REVIEW ARTICLE

A Review of Venomous Animal Bites and Stings in Pregnant Patients

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This is a review of Medline and PubMed articles on venomous animal bites and stings during pregnancy reported in English literature from 1966 to 2002. Eighty-five venomous snakebites were reported in pregnant women. Although there are frequent anecdotal reports of scorpion stings in pregnant women, few case reports are documented. Other venomous animal bites or stings to pregnant women that have been reported include spiders, jellyfish, and insects, and these are described. Adverse reproductive and teratogenic effects of venoms on gravid animals are also briefly reviewed. Although uncommon, venomous bites and stings during pregnancy may have significant adverse effects on the fetus and the mother.

Key words: pregnancy, bites, stings, envenomation, antivenom

Introduction

Millions of people are bitten or stung by venomous animals yearly throughout the world.¹ However, the English literature on envenomation of pregnant women is limited. Reviews since 1966 are few and are largely limited to snakebites.^{2–4} In addition to snakes, numerous other species have the potential for envenoming a person, including various arthropods, coelenterates, fish, amphibians, and mammals, and reports of pregnant women being bitten or stung by these types of species have been published.

Envenomation in the pregnant woman may lead to a poor outcome in both the mother and the fetus. Antivenoms, which may be used in the treatment of the envenomed expectant mother, can cause allergic reactions that may have an adverse effect on the mother or fetus. This review discusses outcomes in pregnant women that suffered from an envenomation.

Methods

A search of the US National Library of Medicine Medline/PubMed database for articles on venomous animal bites and stings and pregnancy for the years 1966

through 2002 was conducted (<http://www.ncbi.nih.gov/entrez/query.fcgi>). Terms used in the search included the following: snake bites, spider bites, scorpion stings, jellyfish, caterpillars, platypus, cone shells, fish stings, frogs, toads, echinoderms, sting rays, salamanders, lizards and pregnancy, bites and stings and pregnancy, envenomation and pregnancy, bites and stings and miscarriage, and venom and pregnancy. Articles in the English language or with English abstracts were reviewed. The bibliographies of those articles were also reviewed for manuscripts that may not have been indexed in Medline/PubMed. Searches of the eMedicine database (<http://www.emedicine.com>) and WebMD database (<http://www.webmd.com>) were also performed.

Discussion

SNAKEBITES

Numerous fatal and nonfatal snakebites occur yearly throughout the world. There are estimates of as many as 3 million bites and more than 150 000 deaths annually.¹ Most fatalities occur in developing countries where venomous snakes are plentiful, human populations are dense, and rapid transport and intensive medical treatment facilities are lacking.

Despite the numerous snakebites that occur, the number of reported snakebites during pregnancy is limited. Few reviews of pregnant women bitten by snakes have

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Table 1. Snake bites reported during pregnancy

Author	No. of patients				
	No. of patients reported	Offending snake	Receiving antivenom	Maternal outcome	Fetal/infant outcome
Singh ²²	1	Saw scaled viper	?	Died	Died (74 h after bite)
Reid et al ⁶	5	Malayan pit viper	?	5 Alive	1 Aborted, 4 alive
Bhat ²³	3	Viper	3*	3 Alive	3 Aborted
Fauveau and Blanchet ²⁴	3	?	?	3 Died	3 Died
Chugh et al ²⁵	1	Viper	?	Died	Died
Entman and Moise ¹⁶	1	Copperhead	+	Alive	Died 4 d after birth (6 wk after bite)
Parrish and Kahn ⁸	4	2 Copperhead 1 Rattlesnake 1 Unidentified	2	4 Alive	1 Aborted (24 h after bite), 3 alive
McNally and Reitz ²⁶	1	Unknown adder	?	Alive	Alive (premature)
Sutherland et al ²⁰	1	<i>Psuedonaja</i> sp.	+	Died†	Died
Zugaib et al ²¹	1	<i>Bothrops jaracaca</i>	+	Alive	Died (abruptio placentae)
Malz ⁵	14	1 <i>Vipera palestinae</i> 4 Viper 9 Unidentified	8	14 Alive	10 Alive 2 Aborted 1 Elective abortion 1 Died‡
Dumavibhat et al ²⁷	1	Green pit viper	+	Alive	Alive
Dunniho et al ²	2	1 Copperhead 1 Unidentified	—	2 Alive	2 Alive
James ¹⁵	4	2 Cobra 2 Viper	3	3 Alive 1 Died	3 Alive 1 Died
Dao et al ⁷	4	Unidentified	—	3 Alive 1 Died	3 Died 1 Unknown (mother lost to follow-up)
Seneviratne et al ⁴	39	11 <i>Bungarus ceylonicus</i> or <i>Da- boia russelli russelli</i> 14 <i>Hypnale hypnale</i> 14 Unidentified	18	39 Alive	11 Aborted 1 Malformation 27 Alive
Total	85	33 Unidentified	38	8 Died	52 Alive 32 Died 1 Unknown

* Presumed to have received antivenom.

† Death attributed to supine hypotensive syndrome.

‡ Malformations and died a few days after birth.

been published. Dunniho et al² reviewed the literature and found 50 cases, but details were only available for 30. Pantanowitz and Guidozi³ reported 12 cases: 9 found in the literature, and 3 reported by oral or written communication (R.S.M. Blaylock, 1966).

In a recent study, Seneviratne et al⁴ reviewed snakebites in women treated at 2 medical centers in Sri Lanka. One center included bites from September 1996 to April 2001, whereas the other included bites only from July 1997 to December 1999. During this study, 39 pregnant women who had been admitted with envenomation caused by a snakebite were evaluated.

Some of the cases included in the 2 studies^{2,3} were reported individually as well as being included in reviews, leading to an overcount. Table 1 lists 85 snakebites in pregnant women reported since 1966, which resulted in 8 maternal deaths and 32 fetal and infant deaths. Limited information on the type of envenoming snake was provided in 52 cases. However, an exact identification was provided in much fewer. For example, many bites by vipers were reported, but only one report named the species. Another study reported envenomation by an unidentified adder. In 33 reports, the snakes were unidentified.

Abortions and deaths in fetuses and infants after a mother has been bitten are not unusual. Seneviratne et al⁴ reported that nearly 30% of the envenomed pregnant mothers had a spontaneous abortion. Malz⁵ reported that 3 of 14 snakebites (21%) resulted in abortion or infant death. Dunnihoo et al² noted that of 30 reports with some detailed information available, 6 spontaneous abortions, 7 fetal deaths, and 1 elective abortion occurred, which is a 43% fetal wastage occurrence (excluding the elective abortion). Reid et al⁶ reported 1 of 5 (20%) women aborted. Dao et al⁷ reported 4 snakebites in pregnant women leading to fetal death or abortion in 3. One mother was in her fifth month of pregnancy and aborted 2 days later, whereas another was at term when a snakebite resulted in the death of the fetus. When these studies are combined, 32 fetal deaths occurred in 85 pregnancies (Table 1).

The average age of the mothers was 25 years (68 individuals). The mean gestational age was 21 weeks (69 individuals). The average age of the mothers that aborted or had fetal demise was 27.4 years (21 individuals). The average length of gestation at the time of fetal demise or abortion was 17.5 weeks.

Pathophysiologic explanations for fetal deaths or abortions include anoxia associated with shock after envenomation, direct effect of the venom on the fetus, hemorrhages into the placenta and uterine wall, uterine contractions initiated by the venom, pyrexia and cytokine release after tissue damage, maternal hemorrhage with acute fetal anemia causing in utero fetal death, and potential anaphylaxis to antivenom.^{3,7,8}

Venom from various species of snakes has been shown to cause uterine contractions in animals and in isolated uterine tissue. Venoms may act directly on uterine muscle or may act indirectly by causing the release of or potentiating the effect of bradykinins on uterine muscle.⁹⁻¹³ Venom components may exert a direct toxic effect on parts of the placenta.¹⁴ Some components may cross the placenta and adversely affect the fetus in the absence of, or before, seriously affecting the mother.¹⁵

Malformations were noted in 3 cases. Seneviratne et al⁴ described a woman bitten by a Russell's viper during her 16th week of pregnancy who later gave birth to a child with hydrocephalus and polydactyly. Malz⁵ reported a woman bitten by a viper in her 12th week of pregnancy that delivered a child with multiple malformations and hydrocephalus 6 months later who died a few days after. Entman and Moise¹⁶ reported a woman with copperhead envenomation and apparent anaphylaxis to antivenom therapy in her 28th week of gestation. Six weeks later, she had a spontaneous rupture of the membranes and delivered an infant with low Apgar scores. Ultrasound of the baby's head disclosed dilation

of the ventricles and echogenic changes consistent with intracranial hemorrhage. The infant died 4 days later.

The venom of *Vipera aspis* causes congenital anomalies in the form of cleft palate and facial deformities in pregnant mice.¹⁷ *Naja nigricollis* venom injected into pregnant mice caused hepatic and myocardial damage as well as pulmonary vascular congestion and extravasated blood in the intestinal lumen of the fetuses.¹⁸ Arvin, the active defibrinating fraction of the Malayan pit viper *Calloselasma rhodostoma*, caused high rates of fetal death and resorption during early organogenesis in pregnant rabbits. Abortions and hemorrhage occurred when Arvin was given during Days 11 to 15 of gestation.¹⁹ Arvin administered to pregnant mice at partial and complete defibrinating doses resulted in many embryonic deaths.

Case reports suggest more severe fetal outcomes if the mother is envenomed earlier in pregnancy.² Most abortions seem to occur before the 20th week of pregnancy.^{2,3} Pregnancy-related disorders that have led to the demise of the mother and or fetus after a snakebite include the supine hypotension syndrome²⁰ and abruptio placentae.²¹ Two cases of abruptio at weeks 32 and 36 of pregnancy were found in this review.^{2,21} Some mothers had systemic envenomation without signs of local envenomation.³ James¹⁵ reports adverse effects on the fetus before or in the absence of signs of systemic poisoning in the mother.

Antivenom is frequently used to treat severe snakebite envenomations. Of the 85 cases, 38 mothers received antivenom. Two mothers that received antivenom died. The effect of antivenom on the fetus is unclear. Seneviratne et al⁴ reported 10 abortions and 1 malformation in 11 of 18 patients (61%) treated with antivenom. However, they did not find the administration of antivenom to be an independent risk factor for adverse fetal outcome. Poor fetal outcome was associated with symptoms of systemic envenomation and the period of amenorrhea. The period of amenorrhea was 18 weeks or less in all cases where the mother aborted.⁴ In Pantanowitz and Guidozi's³ review of pregnant snakebite victims that had received antivenom, 2 maternal deaths (10.5%) and 11 fetal deaths (58%) occurred. Seneviratne et al⁴ note that in many instances, details on the type of antivenom administered or the circumstances of treatment are lacking. The different rates of fetal wastage in people who receive or do not receive antivenom may just be an indication of more severe envenomation in individuals who receive antivenom. In this literature review, 21 of 38 women (55%) that received antivenom experienced fetal death.

Table 2. *Latrodectus* bites during pregnancy

Author	Age	Gestation	Spider	Anti-venom given?	Maternal outcome	Fetal/infant outcome
Sherman (2000)	27	38 wk	Black widow (hour-glass noted on abdomen)	Yes	Alive	Alive; delivered 1 wk after bite
Handel (1994)	36	22 wk	Black widow (identified at hospital)	Yes	Alive	Alive
Scalzone (1994)	30	~31 wk	Black widow (endemic area plus symptoms)	No	Alive	Alive
Russell (1979)	20	16 wk	<i>L. hesperus</i>	Yes	Alive	Alive; delivered at 34 wk by C-section (because of cephalopelvic disproportion)

SPIDER BITES

A few bites by *Latrodectus* species and *Loxosceles* species in pregnant women have been reported (Tables 2 and 3), including 4 envenomations by the black widow spider.^{28–31} Russell et al³⁰ described a case of a pregnant woman bitten by *L. hesperus*. Thirty-five minutes after the bite, she developed abdominal cramps and chest tightness. She was treated with antivenom (*Latrodectus mactans* Lyovac) and became asymptomatic within 20 minutes of administration. It was suggested that severe abdominal cramps provoked by the venom of *Latrodectus* might precipitate spontaneous abortion. Three additional cases of latrodectism during the second, fourth, and eighth month of pregnancy were reported to Russell et al³⁰ (Maretic of Yugoslavia, personal communication, 1976). Despite violent cramps, no abortions or premature births occurred. Russell et al³⁰ also mentioned a

patient of Orusev that was bitten by a *Latrodectus* spider during the sixth month without adverse influence on the pregnancy. In a personal communication (1963) to Dr Russell, Piguelvsky stated that in Russia before the turn of the century, some bites in pregnancy resulted in abortion, but no details were provided.³⁰

All of the 4 women with *Latrodectus* bites experienced an increase in blood pressure, abdominal pain, and cramps. Leg and back pain were also noted. Health care staff reported fasciculations in 2 individuals. One person reported paresthesias of the soles of her feet, described as a burning sensation that began 15 hours after envenomation.³¹ In one individual, slight irregular uterine contractions were noted, the cervix was dilated from 1 to 2 cm, effacement increased from 50% to 75%, and the station changed from –5 to –2, but no further progression of labor occurred after antivenom was given.²⁹

Table 3. *Loxosceles* bites during pregnancy

Case	Age	Gestation	Spider	Antivenom given?	Maternal outcome	Fetal/infant outcome
1	32	7.5 mo	<i>Loxosceles reclusa</i> (identified)	No	Alive	Alive
2	27	8 mo	<i>L. reclusa</i> (identified)	No	Alive	Alive
3	34	6 mo	<i>Loxosceles</i> (typical symptoms and found in house)	No	Alive	Alive
4	28	6 mo	<i>Loxosceles</i> (typical symptoms and found in neighborhood)	No	Alive	Alive
5	?	5.5 mo	<i>Loxosceles</i> (typical symptoms)	No	Alive	Alive

Three of the bite victims received calcium gluconate, but symptoms were not relieved. Two of these also received narcotics (morphine) for pain. Three of the women received antivenom, and their symptoms were markedly improved within 1 hour of administration.

In studies on rodents, Bettini and Cantore³² reported abortion and expulsion of the fetus in mice envenomated by *Latrodectus* spiders.

The genus *Latrodectus*, found throughout much of the world, consists of many species of medical importance such as *L mactans*, *L tredecimguttatus*, *L cinctus*, *L menavodi*, *L hasselti*, *L pallidus*, and *L curacaviensis*.³³ In North America, species of importance include *L mactans* (black widow), *L geometricus* (brown widow), *L bishopi* (red-legged widow), *L variolus* (northern black widow), and *L hesperus* (western black widow).

The neurotoxins in the venom from these North American species are similar and respond to the same antivenom.²⁸ One of the main neurotoxins of *Latrodectus* is alpha-latrotoxin. This toxin combines with a guanosine 5'-triphosphate-binding protein on presynaptic neurons resulting in depolarization of the neuron and the release of acetylcholine at the neuromuscular junction,³⁴ which may lead to uterine contractions. Investigators think that this toxin is so large (molecular weight, 130 000 Da) that it is unlikely to cross the placenta.^{28,29}

The other type of spider bite reported in pregnant women is that of the brown spider *Loxosceles*. Five cases of proven or probable loxoscelism during pregnancy have been reported and are summarized in Table 3. Anderson³⁵ states he has reviewed or managed several other patients with possible loxoscelism in pregnancy, but he did not report them. The spider was recovered and identified as *Loxosceles reclusa* in 2 cases. The other 3 individuals had symptoms typical of *L reclusa* bites. Two developed a red maculopapular rash over their body. Protein and hemoglobin were detected in the urine of 4 individuals. No serum hemolysis or free-serum hemoglobin was reported in 3 cases; it was not mentioned in the other 2. Case 4 developed a necrotic wound that took several months to heal. Three individuals were treated with corticosteroids, and no one received antivenom. No adverse effects on the fetuses were reported.

SCORPION STINGS

Although there are frequent anecdotal reports of scorpion stings in pregnant women, few such reports are documented in detail in the literature. In a study of 52 envenomations by the scorpion *Androctonus crassicauda*, 2 pregnant women were included.³⁶ Little information was provided on these individuals, except that one was 28 years old, and the other was 27 years old when

stung. Both received antivenom, and their fetuses remained stable. No adverse consequences were reported in either mother or fetus.

Analysis of the venom from this scorpion revealed a weak effect on the isolated rat uterus. Ismail et al³⁶ noted that the venom from *A crassicauda* was less potent than *Leiurus quinquestriatus*, *Buthus minax*, *Pandinus eximialis*, *Parabuthus granimanus*, and *Androctonus amoreuxi*.

Kankonkar et al³⁷ reported that a number of pregnant women succumbed to the red scorpion sting in the Konkan region in India, but no details were provided.

Unpublished observations attributed to Ibrahim report that stings from *L quinquestriatus* result in abortion in pregnant women during the first trimester in most cases.³⁸ The venom of *L quinquestriatus* produced a marked increase in the frequency and amplitude of contractions of the rat uterus.³⁹ This action seems to be blocked by meclofenamic acid, suggesting that the venom may produce this response through the release of kinins. Promethazine and chlorocyclizine also are reported to block the uterine stimulant action of the venom.³⁸

Marei and Ibrahim³⁹ found that the uterus of the pregnant rat seems to be more sensitive to the effect of scorpion venom during early pregnancy. They were able to detect 5-hydroxytryptamine in the venom of *L quinquestriatus* and felt that this component may be the cause of abortion during the first trimester in humans. They recommend that pregnant women stung by *L quinquestriatus* during the first trimester be treated with antivenom and a 5-hydroxytryptamine antagonist.³⁹

Other studies of scorpion venoms on the rat uterus and rat fetuses have been performed. *Buthus occitanus* venom was found to contain a peptide with bradykinin-potentiating activity that causes contractions in isolated rat uterine muscle.⁴⁰ Toxin T1 from the scorpion *Tityus serrulatus* causes contractions in the isolated rat uterus.⁴¹ *A amoreuxi* venom caused high fetal resorption rates, especially when injected on Days 9 to 11 of gestation. Vertebral and ossification defects and weight loss were noted in many viable fetuses.⁴²

HYMENOPTERA STINGS

Hymenoptera stings are the leading cause of venomous animal-related deaths in the United States⁴³ and a major cause of animal-related deaths worldwide. Despite the frequency of stings, very few articles on hymenoptera stings in pregnant women could be found.

One report⁴⁴ described a woman in the 27th week of pregnancy that had an anaphylactic reaction after a wasp (*Paravespula germanica*) sting. She was aggressively

treated. Two days later, she experienced uterine pains and contractions, and intravenous ritodrine tocolysis to inhibit uterine contractions was begun. Ultrasound showed a vital fetus. Tocolytic therapy was continued for 3 days. She was found to have some cervical dilation and underwent cervical cerclage. Her postoperative course was stated to be uneventful. She had a premature delivery in the 35th week of gestation felt to be the result of postanaphylactic reaction. The child developed normally after delivery.

A Samsun ant (*Pachycondyla sennaarensis*) stung a 21-year-old woman during her 40th week of gestation. She developed leg swelling and dyspnea, was treated for anaphylaxis, and was stable 1 hour later without evidence of fetal distress. Approximately 16 hours later, she developed vaginal bleeding, abdominal pain, and uterine tenderness. Ultrasound disclosed placental separation with absent fetal heartbeats. Labor was induced and she delivered a stillborn child. Evidence of a retroplacental clot was found. The authors felt that placental abruption was caused by the ant sting.⁴⁵

Multicystic encephalomalacia was reported in an infant whose 31-year-old mother was stung by a bee in her 30th week of gestation.⁴⁶ She developed severe anaphylaxis and was unconscious for several hours, but she was discharged from the hospital 24 hours after admission. Fetal movements ceased for 4 days afterward, and the fetal heartbeat was inaudible. An ultrasound 6 days after anaphylaxis showed an increased biparietal diameter, and it was still increased 10 days later. Spontaneous labor occurred at the 35th week, 34 days after the sting. The amniotic fluid was meconium stained. A limp cyanotic infant was delivered vaginally after a short labor. The infant had genu recurvatum, dislocated hips, hypotonia of the upper limbs, and hypertonia of the lower limbs at birth. The infant died after 64 days. On necropsy, cystic cavitation of the white matter and loss of neurons were noted in various areas of the brain. The authors felt that the fetus had been hypoxic during the period of maternal hypotension from the bee sting, which resulted in severe fetal cerebral edema manifested by an increase in fetal biparietal diameter. The absence of fetal movements for 4 days after the bee sting suggested neuraxial insult, which may explain the limb deformities noted.

An unknown type of insect stung a 24-year-old woman in her fifth month of pregnancy, resulting in collapse after a few minutes and subsequent complete paraplegia.⁴⁷ After 4 months with no improvement, a normal delivery occurred. By this time, the flaccid paralysis had become spastic; she progressively improved and eventually left the hospital 1 year after being stung. No information about the baby was provided.

Whole-bee venom injected into pregnant rats on Days 6 to 14 of gestation produced a reduction in weight and of lactate dehydrogenase and isocitrate dehydrogenase activity in 20-day-old rat embryos. Dead embryos were present in the uterus of treated rats, but no teratogenic alterations were noted.⁴⁸

CATERPILLAR STINGS

In one report,⁴⁹ a woman in her 37th week of gestation came into contact with a *Lonomia obliqua* caterpillar. She developed a hemorrhagic syndrome with gum and genital bleeding and possible abruptio placentae. Labor was initiated, and she delivered a slightly hypoxic live child that left the hospital well after 2 days. The mother had a postdelivery hemorrhage, developed acute renal failure, and required hemodialysis. It required over a month for her renal function to return to normal.

In a study of reproductive loss in mares in Kentucky during 2001, exposure to moderate to large concentrations of Eastern tent caterpillars was one of several factors significantly associated with an increased risk of early fetal loss.^{50,51}

A recent study of pigs fed swine feed mixed with Eastern tent caterpillars found that 2 of 5 pigs aborted their entire litter as compared with 5 control pigs fed uncontaminated swine feed.⁵²

JELLYFISH STINGS

Only one case report⁵³ was found. A 20-year-old woman in her 34th week of pregnancy and her husband were stung by the box-jellyfish *Chironex fleckeri* while sitting in water about 50 cm deep. Immediately after envenomation, she was screaming with pain and walked to the beach with her husband, who was also in pain. She became irrational and unable to stand and reportedly became quiet and pale. Her husband went for help at a kiosk approximately 40 m away. A park official quickly threw methylated spirits on her husband's stings and rushed to the woman's aid. The official described her as "lying still, there was no visible breathing, and her face and limbs were black."⁵³ The official doused the stings and adherent tentacles with methylated spirits and began expired air resuscitation. He soon noticed that her ear lobes were turning pink, and she began to breathe. He returned to the kiosk and summoned a trained nurse (also 37 weeks pregnant at the time). When they came back to the injured woman minutes later, she was again apneic with facial cyanosis and vomitus on her lips. After clearing the airway, expired air respiration mouth-to-nose was begun. After 40 seconds, the victim's face became pink, and spontaneous ventilation resumed. An

ambulance arrived at this time, and the victim was transferred to a hospital. Approximately 30 minutes after envenomation, specific therapy including antivenom was begun. After 4 days of hospitalization, the victim was discharged. Nine weeks later, she delivered a healthy baby by caesarean delivery.

Both rescuers received stings from the tentacles adherent to the victim. However, little information was provided about the pregnant rescuer except that she delivered uneventfully 2 weeks later.

OTHER ANIMALS

No reports of envenomations by platypus, fish, frogs or toads, salamanders, lizards, echinoderms, stingrays, or cone shells in pregnant women were found. Studies with venom from these animals have found contractions of isolated segments of rodent or rabbit uterine muscle, but the implications for humans are not known.^{54–58}

Conclusion

Venomous animal bites and stings during pregnancy are rarely reported. Unfortunately, from cases described in the literature, the occurrence of fetal death is frequent (30%–40%) in snakebite victims. The frequency of fetal deaths after other venomous bites or stings is not known. Envenomations during pregnancy should be reported so that information on medical management and fetal outcomes can be evaluated.

No formal epidemiologic studies of the effects of antivenom on fetal development have been performed. Whereas a large percentage of fetal deaths occurred in mothers who received snake antivenom, it is likely that these deaths were related to the severity of the venom poisoning as opposed to the antiserum. It is generally felt that the risks of significant venom poisoning to the mother and fetus outweigh any concerns about the safety of antivenom to the unborn child. More studies and human investigations are required to evaluate the risk-benefit profiles of snake, spider, and scorpion antivenoms on pregnant mothers, embryos, and fetuses.

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