MEDICAL PRACTICE

Review Article

Adder bites in Britain

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Summary

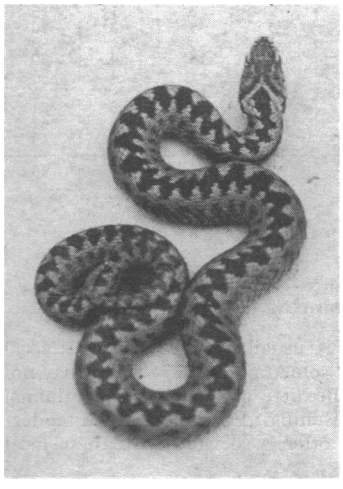
Ninety-five cases of adder bite that have occurred in Britain over the past 100 years are reviewed. Most bites occurred in men who foolishly picked up the adder. Three-quarters of the victims reached hospital within two hours of the bite.

When venom is injected the early symptoms include local swelling and discoloration, vomiting, diarrhoea, and early collapse, which often resolves spontaneously. In severe poisoning persistent or recurrent shock is the main feature. Children recover quickly but adults may take weeks or months to recover, during which there may be considerable disability in the bitten limb. Deaths are rare: only 14 deaths from poisoning were recorded in the past 100 years. In England and Wales only one death from adder bite was recorded in 1950-72, but there were 61 deaths from bee or wasp stings.

In most cases simple symptomatic treatment is enough, but all patients should be carefully monitored. With persistent or recurrent shock Zagreb antivenom is indicated; and it should also be considered in adults seen within two hours of the bite to minimise morbidity from local effects.

Introduction

In his admirable review of 50 adder bite victims Walker[1] recorded that about half the cases caused real anxiety. Effective antivenom against poisoning by the adder *Vipera berus* (see figure) was not available until 1969, when Zagreb antivenom was approved for use in the National Health Service. This antivenom is highly refined,[2] thus lessening the risk of serum reactions, and recent experimental work has confirmed its effectiveness. Monkeys injected subcutaneously with a triple lethal dose of *V berus* venom were saved by intravenous Zagreb antivenom even when it was not given until four hours after the venom injection.[3] In view of this and because many clinicians in Britain are not familiar with the practical aspects of dealing with snake bite, I have reviewed a series of adder bites in Britain. My main purpose was to evolve practical guidelines for dealing with bites. The pathogenesis and other aspects of poisoning by *V berus* venom will be considered elsewhere.



The adder, *Vipera berus*, is the only naturally occurring venomous snake in Britain. Adult specimens are 50-60 cm in length, greyish (though colour can vary), and have characteristic zig-zag markings along their back. Adders are widely distributed throughout Britain, living in clearings, along the edges of woods, on moors, and on mountains. In summer they prefer low-lying damp meadows.

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Patients

The series consisted of 55 cases reported from 1876 to 1971 (in 37 publications) and 40 hospital cases with which I have been concerned through consultation or correspondence from 1957 to 1975. The severity of poisoning was classified as: (*a*) nil (no local or general effects except those of fright); (*b*) mild (local swelling with or without vomiting and sometimes diarrhoea but no recorded evidence of shock); (*c*) moderate (when shock lasted under 2 hours); (*d*) severe (when shock lasted two or more hours or recurred more than two hours after the bite); and (*e*) fatal.

Epidemiological features

Sixty-two per cent of bites occurred in June, July, or August. This was expected, since the adder hibernates during winter. About 10% of bites occurred in each of the months of April, May, and September. Two bites were in March and one was in October. The severity of poisoning was not related to the month of the bite.

Eighty of the 95 victims were bitten in England: 42 in the south coastal counties, 25 in 12 of the more central counties, and nine in Westmoreland, Cumberland, or Northumberland; in four the location was uncertain. Nine people were bitten in south Wales (Glamorgan and Pembrokeshire) and six in the central counties of Scotland. Most (75) victims were male, and no fewer than five out of six males were bitten on the finger, thumb, or hand and only a sixth on the foot or ankle. In contrast, two-thirds of the 20 female victims were bitten on the foot or ankle. Obviously, men have a predilection for picking up snakes not shared by women. For example, a man picked up the severed head of an adder 20 minutes after he had cut it off; he was bitten and suffered severe poisoning.[4]

The site of the bite did not seem to affect the degree of envenoming significantly (table I). The time between the patient being bitten and his reaching hospital was known in 40 cases. This interval was 30 minutes or less in 11 patients, under an hour in 20, and under two hours in 30; in the remaining 10 victims the time varied from three hours up to four days. Thus three-quarters of these victims reached hospital within two hours of the bite.

TABLE I—*Severity of poisoning according to age and site of bite*

	Severity of poisoning					Total
	Nil	Mild	Moderate	Severe	Fatal	
Age (years):						
≤5		3		3	3	9
6–10	1	8	2	3	1	15
11–15		9	3	5	3*	20
16–20		4	1	3		8
≥21	2	12	6	15	4	39
Not recorded					4	4
Site of bite:						
Foot/ankle		9	3	6	3	21
Finger/hand	3	27	9	20	2	61
Not recorded				3	10	13
Total	3	36	12	29	15	95

*One death was due to antivenom.

Early clinical features of poisoning

When venom is injected there is usually immediate pain; local swelling starts within minutes. But sometimes local swelling may not appear until at least an hour after the bite,[5] and pain may be minimal or absent despite severe general poisoning.[6] Enlargement and tenderness of regional lymph nodes are often associated with these local effects.

Vomiting may start within five minutes of the bite[7] and may continue frequently for the next 48 hours. In other cases vomiting does not start until five hours after the bite.[6] Excessive sweating, abdominal colic, and diarrhoea, sometimes with incontinence, often accompany or follow the vomiting. Vomiting, usually with diarrhoea, occurred in almost all the patients with moderate or severe poisoning. Eleven of the 36 patients with mild poisoning vomited, and three also had diarrhoea. Vomiting thus suggests the possibility, though not the inevitability, of serious poisoning.

Shock—as reflected by weakness, sweating, thirst, collapse, confusion, semiconsciousness,[8] loss of consciousness,[9] coldness, cyanosis, absent pulse, and low or unrecordable blood pressure—may start within 10 minutes of the bite[10] or not until 16 hours after the bite.[5] In at least 12 cases this shock was relatively transient, resolving spontaneously within two hours. The rapid onset of this early transient shock suggests activation followed by inhibition of the kinin system.[11]

Bleeding—Generalised bleeding is common in systemic poisoning by many types of viper bite. In adder bites the local oedema is haemorrhagic, as shown by subsequent discoloration, but generalised bleeding is exceptional even in severe adder bite poisoning. Alimentary bleeding has been recorded in an adult victim,[4] in one fatal case (case 12; table II), and in a 14-year-old patient receiving heparin during the first 24 hours after the bite (bleeding promptly ceased when heparin was stopped).

TABLE II—*Deaths due to adder bite poisoning during the last 100 years*

Case No	Sex	Age (years)	Time of bite	Location	Reference No	Hours between bite and death
1	M	Adult	July 1876	Leith Hill, Surrey	24	48
2	M	11	June 1893	Glamorgan	5	33
3	M	4	1901	Ravenglass, Cumberland	1, case 2	60
4	F	3	1903		1, case 3	6
5	M		1903		1	
6	M	Adult	1912	Ramsley, Derbyshire	25	
7	M		1913		1	
8	M	51	1932	Malvern Hills, Worcestershire	1, case 5	26
9	F	6	1934	Whitecliff Hill, Shropshire	1, case 4	36
10	M		1941		21	
11	M		1941		21	
12	F	12	May 1961	Mendip Hills, Somerset	See text	19
13	F	78		Salop	26	
14	M	5	June 1975	Trossachs, Perths	See text	43

Swelling—In 12 of the 29 cases of severe poisoning, swelling of the face and lips or tongue, or both, developed, sometimes immediately after the bite,[12] and lasted for up to two days.[13] The swelling has been attributed to sucking the site of the bite but this is unlikely because the swelling occurred in several victims who did not suck the bite. This feature is also common after bites by *V xanthina palaestinae*[14]; it seems to respond well to antihistamines.

Apart from the depression of consciousness and dilated pupils associated with shock no abnormal neurological signs were recorded.

Later clinical features

Vomiting and diarrhoea may continue for up to two days.[8 15] In severe poisoning shock usually resolves in three to 12 hours. More persistent shock often responded to intravenous fluids, which suggested that hypovolaemia from dehydration and massive local oedema were important causal factors, as suggested by Walker.[1] But sometimes the relief of shock by these non-specific measures was only temporary and shock could recur as late as 30 hours after the bite.[9] Thus persistent or recurrent shock in adder bites is likely to be of multifactorial origin, as in Malayan viperine shock.[16]

Oedema of the bitten limb may increase both in amount and extent to reach a maximum 48-72 hours after the bite. The whole limb may be swollen within five hours of the bite.[17] In severe poisoning oedema extended to the trunk in two-thirds of cases and affected the whole limb in the remaining third. In moderate or mild poisoning the trunk was affected in a third of the cases, the whole limb in a half, and in the remaining sixth swelling was confined to the lower part of the bitten limb. Initially, the oedema is tense, shiny, and non-pitting, and it may be massive. Pain and tenderness in the swollen limb are variable. Sometimes there is remarkably little pain. The oedema starts to resolve three to four days after the bite and then becomes pitting. Initially dusky or mottled in appearance, the discoloration of the swelling subsequently changes, as in a bruise. The swelling has sometimes been attributed to inflammation or venous thrombosis but necropsy findings do not support these theories.

Although blisters occasionally appear at the site of the bite, local necrosis is conspicuously (and fortunately) absent in *V berus* envenoming. Recorded necrosis[18] can be reliably attributed to local injection of ammonia. Acute renal failure may occur in severe poisoning after most types of venomous bites and stings, and anuria for three days has occurred after adder bite.[19]

RECOVERY

Complete recovery in young victims aged 14 years or under was rapid, taking under a week in about a quarter of cases and one to three weeks in the remainder. A 9-year-old boy took six weeks to recover, but this was mainly owing to local incisions made at the hospital. Adults took significantly longer to recover, two-thirds taking three or more weeks and a quarter taking one to nine months. During these months patients often found aching pain and intermittent swelling of the bitten limb disabling. Of the two-thirds who took three or more weeks to recover, less than half had systemic symptoms sufficiently severe to warrant Zagreb antivenom. Recent work in monkeys indicates that this antivenom not only saves life but also greatly reduces the local effects of *V berus* venom.[3] It would therefore be rational to give adults this antivenom to prevent or minimise morbidity from local effects if this can be done, say, within two hours of the bite and provided there are no contraindications. As noted above, three-quarters of the victims reach hospital within two hours of the bite.

Investigations

Non-specific changes in the electrocardiogram (ECG) (mainly T-wave inversions) were recorded in both severe[9] and mild[20] poisoning. Normal ECGs were recorded in two mild cases and one moderate and one severe case. In the severe case the serum creatine phosphokinase concentration was slightly raised. A neutrophil leucocytosis of 16-26 $\times 10^9$/l (16 000-26 000/mm^3), apparent as early as two hours after the bite, was found in four out of six patients with severe poisoning. The white cell count is a useful and simple non-specific test of systemic envenoming, but the neutrophil count was raised in one case of mild poisoning and was normal (11 $\times 10^9$/l) in one case of severe poisoning. In six patients in whom coagulation was studied findings, including Hess test result, clotting time, bleeding time, prothrombin time, fibrinogen levels, platelet counts, thrombin titre, and serum levels of fibrin-fibrinogen degradation products (FDP), were normal. In one case of severe poisoning FDP levels were raised but this may have been due to heparin treatment. Haemoglobin levels may fall slightly during the first three to four days. The erythrocyte sedimentation rate was normal in three severe cases. Plasma bicarbonate concentration was low on admission in a severe case, reflecting the acidosis that is a feature of experimental viper bite poisoning. Potassium levels were slightly raised. Electrolytes were otherwise normal. Plasma urea concentration was slightly raised in a severe case and was 14·0 mmol/l (86 mg/100 ml) in a fatal case (case 12). Liver function and serum aspartate aminotransferase levels were normal in a case of mild poisoning, although the patient developed ECG changes.[20]

Deaths

Table II lists the 14 deaths during the last 100 years. Walker[1] recorded seven deaths in 50 years, but one of his cases (case 1) had been reported[5] (C W Walker, personal communication, 1976); the remaining six deaths were obtained from the Registrar-General. These seven deaths do not include the two deaths in 1941 that were recorded by Birch[21] and also obtained from the Registrar-General. Two deaths, not recorded elsewhere, are reported below (table II).

Case 12—A previously healthy girl was bitten on the ankle and immediately began vomiting violently. Soon afterwards, when her parents reached her, she was collapsed, breathing heavily, and cyanosed with a puffy face, swollen lips, and half-opened eyes under swollen lids. She was admitted to hospital one and three-quarter hours after the bite in severe shock with extreme restlessness and disorientation. Face, eyes, and lips were swollen and cyanosed, blood pressure was unrecordable, and pupils were dilated and fixed. On several occasions she vomited bright red blood, and a motion passed contained bright red blood. Pasteur antivenom was not given because clinically her condition suggested severe anaphylaxis. Despite an intravenous infusion of dextrose solution containing 48 mg noradrenaline and 175 mg prednisolone, the blood pressure remained low and she was very restless. Plasma electrolyte concentrations were normal though the blood urea rose to 14·3 mmol/l (86 mg/100 ml), and she had passed no urine. Nineteen hours after the bite breathing stopped, and despite artificial respiration she died (J Macrae, personal communication, 1961).

Case 14—A boy was bitten on the right ankle at about 1230 on 29 June. He subsequently vomited three times and reached hospital in Glasgow six hours after the bite, when swelling had reached above the knee and blood pressure was 80/60 mm Hg. About an hour later blood pressure was 102/60 mm Hg. Zagreb antivenom was available in the hospital but was not given. No further blood pressures were recorded. According to nursing reports the boy vomited several times during the ensuing 36 hours, and on 30 June he was very pale. At 0700 on 1 July a sudden deterioration was noted and at 0720 an ECG showed no activity. There was no response to cardiac massage. At necropsy the whole of the right leg was very swollen and showed blue-red discoloration. The heart showed a few subendocardial haemorrhages. Posterior aspects of the lungs showed areas of haemorrhage or congestion. No cerebral haemorrhage, pulmonary oedema, or thrombosis in the right thigh vessels were evident.

A notable feature of these fatal cases is the average time of 34 hours between bite and death. There should be ample time to administer Zagreb antivenom if it is indicated.

Death from Pasteur antivenom

In 1957 a 13-year-old boy died from anaphylactic shock due to subcutaneous Pasteur antivenom. The boy had suffered from asthma attacks about four years earlier. He arrived at Poole General Hospital 55 minutes after being bitten on the hand, which was swollen. He was not shocked. Pasteur ER antivenom 10 ml was injected subcutaneously, and seven to 10 minutes later the boy collapsed with arrested breathing. Shortly afterwards the heart stopped. For a few minutes the heart responded to resuscitative measures but he died two and a half hours after the bite (T A J Wickham, personal communication, 1957). Naturally this episode brought antivenom into disrepute and doubtless accounted for the statement in the *British National Formulary 1974-76*[22]: "The bite is less dangerous than the antiserum." This statement is justified in regard to Pasteur ER antivenom, which was unrefined and feeble in neutralising *V berus* venom (P Boquet, personal communication, 1967). But these strictures do not, in my opinion, apply to Zagreb antivenom.[2]

Mortality risks from adder bite and bee or wasp stings

Although 14 deaths from adder bite poisoning occurred in this series of 95 cases, seen over the past 100 years, these two figures are selective and not representative of adder bite in general. It would be grossly misleading to deduce a mortality rate from them. For example, only 9 of Walker's[1] 50 cases are included in the 95 cases—the six unpublished deaths and three cases previously published.[5 8 23] The total number of adder bite victims treated in British hospitals each year is not known. The Office of Population Censuses and Surveys estimate that in 1968-72 an average of 282 people were discharged from hospital in England and Wales each year with a diagnosis of venomous bites and stings (personal communication, 1976). How many of these were adder bites is not known. And how many of those bitten by adders do not go to hospital? From correspondence with herpetologists I know that they rarely go to hospital after such bites. Although the total number of adder bites in Britain is not known it is unlikely that fatal cases are overlooked. During 1959-72 only one death in England and Wales was recorded (case 12, table II), but during these years 61 victims (33 males, 28 females) died from bee or wasp stings (Office of Population Censuses and Surveys, personal communication, 1976). In Scotland during 1950-74 there were no deaths from adder bite and five deaths from bee stings (General Register Office for Scotland, personal communication, 1976).

Discussion

Five years ago it was suggested that a central hospital in each region or each county where adder bite is a possibility (virtually every county in England, Scotland, and Wales) should be designated to stock Zagreb antivenom.[2] This would obviate the nuisance, fuss, and delay of obtaining antivenom urgently from a distance. As well as stocking antivenom the designated hospital should have informed advice immediately available for clinicians dealing with the rare but potentially disturbing problem of adder bite; and all concerned (doctors, ambulance drivers, police, and so on) should be clearly informed of the arrangements. I doubt if this policy has yet been generally adopted in Britain. In the light of experience of dealing with snake bite in various parts of the world, especially in the tropics, and of the findings in the above review, I would make the following suggestions for dealing with adder bites in Britain.

FIRST-AID AND PRE-HOSPITAL PROCEDURE

(1) Reassurance is most important. If available, aspirin or alcohol in moderation are helpful for their calming effects.

(2) The site of the bite should be wiped and covered (mainly for psychological reasons) with a handkerchief or dressing. The site should not be incised as this may seriously delay recovery, introduce infection, aggravate bleeding, and so on.

(3) By compressing the tissues above the bite a ligature may delay absorption of venom into the general circulation during transit to hospital. If hospital treatment is available within 30 minutes no ligature is needed. Otherwise, a firm, but not tight, ligature should be applied just above the bite and should not be released during transit.

(4) If the snake has been killed it should be taken to hospital. Otherwise it should be left alone since attempts to find or kill the snake have resulted in further bites. On no account should the snake be handled, even if dead. Decapitated head reactions can persist for up to an hour.

(5) All victims should be taken to hospital, preferably directly to the designated hospital. The bitten limb should be moved as little as possible because movement spreads the venom even when a ligature has been applied. If retching or vomiting occurs, the victim should be turned on to the side to prevent vomit being inhaled. If vomiting is very troublesome a doctor could inject chlorpromazine.

HOSPITAL TREATMENT

(1) It is important not to panic—there is abundant time to administer antivenom if indicated—but the injury should not be dismissed as trivial without observation. Fatalities have occurred because on admission the victim was thought to have only slight poisoning.

(2) Adequate reassurance is most important, so tetanus toxoid or a placebo injection should be given promptly unless antivenom is already indicated.

(3) The patient should be admitted and carefully observed, preferably in an intensive care unit, at least until the next day.

(4) In *all* cases the following should be monitored and charted: (*a*) vomiting, diarrhoea, and abnormal bleeding; (*b*) hourly pulse rate, blood pressure, and respiration rate; (*c*) white blood count, creatine phosphokinase, serum bicarbonate, and ECG twice daily (ECG more often if hypotension persists); (*d*) local swelling: extent, colour, and amount. Amount is assessed daily by measuring circumference to nearest 0·5 cm at same marked level of both hands or feet, wrists or ankles (thinnest part), forearms or calves (fattest part), or arms or thighs (middle); and (*e*) urine protein, output and blood urea levels.

(5) If a ligature has been applied it should be released. After cleansing, the site of the bite should be left alone.

(6) Cryotherapy is harmful because it may cause local necrosis. Heparin is contraindicated in snake bite as it may seriously aggravate bleeding from vasculotoxic damage. Antibiotics and steroids are not indicated in adder bite poisoning (except that steroids are useful for delayed serum reactions). Chlorpromazine may be needed for vomiting, analgesics for pain, and an intravenous antihistamine for an angioneurotic type of oedema. If restlessness is extreme paraldehyde is suitable. Most patients respond satisfactorily to simple symptomatic treatment.

(7) Zagreb antivenom is indicated if hypotension persists and to reduce morbidity in adults. Antivenom should be given to patients of all ages if hypotension persists or recurs, unless there is a known "allergic" history. If there is a history of allergy the danger of severe poisoning has to be weighed against the danger of intravenous Zagreb antivenom. Further clinical features suggesting that poisoning is severe enough to warrant antivenom include leucocytosis (especially if over 20×10^9/l (20 000/mm^3)), evidence of acidosis, ECG changes, and raised serum creatine phosphokinase levels. If an adult is seen within two hours of the bite and already has swelling extending up the forearm or leg antivenom administration should be considered to minimise morbidity from local effects. This would be contraindicated by a known "allergic" history.

(8) If antivenom is indicated I do *not* advocate a serum sensitivity test. In treating several hundred patients with antivenom I have found sensitivity tests (subcutaneous injection and observation for 30 minutes for reaction) most misleading. When the antivenom was infused reactions sometimes occurred despite negative test results, and in some severe cases with a positive test reaction intravenous antivenom was subsequently infused without any reaction. When immediate reactions occurred adrenaline was invariably successful provided it was *promptly* injected.

(9) Adrenaline should be in the syringe at the bedside before the infusion is started. The contents of 2 ampoules of Zagreb antivenom should be diluted in about 100 ml of isotonic saline and the intravenous drip started slowly (15 drops a minute). If a reaction occurs the drip should be temporarily stopped and 0·5 ml adrenaline 1/1000 solution injected intramuscularly. It is almost always quickly effective and usually the drip may be restarted cautiously. In some cases several injections of adrenaline are needed. The speed of administration is progressively increased so that the infusion is completed within about an hour. If by then there has been little significant improvement further antivenom should be considered. The dose of 2 ampoules is suitable for patients of all ages.

(10) Monitoring and charting should continue at suitably decreasing intervals until all evidence of systemic poisoning has resolved.

I thank patients and colleagues too numerous to name individually for their helpful correspondence and for allowing me to include their cases.

Details of the 17 cases not cited are available from the author.

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Is Raynaud's disease a contraindication to a woman taking the contraceptive pill?

Raynaud's phenomenon does not appear in the lists of contraindications to using contraceptive pills. Nevertheless, there may be individual women in whom such pills may seem to exacerbate the symptoms of vasospasm. These are much improved in pregnancy, as Raynaud himself[1] observed, but how much of the vasodilatation of pregnancy is due to sex steroids is not known.

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