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Mini review



## Nomenclatural instability in the venomous snakes of the Bothrops complex: Implications in toxinology and public health





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#### ABSTRACT

Since nomenclature is intended to reflect the evolutionary history of organisms, advances in our understanding of historical relationships may lead to changes in classification, and thus potentially in taxonomic instability. An unstable nomenclature for medically important animals like venomous snakes is of concern, and its implications in venom/antivenom research and snakebite treatment have been extensively discussed since the 90s. The taxonomy of the pitvipers of the Bothrops complex has been historically problematic and different genus-level rearrangements were proposed to rectify the longstanding paraphyly of the group. Here we review the toxinological literature on the Bothrops complex to estimate the impact of recent proposals of classification in non-systematic research. This assessment revealed moderate levels of nomenclatural instability in the last five years, and the recurrence of some practices discussed in previous studies regarding the use of classifications and the information provided about the origin of venom samples. We briefly comment on a few examples and the implications of different proposals of classifications for the Bothrops complex. The aim of this review is to contribute to the reduction of adverse effects of current taxonomic instability in a group of medical importance in the Americas.

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#### 1. Taxonomic instability

Systematics is the study of the diversity of organisms and the natural relationships among them. Taxonomy, closely linked to systematics, seeks to reflect our understanding of the phylogenetic relationships among organisms in classifications of biodiversity. Official codes, such as the International Code of Zoological Nomenclature for animals, governs the translation of that into a system of formal nomenclature (i.e. names applied in a classification).

Classifications are not static systems of names but potentially dynamic ones that may change through time. Given the incompleteness of our understanding of the diversity of life, the regular publication of new scientific research advances, including new insights into evolutionary relationships and species boundaries, may lead to changes in the nomenclature to better reflect those findings (Sangster et al., 1999; Morrison et al., 2009; de Carvalho et al., 2013; Kaiser et al., 2013). Hence, some degree of taxonomic instability is expected. Changes in nomenclature, being a result of scientific progress, may cause temporary confusion and nomenclatural instability, but should reflect a better understanding of biodiversity and lead to stable classifications in the long term. Additional and less beneficial causes of taxonomic instability include proposals of classifications that ignore fundamental taxonomic principles, and the unknowing or uncritical adoption of erroneous classifications by researchers in non-systematic disciplines. Previous studies have extensively discussed these issues (Wüster, 1996; Wüster et al., 1997; Williams et al., 2006; Kaiser et al., 2013).

#### 2. Taxonomy and venomous snakes

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In the case of venomous snakes and other organisms of medical

importance, taxonomic instability may have implications in a variety of scientific disciplines that includes biomedical studies applicable to public health. For instance, confusion generated by changes in nomenclature may lead to taxonomic inaccuracy, which may have serious consequences in antivenom therapy (Wüster, 1996). In toxinological studies, taxonomic inaccuracy may hinder the identifiability of venoms samples, the interpretation of results (e.g. differences in venom composition), and the repeatability of experiments (e.g. isolation of toxins of potential pharmaceutical interest).

Venomous snakes are animals of biomedical importance. Human envenomation by snakes of the families Elapidae and Viperidae is an important public health problem in tropical countries, particularly rural areas, as well as countries in temperate zones (Chippaux, 1998; Gutiérrez et al., 2006; Kasturiratne et al., 2008; Mohapatra et al., 2011; Williams et al., 2011; Chippaux et al., 2013; Chippaux and Postigo, 2014; Nori et al., 2014; Kipanyula and Kimaro, 2015). On the other hand, snake venoms also bear therapeutic potential; for example, some components have found to be useful in the treatment of hypertension, parasites and cancer (Rocha e Silva et al., 1949; Markland, 1998; Lipps, 1999; Fernandez et al., 2004; Koh et al., 2006; Deolindo et al., 2010; Koh and Kini, 2012; Vyas et al., 2013; Calderon et al., 2014; Shanbhag, 2015).

Variation in the composition of snake venoms is ubiquitous and the knowledge of that variation is essential for an efficient treatment of snakebites (Chippaux et al., 1991; Warrell, 1997; Fry et al., 2003: Calvete et al., 2009a: Casewell et al., 2014). The venom's main function is the subduing and ingestion of prey, and many studies have found strong evidence that venom's variation may be the result of natural selection for differences in diet (Daltry et al., 1996; Creer et al., 2003; Sanz et al., 2006; Barlow et al., 2009). However, diet alone is insufficient to explain the variation in venom composition and toxicity in all cases; other ecological and evolutionary factors, such as ontogeny, geographic distance and/or phylogenesis, need to be considered (Minton and Weinstein, 1986; Mackessy, 1988; Daltry et al., 1996; Rodrigues et al., 1998; Andrade and Abe, 1999; Mebs, 2001; Calvete et al., 2007, 2011; Barlow et al., 2009; Gibbs and Mackessy, 2009; Zelanis et al., 2010; Casewell et al., 2013). For that matter, venomous snake systematics is fundamental (Wüster, 1996; Wüster and McCarthy, 1996; Wüster et al., 1997; Fry et al., 2003; Williams et al., 2006). When predicting venom variation, phylogeny should be considered as the null hypothesis (i.e. closely related taxa would be predicted to have similar venoms), whereas departures from this hypothesis may indicate the action of other causes, such as natural selection for ecological factors. Examples of venom divergence tracking phylogeny can be found in Notechis (Williams et al., 1998), Bothrops (Wüster et al., 2002a), and Agkistrodon (Lomonte et al., 2014). On the other hand, a study on Sistrurus (Gibbs et al., 2013) found no evidence for significant phylogenetic signal in venom variation, and found the variation related to diet. Regardless of the degree to which phylogeny may explain the variation in venoms, any attempt at an evolutionary interpretation of that variation relies critically on the information of the historical relationships among taxa contained in phylogenies, which is reflected in nomenclature. The aim of this review is to estimate the impact of recent nomenclatural changes in the venomous snakes of the Bothrops complex on toxinological research.

## 3. Taxonomic instability in the pitvipers of the *Bothrops* complex

#### 3.1. The Bothrops complex (Viperidae: Crotalinae)

This group of pitvipers is widely distributed in the Americas,

from Mexico to southern Argentina, and is the main medically important group of snakes in that region (Campbell and Lamar, 2004; Warrell, 2004; Gutiérrez et al., 2006; Segura et al., 2010). It comprises at least 50 species, some of them described recently (Campbell and Lamar 2004; da Silva and Trefaut Rodrigues, 2008; Barbo et al., 2012, 2016). The group is present in different ecoregions of the continent, from tropical and subtropical forests to arid and semiarid regions, and from sea level to altitudes of more than 3000 m (Campbell and Lamar, 2004; Carrasco et al., 2009, 2010).

The Bothrops complex (Bothrops sensu lato) is extremely diverse in its morphological and ecological traits. It includes terrestrial, arboreal and semiarboreal species. Many species show ontogenetic shifts in their diet, feeding mainly on ectotherms as juveniles and mammals as adults; others show specialized diets (e.g. on rodents or birds) (Martins et al., 2002). Phylogenetic studies of the group have repeatedly recovered groups of species commonly known as: the "alternatus" and "neuwiedi" groups, present in open vegetation biomes like those of the South American "dry diagonal", and the "jararaca", "jararacussu", "taeniata", "atrox" and "microphthalmus" groups, present in highly forested regions like Atlantic forests, Andean forests or Amazonia (Martins et al., 2002; Campbell and Lamar 2004; Werman, 2005). All of these groups include species that are medically important in terms of human ophidism (e.g. Otero et al., 1992; França and Málaque, 2003; Smalligan et al., 2004; Warrell, 2004; Gutiérrez, 2009).

#### 3.2. Nomenclatural changes in the Bothrops complex

The genus name Bothrops Wagler, 1824, was widely used for almost all Neotropical pitvipers through much of the 20th century until its division (e.g. Burger, 1971) was popularised by Campbell and Lamar (1989), who restricted the concept of Bothrops to a mostly South American group of species. By the early 2000s, the Bothrops complex was classified into three genera: Bothrops Wagler, 1824, Bothriopsis Peters, 1861, and Bothrocophias Gutberlet and Campbell, 2001 (Campbell and Lamar, 2004). Before the genus Bothrocophias (the "microphthalmus" group) was described, phylogenetic studies had revealed the paraphyly of Bothrops with respect to the species of the genus Bothriopsis (the "taeniata" group) (Werman, 1992; Salomão et al., 1997; Parkinson, 1999). Subsequent studies, incorporating more taxa/data in phylogenetic analyses, further confirmed this. All found Bothrops to be paraphyletic but the supported monophyly of the Bothrops + Bothriopsis + Bothrocophias group (Gutberlet and Harvey, 2002; Parkinson et al., 2002; Wüster et al., 2002b; Castoe and Parkinson, 2006).

In view of this evident systematic problem, different taxonomic rearrangements to rectify the paraphyly of *Bothrops* were proposed. One of the proposals was to maintain Bothriopsis and to split Bothrops into multiple monophyletic genera, consistently with the wider trend in pitviper systematics of splitting large genera into smaller, more homogeneous genera (Gutberlet and Campbell, 2001; Parkinson et al., 2002; Malhotra and Thorpe, 2004; Harvey et al., 2005; Castoe and Parkinson, 2006). Other authors (Salomão et al., 1997; Vidal et al., 1997; Wüster et al., 2002b) proposed to synonymize Bothriopsis with Bothrops, some of them arguing that the morphological and ecological diversity of the group is probably the result of a single adaptive radiation, and that splitting the genera would obscure this biogeographical pattern. Fenwick et al. (2009) performed phylogenetic analyses of the *Bothrops* complex combining morphological and molecular data, and proposed to maintain Bothriopsis and to split Bothrops into three genera: Rhinocerophis Garman, 1881 ("alternatus" group), Bothropoides gen. nov. ("neuwiedi" and "jararaca" groups), and Bothrops sensu stricto ("jararacussu" and "atrox" groups). Carrasco et al. (2012) analysed Download English Version:

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