symptoms. Moreover, all close contacts should be treated simultaneously. If performed differently, the coming and going of scabies is almost unavoidable: some are cured, but others acquire the parasite again and the outbreak continues.

In developed countries, including Brazil, the price of the drugs used to kill the mite is a critical issue. Benzyl benzoate, the cheapest topical acaricide, has not a well-defined resistance because it is not much used in developed countries that study this condition; moreover, since it irritates the skin, it is less often prescribed. The permethrin derivatives are very much used in Australia and in other countries but they are more expensive and cases of resistance has been described in lice and in \textit{Sarcoptes}\(^2-3\). When ivermectin was launched, it seemed to be the perfect treatment: a single-dose drug for oral or intravenous administration, not topical administration. Unfortunately, 30 years later, there is evidence that ivermectin also causes selection pressure and resistance\(^4\).

It is noteworthy mentioning that monosulfiram (Tetmosol\(^6\)), a drug widely used in Brazil to treat scabies seems to be used only in this country, since there are no reports on its use or resistance in the medical literature, which does not mean that there is
no resistance. As a famous medical philosopher, whose name I do not recall, said: absence of evidence is not evidence of absence.

What are the molecular mechanisms of these resistances? As to pyrethroids, such as permethrin, it is known that the resistance in some incepts is related to mutation in the voltage-sensitive sodium channel. Concerning ivermectin, in some worms, there are reports of mutations in the chloride channels or in excretion pumps bound to protein P, which may have a hyperexpression in resistant strains. There are scarce genetic studies on Sarcoptes scabei, and the first investigation are from 1995\(^{(5)}\). There is evidence of genetic mutations related to permethrin resistance\(^{(6)}\).

The future perspectives indicate more resistance, as it occurs in any parasite. The more antiparasitary drugs we use, the greater is the selection pressure which leads to resistance. When these drugs are used empirically, repetitively, over the counter and inappropriately – night pruritus does not necessarily means scabies, and if someone who had scabies presents pruritus again, it do not always represent recurrence – there is an immune response to parasite eggs as well as irritation caused by topical drugs. However, we saw patients treated more than five times for scabies and others who were treated just once, which is known to be insufficient for cure. These are excellent occasions for Sarcoptes to do graduation and post-graduation courses in resistance.

Moreover, there are therapeutic perspectives. Regardless of medicines that will derive from new knowledge about resistance and genomic mechanisms, some drugs may be useful, such as the oil of Melaleuca alternifolia, a traditional tree in Australia, where it is known as tea tree; however, in Florida it is a pest for being one of the most successful invasive species\(^{(6)}\). We do not know if veterinary therapies for other species of mites may lead to human contact with other pyrethrins, for instance, and selection by resistance suboptimal dose in our mites.

**REFERENCES**