# [総説] Skin Injuries Due to Poisonous Snake Bites

# Skin Injuries Due to Poisonous Snake Bites

Hiroshi Uezato[1] and Masatoshi Nozaki[2]

[1] *Division of Dermatology, Department of Organ-oriented Medicine School of Medicine, Faculty of Medicine University of Ryukyus, Okinawa, Japan*
[2] *Department of Health Science, Okinawa Prefectural Institute of Health and Environment*

## ABSTRACT

We present an overall view of poisonous snake bites in Japan. In Main Land, Japan north of the Tokara Straits or "Tose Line", poisonous snake bites by the Nihon mamusi (a species of a viper native to Main Land Japan), and Yamakagashi (tiger keelback) are of major clinical importance, whereas in the South-West Islands south of the Tokara Straits, serious problems occur due to the snake bites by the Habu (a pit viper native to the Ryukyu Islands). In Main Land Japan, approximately 10 mortality cases by the Nihon mamusi have been reported recently, whereas in Okinawa, no mortality cases due to the Habu bites have been observed. However, poisonous snake bites are still important diseases, and we should not disregard them even in our days of urbanization. *Ryukyu Med. J., 23(1,2) 11～20, 2004*

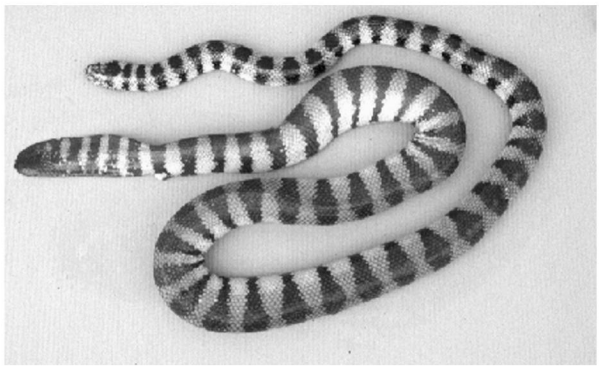
Key words: snake bites, skin injuries

## Definitions and General Concepts

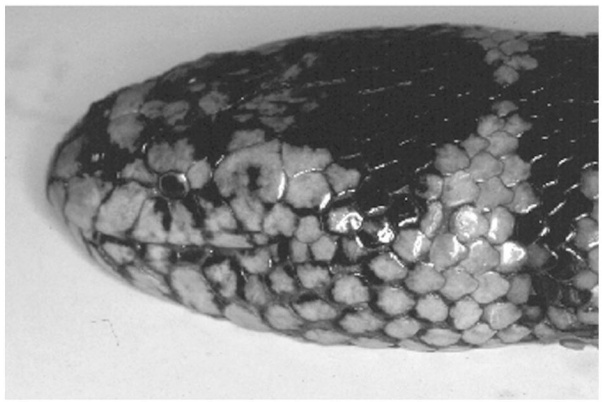
Snake bites are divided into two categories: first, venomous bites or envenomations and second, harmless bites or blunt traumas. There are approximately 2,900 species of snakes in the world, of which 500 are venomous[1]. In Japan, venomous snake bites caused by the Nihon mamusi (a species of a viper native to Main Land Japan), Habu (a pit viper native to the Ryukyu Islands), and Yamakagashi (tiger keelback), which for long time was believed to be non-poisonous, are of major clinical importance. Reports of snake bites by those other than the above three are few.

According to the taxonomy of higher animals, snakes belong to the suborder Serpentes, the order Squamata, and the class Reptilla. Four major families are known in the suborder Serpentes that thrive in Japan. 1) The family Typhlopidae are primitive snakes with small eyes. In Okinawa, only one species of this family thrives. It is harmless, and is without fangs. 2) The family Colubridae includes most of the snakes. There are more than 1,530 species, most of which are nonpoisonous. However, the Yamakagashi (*Rhabdophis tigrinus*), which belongs to this family is known to have venom (Fig. 1). 3) The family Elapsidae are poisonous snakes, represented by a cobra with neurotoxins and a krait in South Asia. Nine species of this family thrive in Okinawa, including the Hyan (*Hemibungarus japonicus japonicus*), Hai (*Hemibungarus japonicus boettgeri*) Iwasaki-Wamon-Beni-Hebi (Iwasaki's coral snake) (*Hemibungarus macclellandii iwasakii*), and sea snakes with neurotoxins living of Okinawa such as Madara-Umi-Hebi (*Hydrophis cyanocinctus*) (Fig.2 a, b, c), and

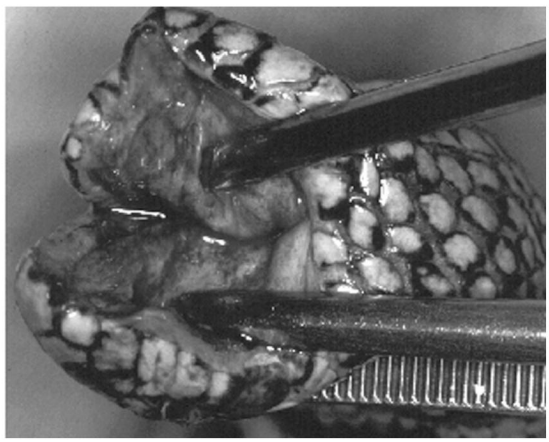
Fig. 1 A Yamakagashi snake (*Rhabdophis tigrinus*).



a



b



c

Fig. 2 a, b, c A Madara-Umi-Hebi snake (*Hydrophis cyanocinctus*) and its oral region. It was caught at the time of its bite on a 52-year-old man in May, 1989.

Erabu-Umi-Hebi (Erabu sea snake) (*Laticauda semifasciata*)[2-4]. 4) The family Viperidae mostly has hematoxins. Over 150 species are known, including the rattle snake, Nihon-mamusi (*Agkistrodon blomhoffii*) (Fig.3), Tsushima-mamusi (*Agkistrodon tsushimaensis*) and Habu with its subspecies. The Habu (*Trimeresurus flavoviridis*) (Fig.4), Sakishima-habu (*Trimeresurus elegans*) (Fig.5), Tokara-habu (*Trimeresurus tokarensis*), Hime-habu (*Ovophis*

Fig. 3 A Nihon Mamusi snake (*Agkistrodon blomhoffii*).

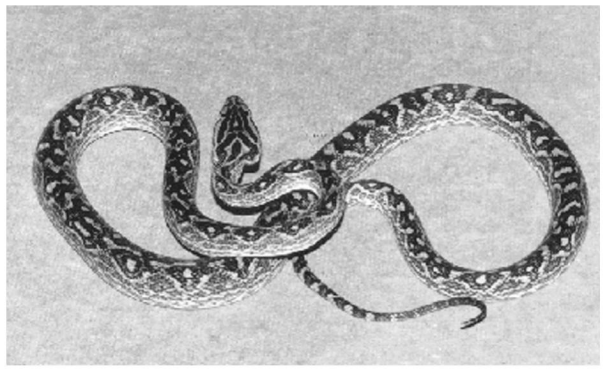


Fig. 4 A Habu snake (*Trimeresurus flavoviridis*).

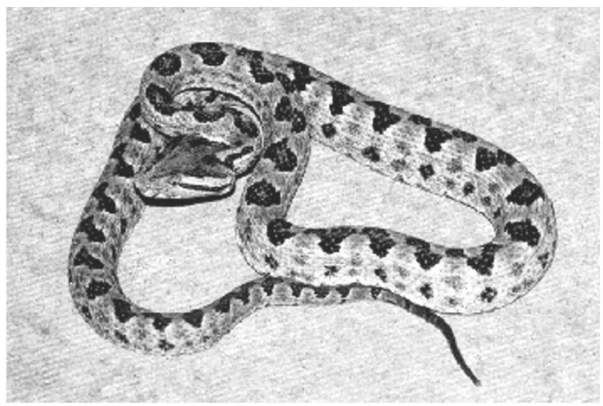


Fig. 5 A Sakishima-habu snake (*Trimeresurus elegans*).

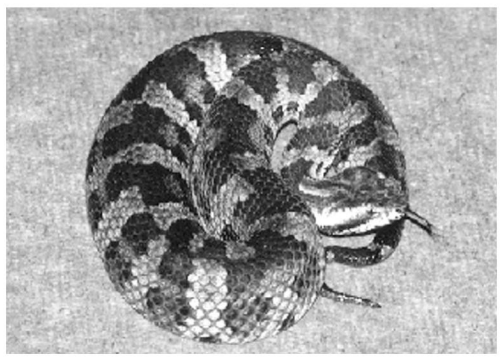


Fig. 6 A Hime-habu snake (*Ovophis okinavensis*).

Table 1 Species of snake in Japan

| **northward of Kyushyu** | | | |
|---|---|---|---|
| **Venomous land snakes** | | **Non-venomous land snakes** | |
| Common Japanese name | Latten name | Common Japanese name | Latten name |
| 1) Yamakagashi | *Rhabdophis tigrimus tigrimus* | 1) Takachiho-hebi | *Achalinus spinalis* |
| 2) Nihon-mamusi | *Gloydius dlomhoffii* | 2) Aodaisho | *Elaphe climacophora* |
| 3) Tsusima-mamusi | *Gloydius tsushimaensis* | 3) Shima-hebi | *Elaphe quadrivirgata* |
| | | 4) Jimuguri | *Elaphe conspicillata* |
| | | 5) Shiromadara | *Dinodon orientalis* |
| | | 6) Akamadara | *Dinodon rufozonatum rufozonaturn* |
| | | 7) Hibakari | *Amphiesrna vibakari vibakari* |
| | | 8) Danzyo-hibakari | *Amphiesrna vibakari banjoense* |
| | | | |
| **Nansei-Islands** | | | |
| **Venomous land snakes** | | **Non-venomous land snakes** | |
| Common Japanese name | Latten name | Common Japanese name | Latten name |
| 1) Iwasaki-monbeni-hebi | *Siromicrurus macclellandi iwasakii* | 1) Buramini-mekura-hebi | *Ramphotyphlops braminus* |
| 2) Hyan | *Siromicrurus japonicus japonicus* | 2) Iwasaki-sedaka-hebi | *Pareas iwasakii* |
| 3) Hai | *Siromicrurus japonicus boettgeri* | 3) Amamitakachiho-hebi | *Achalirus werneri* |
| 4) Kum ehai | *Siromicrurus japonicus takarai* | 4) Yaeyamatakashiho-hebi | *Achalirus formosarus chigirai* |
| 5) Habu | *Trimeresurus flavoviridis* | 5) Miyako-hime-hebi | *Calamaria pfefferi* |
| 6) Hime-habu | *Trimeresurus okinavensis* | 6) Miyara-hime-hebi | *Calamaria pavimentata miyarai* |
| 7) Sakisima-habu | *Trimeresurus elegans* | 7) Sakisima-sujio | *Elaphe taeniura schmackeri* |
| 8) Tokara-habu | *Trimeresurus tokarensis* | 8) Taiwan-sujio | *Elaphe taeniura friesei* |
| 9) Taiwan-habu | *Trimeresurus mucrosquamatus* | 9) Yonaguni-shoda | *Elaphe carinata yonagumiensis* |
| | | 10) Shoda | *Elaphe carinata carinata* |
| | | 11) Ryukyu-aohebi | *Cyclophiops semicarinatus* |
| | | 12) Sakisima-aohebi | *Cyclophiops herminae* |
| | | 13) Kikuzato-sawa-hebi | *Opisthotropis kikuzatoi* |
| | | 14) Sakishima-madara | *Dinodon rufozonaturn walli* |
| | | 15) Sakishima-baikada | *Lycodon ruhstrati multifasciatus* |
| | | 16) Akamata | *Dinodon semobarinatum* |
| | | 17) Garasu-hebi | *Amphiesma pryeri* |
| | | 18) Yaeyama-hebi | *Amphiesma ishigakiense* |
| | | 19) Miyako-hebi | *Amphiesma concelarum* |
| | | | |
| **Venomous sea-snakes** | | | |
| Laticaudinae | | Hydrophiinae | |
| Common Japanese name | Latten name | Common Japanese name | Latten name |
| 1) Irabu-umi-hebi | *Laticauba semifasciata* | 1) Kurogasira-umi-hebi | *Hydrophis melanocephalus* |
| 2) Hirro-umi hebi | *Laticauba laticaudata* | 2) Madara-umi-hebi | *Hydrophis cynanocinctus* |
| 3) Aomadara-umi-hebi | *Laticauba colubrine* | 3) Kuroboshi-umi-hebi | *Hydrophis ornatus maresinensis* |
| | | 4) Iijima-umi-hebi | *Emydocephalus ijimae* |
| | | 5) Seguri-umi-hebi | *Pelamis platurus* |
| | | 6) Toge-umi-hebi | *Lapemis curtus* |

*okinavensis*) (Fig. 6 ) inhabit Okinawa and the South-West Islands. The Taiwan-habu (Trimeresurus mucrosquamatus), an imported species from Taiwan, also thrives in Okinawa.

For physicians, it is essential to divide snake bites into venomous and nonvenomous. Sakai *et al.* classified Japanese snakes into poisonous and non-poisonous groups, considering their geographical distributions[5]. This classification is useful for physicians. It states that the important poisonous snakes living north of Kyushu are the Nihon-mamusi, Tsushima-mamusi, and Yamakagashi (Table 1). In the South-West Islands south of the Tokara Straits or "Tose Line", serious problems occur due to the snake bites by the Habu, Sakishima-habu, and Hime-habu.

There are 9 kinds of sea snakes in Japan, all of which belong to the strongly venomous group. These snakes are usually gentle. In the South-West Islands, mortality and severe cases due to sea snake

Table 2 Annual transition of incidence of the Habu (Hime-habu, Sakishima-habu, Habu) bites in Okinawa in the last 10 years

| | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 |
|---|---|---|---|---|---|---|---|---|---|---|
| No. of death | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| *Trimeresurus okinavensis* | 28 | 18 | 15 | 15 | 8 | 14 | 18 | 7 | 17 | 6 |
| *Trimeresurus elegans* | 37 | 40 | 44 | 42 | 25 | 23 | 28 | 27 | 36 | 30 |
| *Trimeresurus flavoviridis* | 86 | 103 | 100 | 124 | 104 | 109 | 93 | 81 | 82 | 61 |

bites have been reported[6,7].

As for morphological characteristics of typical Japanese venomous snakes, the Nihon mamusi and Habu have movable long fangs on the anterior part of the maxilla. The fang has an opening located laterally at its tip, through which the venom is injected. Therefore, the venom can be transferred to the victim only when the lateral opening of the fang penetrates the tissues. The Habu stores 1 ml of its venom in the poison glands, and 0.1ml of the venom is injected at each single bite[2,8,9]. The Yamakagashi thrives throughout Japan, except Hokkaido, and the South-West Islands. It has two poison glands, i.e., the Duvernoy gland that forms the lower half of the upper lip gland and neck gland. Its long fangs are attached at the upper maxilla, through which venom (saliva) is secreted from the Duvernoy gland. The Yamakagashi also has a blind gland without openings on the dorsal part of the neck. When pressure is introduced, the gland secrets a yellowish viscous liquid through the body squamae, which causes violent inflammation[10-12].

## Epidemiology

It is difficult to know an accurate incidence of poisonous snake bites because not all such cases have been reported in Japan. It is estimated, however, that about 100 cases of Habu bites in Okinawa[13] and about 500 cases of Japanese mamusi bites in Main Land Japan occur annually[14]. As for Yamakagashi bites, over 21 cases attributed to the Duvernoy gland and 16 cases where the venoms from the neck gland spouted into the victims' eyes have been reported[15,16]. Mortality and severe cases with bleeding tendency due to hemagglutination deficiency by the Yamakagashi bites have been reported[17-19]. Table 2 shows the annual transition of incidence of Habu bites in Okinawa[20].

**Occurrence of snake bites:** Occurrence of snake bites varies in area and season. The Nihon mamusi bites most often from April to October when it is most active[21,22]. The occurrence of Habu bites in Okinawa shows an annual distribution with two peaks in May and October. Even in winter snake bites occur in warm, subtropical Okinawa[20,23,24]. The optimal average temperature for the Habu bites is 25℃. The occurrence of the Habu bites decreases in temperature higher than this[25].

**Location of snake bites:** The Nihon mamusi bites most often in fields, roads, gardens, and mountains in a decreasing order of occurrence. Many of the victims are attacked during farm work[22]. The Habu, almost similarly to the Nihon mamusi, bites most often in fields, gardens, meadows, and mountains[20].

**Region of snake bites:** The Nihon mamusi bites most frequently the hands and feet, and very rarely the trunks[22]. On the contrary, the Habu bites even the head and the trunk[20].

## Etiology and pathogenesis

Envenomations by poisonous snakes are usually composed of the following: (1) neurotoxic reactions inducing paralysis; (2) necrotic reactions destroying the tissues; (3) edema formation and vascular injuries due to hemorrhage, hemolysis, blood circulation deficiencies, and hemagglutination deficiencies caused by procoagulant and anticoagulant activities. Neurotoxic reactions are divided into two: (1) peripheral paralysis, i.e., motor and sensory paralyses caused by curariform activities; (2) central paralysis inducing respiratory paralysis. Peripheral paralysis is mostly observed in the victims bitten by cobras and sea snakes. Neurotoxins from these snakes acts on the postsynaptic acetylcholine receptors displaying neuromuscular blocking activities like flaccid paralysis. Crotoxin, an acid protein, isolated from the tropical rattlesnake (*Crotalus durissus terrificus*) and viperotoxin from Palestine vipers cause central paralysis[10,26]. Hemorrhagic factors are found in all the snakes belonging to the family Viperidae that cause injuries to red blood cells and peripheral blood vessels[27]. The venom from the Japanese mamusi, Habu and sea snakes contain strong myonecrotic factors that cause sequelae such as myoglobulinuria and

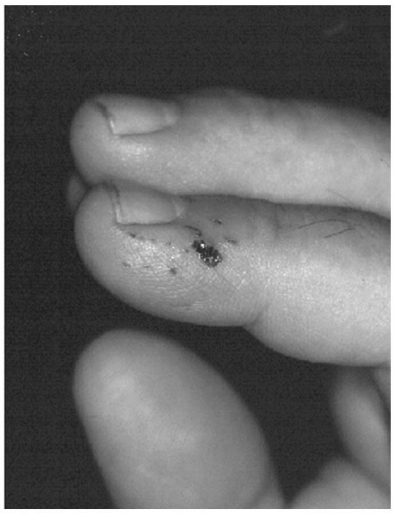


Fig. 7 A case of sea snake bite by the Madara-Umi-Hebi (*Hydrophis cynanocinctus*). The fang marks are on the right forefinger of a 52-year-old male.

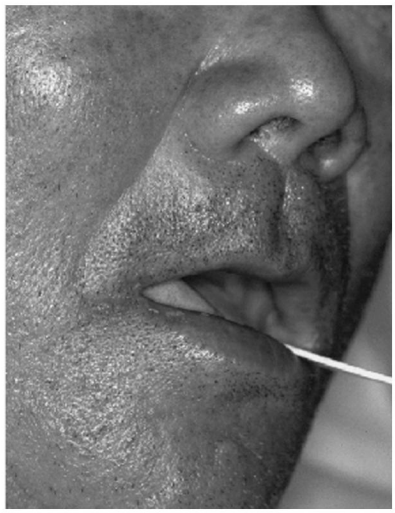


Fig. 8 The trismus due to myoparalysis in the case of Fig.7.

muscular contracture after skeletal muscle necroses occur[5, 28]. The venom from the Nihon mamusi contains enzymes such as phosphodiesterase, monoesterase, 5'-nucleotidase, hyaluronidase, endopeptidase, kininase II, phospholipase and so on. These enzymes are found in almost all the other venomous snakes as well. It also contains HR-I and HR-II that are assumed to be its essential lethal factors with hemolytic activities[5, 28-30]. The clinical manifestations of the Nihon mamusi bites are very complex and many-sided because of the variety of the actions of these enzymes. The local symptoms at the bite sites include pain, swellings, redness, subcutaneous bleedings, and vesicle formation; the systemic symptoms include nausea, vomiting, palpitation, decrease of blood pressure, shock, hemolysis, diplopia, and so on[5, 31].

The venom from the Habu contains hemorrhagic and neurotoxic factors as well as those enzymes that are found in the venom of the Nihon mamusi. HR-I (105,000 molecular weight) and HR-II (24,500 molecular weight), acid and basic proteins respectively, are well known hemorrhagic factors from the Habu venom. On the average, 0.1ml of the venom (20mg of protein) is ejected at each bite. When compared in terms of the lethal activity ratios, the Habu, Sakishimahabu, Himehabu, and Tokarahabu are, 10 to 7 to 3 to 3 in descending order of strength. Incidentally, the lethal dose of the Habu venom is about 150～200mg/60kg, which is 3 to 4 times as large as that of cyanide (50mg/60kg)[2, 9, 26].

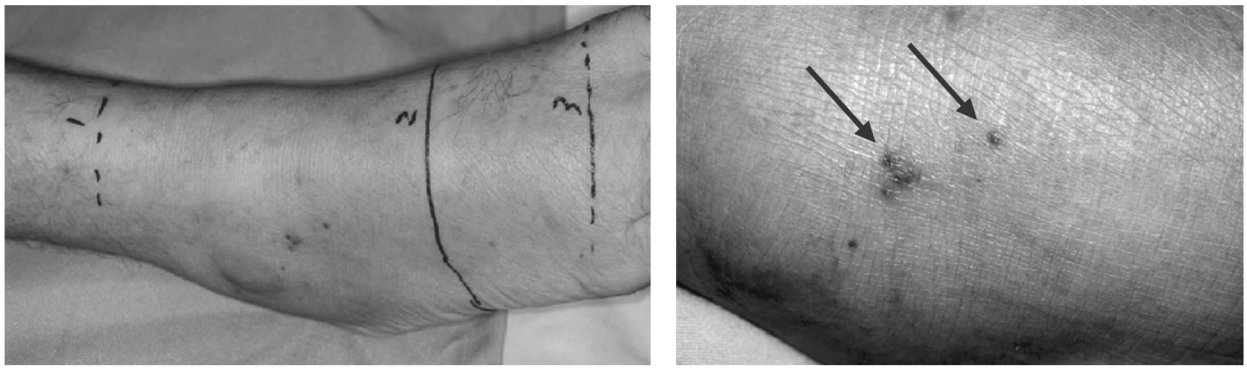
As mentioned before, the Yamakagashi is a venomous snake with the Duvernoy gland and neck gland. The venom from the Duvernoy gland contains prothrombin activation enzymes, therefore, has anticoagulant activity that causes clinical manifestations such as hemorrhage[11, 32]. However, the bite sites usually do not show severe local changes such as swelling and pain, which may appear in the cases of the Nihon mamusi bites. The neck glands, which are subcutaneous blind glands without openings, are distributed on the dorsal part of the body from the neck to the tail. When pressure is applied, the glands spout venoms through the body squamae, which may cause eye injuries[12].

Many sea snakes have neurotoxins. Therefore, it is commonly assumed that sea snake bites cause myoparalyses that may result in death due to respiratory dysfunction. The neurotoxins act on the acetylcholine receptors at the postsynaptic sites of the motor end plate. No nerve impulse can be transmitted with this receptor blocked and symptoms such as respiratory paralysis may occur. It has been reported recently that acute renal failure may also occur due to hyperkalemia and myoglobulinemia from the myolysis by the myotoxins in the venoms[6, 33-35] (Fig.7, 8).

## Clinical Manifestations

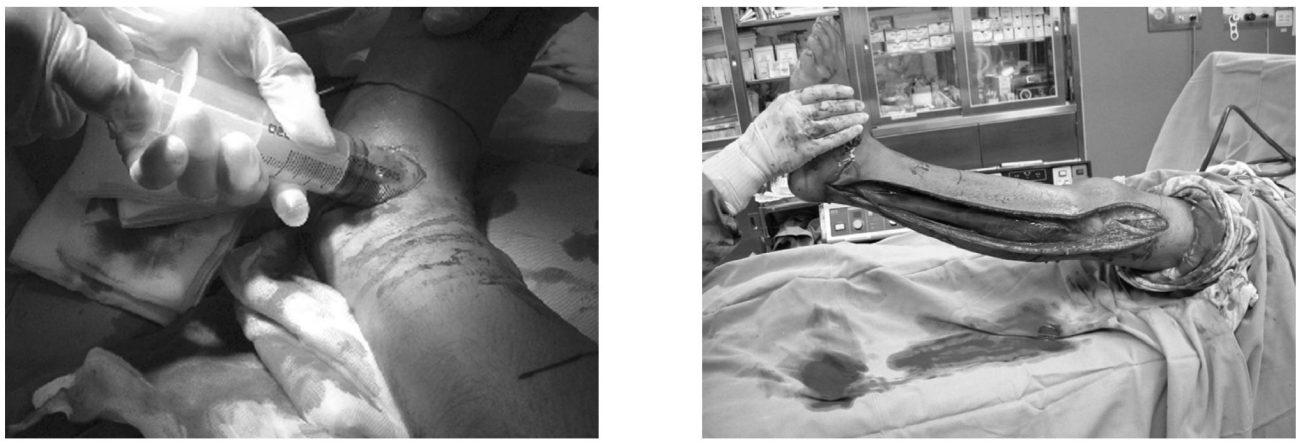
### (1) Nihon mamusi bites

It is said that the characteristic manifestations of Nihon mamusi bites are two fang marks, swelling and pain. However, the fang marks are not always



a b

Fig. 9 a, b The parallel fang marks (arrows) on the right foot of a 78-yaer-old male after the Habu bite. Marks were made proximally every 10cm and the diameters of the swelling were measured every 30 minutes.



a b

Fig. 10 a, b Suction of the venoms after the incision of the bite site using an improvised suction device of syringe. A case of the Habu bite on the left foot of a 13 year-old boy. A striking swelling edema of the left limb appeared with an elevated CPK. Fasciotomy was done to evade compartment syndrome.

necessarily two[21]. The systemic symptoms include nausea, vomiting, anxiety of the breast, palpitation, decrease of blood pressure, and eye symptoms such as diplopia, blepharoptosis and so on. About a dozen or so % of the victims show misty and/or multiple visions. The patients with these eye symptoms tend to be hospitalized longer than those without them. These symptoms recover naturally and are commonly assumed to be the direct results of the Nihon mamusi venom[36]. The main cases of death from Nihon mamusi bites include acute renal failure, disseminated intravascular coagulation (DIC), myocardial degeneration and so on, most of which occur about 50 hours after the bites[22].

**(2) Yamakagashi (tiger keelback) bites**

Dozens of minutes or several hours after the Yamakagashi bites, a systemic bleeding tendency, i.e., DIC may occur including local continuous bleeding without hemostatic tendency, subcutaneous bleeding, rhinorrhagia, stomatorrhagia, hemosialemesis, hematuria, melena and so on. Mortality due to multiple organ failure have also been reported[16-19]. Therefore, it is necessary to recognize that severe bleeding symptoms may occur at a later stage in Yamakagashi bites, even though the pain and swellling are not severe on the early stages. Local pain in the Yamakagashi bites is assumed not to be so characteristic as the bites of the Nihon mamusi or the Habu. Subcutaneous neck poison glands on the back, spout venom when pressure is applied. If the venom falls into the eye, symptoms such as eye irritation, conjunctival edema, conjunctival congestion, visual disorders, corneal erosion, corneal opacity, iritis, linear cloudiness of facies posterior

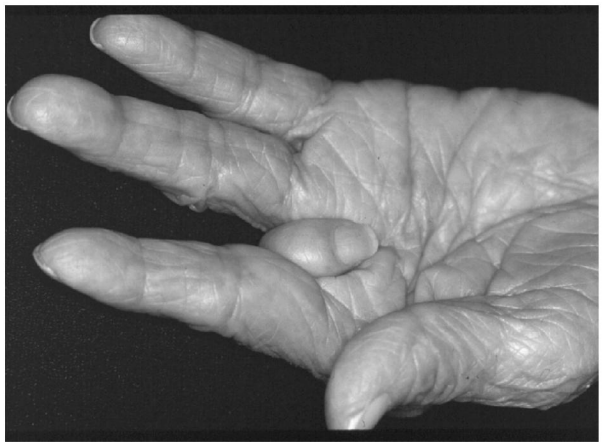


Fig. 11 Contracture of the left middle finger of a 85-year-old female after a Habu bite.

corneae and so on occur[12, 37, 38].

**(3) Habu bites**

Immediately after the Habu bites, varying degree of pain from light pain to burning and/or fulminant pain may appear. The degree of pain runs parallel to the clinical symptoms. At the bite sites fang marks are seen, but not necessarily two (Fig. 9 a, b). Twenty to thirty minutes after the bites, swellings at the bite sites appear and extend proximally. However, some 20% of the Habu bites are nonpoisonous without swellings. If the swellings become worse, compartment syndrome may occur with myonecroses (Fig. 10 a, b) resulting in motion dysfunction such as contracture (Fig. 10). Several % of the Habu bites show headache and gastrointestinal symptoms such as nausea, vomiting, abdominal pain, diarrhea, and so on. If proper treatments for the swellings delay, dehydration, decrease of blood pressure, decrease of urine, and, eventually, acute renal failure may occur. Laboratory examinations reveal transient proteinuria and myoglobulinuria in about 20% of the cases. More than 90% of the moderate to severe cases that require hospitalization show these abnormalities that are an index of the degree of severity[39-41].

## Diagnosis

Diagnosis is confirmed if the snakes in question can be caught and brought in for identification[39-41]. When it is not possible to catch the snakes, diagnosis is made on the basis of the observation from the clinical symptoms. Enzyme-linked immunosorbent assay (ELISA) with the victim's serum is used to detect the snake venoms[15, 42].

## Treatments

**(1) Nihon mamusi bites**

Local treatments for the Nihon mamusi bites include application of suction with a mobile suction device immediately after the bites[43]. It is recommended to use antivenin for cases with systemic symptoms or for those where the swellings extend beyond the knee and/or elbow joints. To evaluate the degree of severity, it is important to observe the courses. If the swellings at the bite sites extend beyond the inguinal joints to the trunk in a short period, a severe outcome must be anticipated. Factors such as maximal area of swelling and time to reach it can be used as an index of the severity[36]. Antivenin should be used for the cases where the swellings extend beyond the wrists and/or ankles (more than Grade II). It should be administered within one or two hours after the bites, and within 24 hours at most. The use of cepharanthin is controversial. It can be indicated for the light cases, but for severe cases antivenin should be used[22, 31].

**(2) Yamakagashi bites**

Special precautions need to be taken against bleeding tendencies in the treatment of Yamakagashi bites. The effects of cepharanthin and many hemostatic agents are of doubtful value in the cases with bleeding tendencies. It is reported that antivenin specific for Yamakagashi is effective. Blood transfusion, exchange transfusion, plasma exchange, and hemodialysis had been used to cope with the complications before the use of antivenin. Recently, remission from DIC by the antivenin has been reported[12, 19]. As mentioned above, local pain in the Yamakagashi bites is not so characteristic as in the bites of the Nihon mamusi or the Habu. If the venom from the neck glands falls into the eye, symptoms such as eye irritation, conjunctival edema, conjunctival congestion, visual disorders, corneal erosion, corneal opacity, iritis, linear cloudiness of facies posterior corneae and so on occur. In such cases, corticosteroids (e.g., cortisone eye drops) should be administered[12].

**(3) Habu bites**

First aid measures for the Habu bites in the field include application of a constriction band proximal to the bite sites just tight enough to lightly occlude the subcutaneous veins. Excessively tight tourniquet may cause block of arterial flow, which promote myonecrosis. As an emergency treatment, parallel incision through the fang

marks, about 1 ～2 mm long, should be made for suction of the venoms. Two hypodermic syringes are used for the suction in such a manner as to make suction blisters. That is, the outer tube of one hypodermic syringe is pressed upside down on the bite sites with its smaller end connected to a Nelaton's catheter. The other end of the catheter is connected to another hypodermic syringe for suction. In Okinawa Prefecture, a mobile suction device is commercially available for emergency use.

Intravascular access with lactated Ringer's solution should be done for all the victims while the bite site is observed for swelling. If no swelling occurs 30 minutes after the bites, no antivenins are needed for the treatment. The diameter of swelling should be measured every 30 to 60 minutes to determine if the swelling is continuously progressing or not. Antivenins should be administered intravenously for all the cases in which progressive swelling is confirmed. About 5 % of these cases show immediate reactions such as wheeze, urticaria, and shock due to the antivenins. It is necessary therefore to prepare for these adverse reactions with epinephrine and endotracheal intubation when the antivenins are introduced. One vial of the antivenin neutralizes 30 mg of the venom. Additional administration of the antivenin should be continued until the swelling ceases to progress. In treating shock, all the drugs should be administered intravenously. Children require the same amount of the antivenins as adults. Tetanus toxoids (e.g., Tetanoblin) and wide spectrum antibiotics are used to prevent tetanus and secondary infections at the bite sites. Excessive swellings induce compartment syndrome and myonecroses. These cases may be caused by the injection of large amount of the venom from the bites, promotion of their absorption by running around for help, improper use of the antivenins and so on. One of the keys for diagnosis of compartment syndrome is to recognize increase of pain when the victim's fingers and toes are passively moved. Fasciotomies should be done without hesitation if ultrasonography reveals hyper-echoic areas in the muscle layers and/or additional use of the antivens fails to decrease local compartment pressures[39-41].

## Acknowledgements

I would like to express our sincere thanks to Drs. M. Nishimura, S. Iwanaga, T. Nakasone at Department of Health Science, Okinawa Prefectural Institute of Health and Environment, Dr. J. Sakai at Nihon-jazoku-gakujitsu-kenkyujo, Drs. O. Ota, H. Taira, and K.Nakao at the Surgical Division and Dr. T. Isa at the Orthopedic Division of Yonabaru Central Hospital, Dr. H. Higa at the Division of Internal Medicine of Naha City Hospital, and Dr. S. Nakamoto at Nakamoto Internal Medicine Clinic of kindly offerings for many data and advices.

## REFERENCE

1) Ueyz P.: How many reptile species? Herpetol. Rev. 31: 13-15, 2000.
2) Shirai S.: Reptiles, Snakes, Okinawa: Encyclo pedia of Harmful Creatures in Okinawa, pp580-631, Shinseitosho Shuppan, 1982 (in Japanese).
3) Nishimura M.: The Habu bites (First aid measures and guidelines for treatments): Biology of snakes in Okinawa, Okinawaken-habutaisaku-kenkyuukai, pp.23-26, 1987 (in Japanese).
4) Ernst CH. and Zug GR.: Snakes in question (translated by Iwamura K.), pp.300-301, Heibonsha, Tokyo, 1999 (in Japanese).
5) Sakai J., Moriguchi H. and Toba T.: A guide to poisonous snake bites for field workers. Bulletin of the Herpetological Society of Japan, No. 2: 75-92, 2002 (in Japanese).
6) Higa H., Uezato H. and Araki Y.: A case of sea snake bite in Okinawa, Japan. Snake 22: 100-105, 1990.
7) Araki Y. and Tomihara Y.: Sea snake bites in Okinawa Ⅱ. Koudokuso-kenkyu-houkokusho: 39-44, 1989 (in Japanese).
8) Takara T.: Habu=Hanpi snake, Okinawa, pp1-52, Ryukyu-bunkyotosho Co., 1973 (in Japanese).
9) Tomihara Y.: Habu Venoms: Okinawaken-eiseikankyo-kenkyujo the 61st year of Showa Koudokuso-kenkyu-houkokusho, pp.35-48, 1986 (in Japanese).
10) Mishima A.: Snake venom envenomation. Gendaiiryo 21: 979-985, 1989 (in Japanese).
11) Sugai K., Mori K., Akutu Y., Suzuki S., Ishikawa M., Sakai H., Takechi H. and Nemoto S.: Study of the Yamakagashi (*Rhabdophis tigrinus*) venoms. Igaka-no-ayumi 135: 165-168, 1985 (in Japanese).
12) Watanabe S., Tsuneto S. and Matumoto Y.: The Yamakagashi. Kyukyu-igaku 12: 441-450, 1988 (in Japanese).

13) Nishimura M.: The literature of the Habu bites in Okinawa Islands after World War II and estimated number of the Habu bites during the years 1964-1996. Okinawaken-eiseikankyo-kenkyujohou 32: 125-135, 1998 (in Japanese).
14) Sawai Y.: Venomous snakes and snakebite treatments in Asia. Snake 24: 129-141, 1992.
15) Akabori H.: Snakes (The Yamakagashi, Mamusi, Habu). Kyukyu-igaku 20: 1672-1675, 1996 (in Japanese).
16) Kato M., Yoshikawa S., Kiyohara S., Suzuki T., Tsuchida T., Kohama M., Tsubokura H., Miura N. and Sasaki N.: A case of the Yamakagashi bite. Hifu-rinsho 45: 133-136, 2003 (in Japanese).
17) Murase H., Hasegawa Y. and Ogawa H.: A mortality case due to brain hemorrhage after the Yamakagashi bite. Rinsho-kensa 30: 1017-1020, 1986 (in Japanese).
18) Ishihara Y., Ono T., Okawa S. and Maeda K.: A child case of snake bite (the Yamakagashi) with extreme hypofibrinogenemia. Japanese Journal of Pediatric Medicine 18: 1001-1005, 1986 (in Japanese).
19) Takamura T. and Kikuchi H: A case of the Yamakagashi bite with DIC. Kyukyu-igaku 13: 105-108, 1989 (in Japanese).
20) Katuren M. and Nozaki M: Poisonous snake bites in the 13th year of Heisei in Okinawa: Okinawaken-eiseikankyo-kenkyujo the 13rd year of Heisei Koudokuso-kenkyu-houkokusho, pp.35-49, 2002 (in Japanese).
21) Ishihara M., Abe M., Urashima R., Sano Y. and Mihara M: Clinical Investigation of 39 cases of the Mamusi bites in the last 4 years. Jpn. J. Dermatol. 105: 1431-1437, 1995 (in Japanese).
22) Suehiro K., Yamashita Y., Otani M., Akata B., Kamihira A. and Masuya M.: Clinical Investigation of 155 cases of the Mamusi bites. Journal of Clinical Surgery 41:1819-1823, 1986 (in Japanese).
23) Teruya H.: Epidemiological study of the Habu bites in Ryukyu Islands. Medical Entomology and Zoology 10:115-127, 1959 (in Japanese) .
24) Sawai Y.: Snake bites in Asia. Snake 5: 29-75, 1973.
25) Tomari J., Wakisaka I. and Yanagibashi T.: Comparative study of epidemiological views on the Habu bites in Amamioshima, Tokunoshima and Okinawa. Minzoku-eisei 53: 87-96, 1987 (in Japanese).
26) Hunatsu M.: Poisonous snakes, Protein toxins. Vol. 2, pp.622-811, Kodansha Scientific, Tokyo, 1972 (in Japanese).
27) Aisaka A.: An approach to mechanism of bleeding. Seitai-no-kagaku 24: 2-29, 1973 (in Japanese).
28) Chinzei H.: Poisonous snakes and their neighborhoods. Chemistry and Biology 25: 130-140, 1987 (in Japanese).
29) Maruyama S.: Poisonous snakes. Internal Medicine 46: 1004-1005, 1980 (in Japanese).
30) Maruyama S. and Igata A.: Poisonous snakes. Internal Medicine 47: 1239-1242, 1981 (in Japanese).
31) Kosaka M., Goto K., Ota Y., Hirakawa H. and Ogino k.: Investigation of antivenin therapy and cepharanthin therapy for the Mamusi bites. ICU and CCU 20: 243-249, 1996 (in Japanese).
32) Sakai A., Honma M. and Sawai Y.: Study on the pathogenesis of envenomation of the Japanese colubrid snake, Yamakagashi, *Rhabdophis tigrinus tigrinus* (*Boie*): 1. Study on the toxicity of the venom. Snake 15: 7-13, 1983.
33) Marsden A.T.H. and Reid H.A.: Pathology of sea-snake poisoning. Brit. Med. J. 1: 1290-1293, 1961.
34) Reid H.A.: Myoglobinuria and sea-snake-bite poisoning. Brit. Med. J. 1:1284-1289, 1961.
35) Okonogi K.: Sea snake bites. Snake 5: 156-161, 1973.
36) Eto K., Okada K., Takahashi S., Ichiba Y., Takahashi M., Matsuda M., Sugi K., Shimizu Y., Watanabe R. and Yoshida A.: Study of the 41 cases of the Mamusi bites at our clinic. Kyukyu-igaku 20: 737-741, 1996 (in Japanese).
37) Suzuki R.: Distaurbance of the eye by snake venoms (*Natrix trina* (Boie). Rinsho-ganka 14: 1384-1387, 1960 (in Japanese).
38) Kawamoto F. and Kumada N.: A case report of eye-injury caused by cervical gland venom of a snake, *Rhabdophis tigrinus* (Boie). Eiseidobutu 40: 211-212, 1989 (in Japanese).
39) Maeshiro M.: Bites and stings. Kyukyu-igaku 13: 1551-1555, 1989 (in Japanese).
40) Maeshiro Y.: The Habu bites (First aid meas ures and guidelines for treatments): Treatments for the Habu bites, Okinawaken-habutaisaku-

kenkyuukai, pp.1-8, 1987 (in Japanese).
41) Miyagi Y. and Maeshiro M.: Statistical observation of the Habu bites for the last 14 years. Chudokukenkyu 7: 147-152, 1994 (in Japanese).
42) Sakai J.: The Mamusi, Yamakagashi and Habu. Kyukyu-igaku 25: 162-164, 2001 (in Japanese).
43) Maie O.: The Mamusi bites and mobile suction devices. Rinsho-hifu 55: 176-178, 2001 (in Japanese).