



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 long-standing 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

In the case of venomous snakes and other organisms of medical

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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 toxicological 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 toxicological 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 Málague, 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 supported the 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: *Rhinocerocephis* Garman, 1881 (“*alternatus*” group), *Bothropoides* gen. nov. (“*neuwiedi*” and “*jararaca*” groups), and *Bothrops* sensu stricto (“*jararacussu*” and “*atrox*” groups). Carrasco et al. (2012) analysed

additional data for the complex. They demonstrated that the paraphyly of *Bothrops* was not rectified in the taxonomic rearrangement proposed by Fenwick et al. (2009), and that their classification was based on a phylogeny that excluded the information of species with no molecular data, which in turn could lead to the paraphyly of the genera proposed. Carrasco et al. (2012) also found conflicting phylogenetic signal among two mitochondrial genes (cytb, ND4) and the rest of the characters analysed (12S and 16S rRNA, ecology, and morphology). The conflict involved considerable differences in relationships of “*neuwiedi*” and “*jararaca*” with the rest of the groups of species. This led to an alternative phylogenetic hypothesis noted in previous studies (e.g. Werman, 1992; Salomão et al., 1999) (Figs. 1 and 2). In view of those results, Carrasco et al. (2012) argued that splitting *Bothrops* into additional genera was premature, and instead proposed to synonymize *Rhinocerocephis*, *Bothropoides* and *Bothriopsis* with *Bothrops*, and to maintain *Bothrocophias*, assigning *Bothrops andianus* to that genus. This classification followed previous taxonomic suggestions and rectified the paraphyly of *Bothrops* by acknowledging two supported monophyletic groups.

In summary, the published results have demonstrated that the phylogeny of the *Bothrops* complex is not yet robustly resolved, and that conflicting phylogenetic relationships and the resulting nomenclatural instability involve several medically important species.

4. Taxonomy of the *Bothrops* complex and non-systematic research

In order to estimate the impact on toxinological research of the recent genus-level rearrangements of the *Bothrops* complex, we reviewed the classification used for the group in articles published from 2010 to 2015 in two peer-reviewed journals, *Toxicon* and the *Journal of Proteomics* (Appendix A). This assessment is in part similar to that performed by Wüster and McCarthy (1996) for Asiatic cobras (*Naja*) and saw-scaled vipers (*Echis*). We selected

Toxicon and the *Journal of Proteomics* on the basis that they frequently publish studies on venoms of the *Bothrops* complex, thus allowing the evaluation of the existence of nomenclatural instability in the short period considered for this review. The articles were selected when any of the following genera were present in their title: *Bothrops*, *Bothriopsis*, *Bothrocophias*, *Bothropoides*, *Rhinocerocephis*. The classifications were scored as CI (*Bothrops*, *Bothriopsis*, and *Bothrocophias*, classification adopted in Campbell and Lamar, 2004), CII (*Bothrops*, *Bothriopsis*, *Bothrocophias*, *Bothropoides*, and *Rhinocerocephis*, classification proposed by Fenwick et al., 2009), and CIII (*Bothrops* and *Bothrocophias*, classification proposed by Carrasco et al., 2012, and previously suggested by Wüster et al., 2002). When the article could be equally scored as CI or CIII (these classifications are similar except for *Bothriopsis*), the scoring was made according to the date of the article’s publication. A fourth category was applied to those articles dealing with species that are not affected by the recent rearrangements, which are species whose assignment to the genus *Bothrops* (“*jararacussu*” and “*atrox*”) and *Bothrocophias* (“*microphthalmus*”) remained unchanged. Following Wüster and McCarthy (1996), we also reviewed two additional items: if the articles contained taxonomic comments and/or citation of taxonomic literature, and information on the origin of venom samples.

As summarized in Table 1, the most frequently adopted classification was CI, which assigns the complex to three genera (*Bothrops*, *Bothriopsis* and *Bothrocophias*). That can be expected since this classification was the one used through almost a decade before the most recent taxonomic rearrangements were proposed. A small proportion (18.6%) of the articles included taxonomic comments and/or citations of taxonomic literature, and rarely included an explicit argument for the choice of classification. Nearly 75% of the articles provided information on the origin of venoms; but most of them mentioned only institutions, while a small percentage (15.7%) included localities of origin of specimens that provided the venoms.

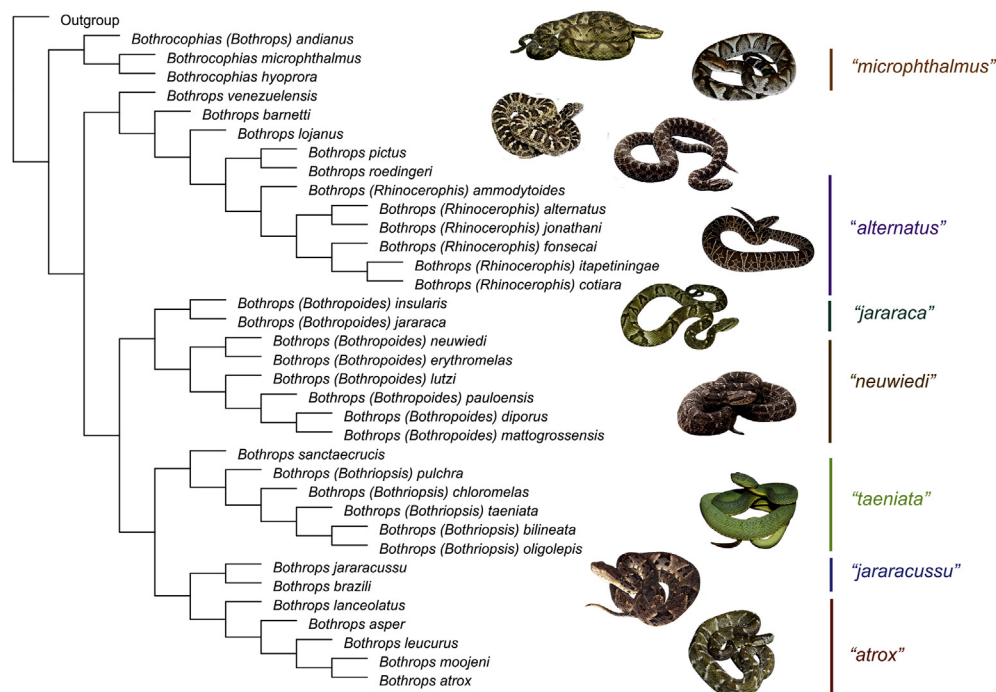


Fig. 1. Phylogeny of the *Bothrops* complex obtained from morphology, ecology, and mtDNA (12S and 16S rRNA, ND4 and cytb) (Carrasco et al., 2012). (Images from top to bottom: *B. andianus*, *B. microphthalmus*, *B. pictus*, *B. ammodytoides*, *B. alternatus*, *B. jararaca*, *B. diporus*, *B. bilineata*, *B. brazili*, *B. atrox*).

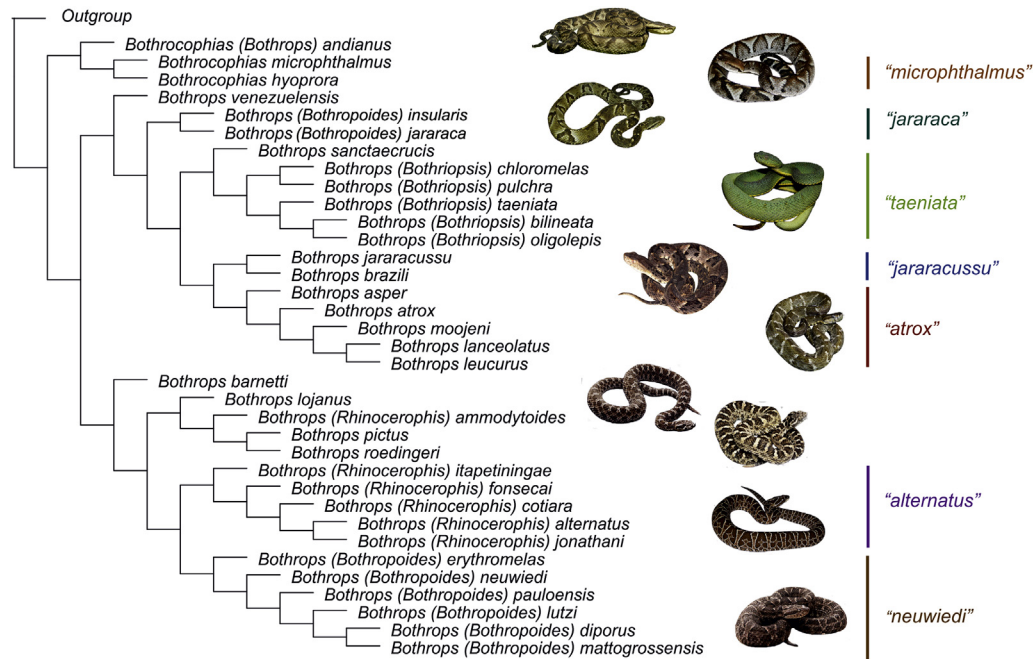


Fig. 2. Phylogeny of the *Bothrops* complex obtained from morphology, ecology, and mtDNA (12S and 16S rRNA) (Carrasco et al., 2012). (Images from top to bottom: *B. andianus*, *B. microphthalmus*, *B. jararaca*, *B. bilineata*, *B. brazilii*, *B. atrox*, *B. ammodytoides*, *B. pictus*, *B. alternatus*, *B. diporus*).

Table 1
Summary of reviewed articles and the classifications used for the *Bothrops* complex.

Year	N° art. Rev.	CI	CII	CIII
2010	24	14 (58.3%)		
2011	13	9 (69.5%)		
2012	21	9 (42.8%)	4 (19.1%)	
2013	19	2 (10.5%)	1 (5.3%)	9 (4.7%)
2014	15	2 (13.3%)	2 (13.3%)	6 (40.0%)
2015	10	1 (10.0%)	1 (10.0%)	2 (20.0%)
Total	102	37 (36.3%)	8 (7.8%)	17 (16.7%)

In general, this review showed moderate levels of nomenclatural instability since 2010 to date. Note, however, that nearly 40% of the articles dealt with species whose generic assignment remain unchanged, like the widely distributed and frequently studied *Bothrops atrox* and *B. asper*. Instability was associated with species of “*taeniata*”, “*neuwiedi*”, “*jararaca*” and “*alternatus*” (Figs. 1 and 2), which are the groups involved in the recent generic rearrangements.

As an example of some of the problems surrounding the issue of taxonomic instability, we comment here one recently published article on the venom of eleven Peruvian species of the *Bothrops* complex (Guerra-Duarte et al., 2015). We selected this article as an example given that it is one of the few studies reviewed herein that performed a comparative study of venoms using a phylogenetic framework, and because most of the species studied are systematically controversial. Additional motivation to comment on this article is that the Peruvian herpetofauna in general is undergoing intense systematic revision. The study of Guerra-Duarte et al. (2015) contributed with significant information on the venom of poorly known species and species that are medically important in Peru and nearby countries; unfortunately, the nomenclature used by the authors may cause confusion about the recent proposals of classifications for the *Bothrops* complex and the specific status of some of its populations.

Peru shows one of the highest levels of snake diversity in the

Americas (Campbell and Lamar, 2004; Pesantes, 2000; Yarlequé, 2000). Fourteen species of the *Bothrops* complex are present in Peru, which represents near 30% of the total diversity of the group; four species (*B. pictus*, *B. roedingeri*, *B. barnetti*, *B. chloromelas*) are endemic to the country and three (*B. andianus*, *B. oligolepis*, *B. pulchra*) are endemic to the Yungas of Ecuador, Peru and Bolivia. While some Peruvian species clearly belong to one of the commonly recognized clades of species, others remain incertae sedis or their phylogenetic affinities remain unclear (Fenwick et al., 2009; Carrasco et al., 2012). Furthermore, the general biology of many remains poorly known, for example species that inhabit Andean areas of difficult access and/or are infrequently found. The species studied by Guerra-Duarte et al. (2015) were *B. microphthalmus*, *B. andianus*, *B. pictus*, *B. barnetti*, *B. atrox*, *B. chloromelas*, *B. taeniata*, *B. oligolepis*, *B. castelnaudi*, *B. peruviana*, and *B. neuwiedi*. The former *B. neuwiedi* sensu lato was revised taxonomically by da Silva and Trefaut Rodrigues (2008) (see also Campbell and Lamar, 2004), who changed our concept of the group from twelve long-established but poorly diagnosed subspecies of *B. neuwiedi* to the recognition of seven species. Guerra-Duarte et al. cited da Silva and Trefaut Rodrigues (2008) and mentioned that the venom they used corresponded to *B. neuwiedi mattogrossensis*; hence, according to da Silva and Trefaut Rodrigues (2008), the venom had to be attributed to *B. mattogrossensis* and not to *B. neuwiedi*. Among the articles reviewed, another confuses the specific status of populations of the “*neuwiedi*” group (Costa de Oliveira et al., 2011) attributing *B. neuwiedi* to the species widely distributed in Argentina, mentioning that the species is also present in Peru. Hence, it is important to clarify that, according to the last taxonomic revision of the group (da Silva and Trefaut Rodrigues, 2008), *B. neuwiedi* is present in southern Brazil, the species distributed widely in Argentina (and the one involved in the majority of reported snakebites in the country) corresponds to *B. diporus* (see distribution maps in Di Cola and Chiaraviglio, 2011; and Nori et al., 2014), and the species present in Peru should be attributed to *B. mattogrossensis*. Additionally, it is important to remark that although Campbell and Lamar (2004) and da Silva and Trefaut

Rodrigues (2008) reported *B. mottogrossensis* from Peru, precise localities have not been published, and taxonomic revisions are necessary to corroborate the presence and specific status of representatives of “*neuwiedi*” in Peru. Two of the species included by Guerra-Duarte et al., *B. castelnaudi* and *B. peruviana*, were long ago synonymized with *B. taeniata* and *B. oligolepis*, respectively (see Campbell and Lamar, 2004). The authors considered *B. castelnaudi* and *B. peruviana* as valid species, and found differences between their venoms and those of *B. taeniata* and *B. oligolepis*. The article provides a regional map of Peru where the reported species are commonly found, with points that correspond to reports taken from the bibliography. This map showed one record for *B. taeniata* that is outside the known range of distribution of the species (see maps in Campbell and Lamar, 2004); this record is located in San Martín Department where *B. pulchra* can be found. Records for *B. castelnaudi* and *B. peruviana* were located in the Departments of Huánuco and Junín respectively, areas that include the range of distribution of *B. chloromelas* (see maps in Campbell and Lamar, 2004). Hence, it seems probable that the authors misidentified the samples, thus their results may have a different interpretation; but that is difficult to establish because they did not include the localities of origin of the specimens that provided the venoms. Wüster (1996), Wüster and McCarthy (1996), and Wüster et al. (1997) pointed out problems associated with the use of old nomenclature and the importance of providing precise localities of origin of specimens. Regarding the generic level, Guerra-Duarte et al. used the CII, which divides the *Bothrops* complex into five genera. As mentioned before, Fenwick et al. (2009) proposed this classification, but Guerra-Duarte et al. erroneously attributed it to Carrasco et al. (2012). Authorship and date are necessary to track the history of the taxonomy of a group, so caution should be taken on this aspect of nomenclature. Some of the results of Guerra-Duarte et al. support their proposal that venom composition is a feature that may contribute to recognize phylogenetic relationships (as also suggested previously, Calvete et al., 2007, 2009b). For example, the authors identified four venom profiles in their study, one of them including *B. microphthalmus* and *B. andianus*. The latter is a poorly known species and a potentially medically important one, particularly in highly touristic places like the Machu Picchu Sanctuary in the Peruvian Andes (type locality of *B. andianus*). The species has not been included in phylogenetic analyses until recently, and then based only on morphological data. As mentioned by the authors, their results supported the phylogenetic results of Carrasco et al. (2012), which showed *B. andianus* closely related to “*microphthalmus*” (*Bothrocophias*). Fenwick et al. (2009, suppl. mat.) obtained similar results. The classification used by Guerra-Duarte et al. assigns *B. andianus* to *Bothrops* sensu stricto, which does not reflect the phylogenetic affinities of the species shown to date by the available evidence.

5. A reappraisal of recent generic-level rearrangements for the *Bothrops* complex

There is wide consensus in taxonomy and other evolutionary disciplines that names are applied only to monophyletic groups, avoiding the recognition of paraphyletic taxa, which would introduce unnecessary and misleading subjectivity to the definition and interpretation of taxa. The current taxonomic and nomenclatural instability in the *Bothrops* complex lead to some degree of persistence of paraphyly in the β taxonomy of the group.

Morphological and molecular evidence support the monophyly of the *Bothrops* + *Bothriopsis* + *Bothrocophias* group; therefore, considering the group as a single genus *Bothrops* or splitting *Bothrops* into additional genera are both applicable approaches in terms of taxonomic principles, except that splitting *Bothrops* would

require the existence of diagnosable and supported monophyletic groups among its species. The latter is not yet clear according to the most recent phylogenetic studies (Fenwick et al., 2009; Carrasco et al., 2012). The phylogenetic affinities of some species are still uncertain (*B. barnetti*, *B. pictus*, *B. roedingeri*, *B. lojanus*) and the position of several others requires re-evaluation, whether from morphological or molecular evidence or both (e.g. *B. andianus*, *B. ammodytoides*, *B. pirajai*, *B. sanctaerucis*, *B. venezuelensis*). There are four main problems with splitting *Bothrops* into *Rhinocerophis*, *Bothropoides* and *Bothrops* sensu stricto, which arise from phylogenetic considerations: a) the variation in the phylogenetic position of some of the species mentioned before may lead to the paraphyly of the genera; b) assigning *B. andianus* to *Bothrops* sensu stricto does not reflect the apparent phylogenetic affinities of the species and retains the paraphyly of *Bothrops*; c) *Bothropoides* is defined solely on molecular data and no morphological synapomorphy; a genus diagnosed solely on the basis of molecular characters from mitochondrial genes seems of little practical value since morphological identification is an essential “first-hand” tool in the field, the laboratory, the museum, and the medical institution; d) the phylogenetic affinities of the “*neuwiedi*” and “*jararaca*” groups, which constitute *Bothropoides*, are strongly conflicting among alternative supported phylogenies. As shown in Figs. 1 and 2, the differences in both phylogenetic hypotheses involve deep nodes in the cladograms, and consequently most species of the complex. These differences (discussed in Carrasco et al., 2012) are mainly due to the discrepancy of positions of “*neuwiedi*” and “*jararaca*”.

The alternative phylogenies for the *Bothrops* complex require re-evaluation from additional data, which is necessary not only for taxonomic purposes but also because they can lead to radically different evolutionary interpretations about their historical biogeography, morpho-ecology, and venoms, among others attributes. For example, the dichotomy shown in the phylogeny of Fig. 2 would imply that similarities within each group in features from morphology (e.g. patterns of coloration) and ecology (e.g. macro-microhabitat, feeding habits) (Martins et al., 2002; Carrasco et al., 2010, 2012) may be attributed to ancestor-descendant relationship. On the other hand, the phylogeny of Fig. 1 would imply that morpho-ecological similarities among “*neuwiedi*” and “*jararaca*” with other groups of species respectively, might be attributed to convergent evolution because of inhabiting similar habitats.

In conclusion, results of phylogenetic studies to date suggest that, at least until ongoing research clarifies the uncertain and conflicting phylogenetic relationships, synonymizing *Bothriopsis* with *Bothrops* seems the most appropriate taxonomic approach. The synonymization follows taxonomic principles and may promote taxonomic stability while reflecting evolutionary information.

6. Final considerations

This review highlights that some problems pointed out two decades ago (Wüster, 1996; Wüster and McCarthy, 1996; Wüster et al., 1997) regarding taxonomy in non-systematic research of venomous snakes, are still recurrent. Here we reiterate the importance of providing precise information on the geographical origin of specimens that provided the venom, and the importance of the deposition of specimens in scientific collections. Both are essential to allow replicability, correct identification of venom samples, and development of further research (Cotterill, 1997; Wüster et al., 1997; Kaiser et al., 2013). We also emphasize the necessity that toxinologists and biomedical researchers working with venomous animals are informed regarding their systematics. Critical and explicitly founded choices of classifications by researchers on the *Bothrops* complex can contribute to the reduction

of adverse consequences of current taxonomic instability. This review also highlights that evolutionary and biomedical studies on venomous snakes can greatly benefit from some degree of articulation between disciplines as toxinology, systematics and ecology.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical statement

Not applicable.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.toxicon.2016.05.014>.

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