

should be as well assured as in pulmonary tuberculosis. However, healing may give rise to scarring and stenosis and this in turn may lead to mechanical difficulties. In all cases of renal tuberculosis, streptomycin levels in the serum should be estimated early in treatment in case there is retention of the drug. In all severe forms of extrapulmonary tuberculosis it is wise to continue chemotherapy for at least eighteen months.

### Conclusions

Provided proper sensitivity tests have shown that the patient's organisms are sensitive to the standard drugs and that chemotherapy is scrupulously prescribed and scrupulously taken, it should be possible to arrest the disease permanently in the vast majority of cases. There may be very occasional failures in patients admitted moribund, in cases of severe tuberculous meningitis, or in miliary tuberculosis in young infants. But any carelessness by the doctor in prescribing, or by the patient in taking, his drugs are liable to result in ultimate drug resistance and often in subsequent disaster for the patient. Unfortunately such carelessness is still all too common. Treatment of its results will be discussed in the next article in this series.

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## ADDER-BITES IN CORNWALL

BY

T. C. MORTON, C.B., M.D., F.R.C.P.

*Air Vice-Marshal, R.A.F. (Ret.); Pathologist, West Cornwall Clinical Area*

In the last eight years I have seen 12 cases of adder-bites in adults and children and have been consulted about another six. In 14 years in the Middle and Far East I have treated only two cases of snake-bite in Europeans. What is the reason for this anomaly?

During the holiday season, from mid-June until mid-September, Cornwall is faced with an influx of visitors, mainly from the industrial north. The majority are town-bred people, complete strangers to our countryside, in holiday mood, and intensely curious and interested in their unfamiliar environment of tent, caravan, or bed-and-breakfast with its compulsory accompaniment of alfresco meals by lane, wood, or beach.

This period coincides with the breeding season of *Vipera berus*, our only venomous snake. Nearly all the bites I have been consulted about have occurred on the fingers or arms due to foolish attempts to capture or handle the vipers.

### The Criminal

The adder (*Vipera berus*) is not an aggressive snake, it strikes only in self-defence when handled or trodden on; where the human race is concerned it is never the aggressor. It is a short stumpy snake; the largest recorded British specimen was 2 ft. 3 in. (68.5 cm.) in length—this was a female; the male is 2 to 3 in. (5 to 7.5 cm.) shorter. It is usually possible to distinguish the sexes by the coloration: whitish or pale-grey specimens with a black belly and jet-black dorsal markings are males; brown and brick-red specimens with the markings of a darker brown or red are females.

The markings vary considerably; those on the back usually consist of a wavy or zigzag longitudinal band; rarely, the markings may be absent altogether and occasional black melanistic specimens occur (Boulenger, 1913).

*Vipera berus* is the only poisonous snake in Great Britain; it is absent in Ireland. As in all vipers, the two poison fangs are hollow and are present in the posterior extremity of the erectile maxilla; the venom from the poison gland (a modified salivary gland) is injected into its prey to immobilize it and facilitate swallowing and also digestion. The venom of *Vipera berus* is not very toxic; the minimum lethal dose (M.L.D.) for a 600-g. guinea-pig is 40 mg., as compared with the M.L.D. of a Russell viper which is 1 mg. for a similar-sized guinea-pig. The venom contains a small amount of neurotoxin, which varies considerably in the different species of the same genus. Haemorrhagins are also present. The haemorrhagin has a special affinity for the endothelial cells of the finer capillaries, causing lysis of the cells and subsequent haemorrhagic oedema or small petechiae. The latter may be present at the site of the bite and may spread up the affected limb. Oozing of blood from the site of the bite occurred in only one of our Cornish cases; no sloughing of tissues occurred, so the cytotoxins present in the venom, although responsible for the oedema and swelling, are not very toxic.

### Feeding Habits

The food of the adder is very varied; baby rabbits, weasels, mice, voles, shrews, moles, birds, lizards, slow-worms, frogs, and large slugs have been found in the stomach. It swallows its prey whole, the neurotoxin paralyzing it and the cytotoxins and haemorrhagins injected deeply into the victim facilitating digestion.

Hibernation occurs during the colder months of the year, but bites have been recorded from March until October.

I am convinced that the varying severity of adder-bites in this country is dependent on whether the snake has bitten anything recently. This is well exemplified in the case of a boy aged 11, who was bitten on the left index finger and then on the right index finger. No haemorrhagic bullae developed on the right index finger, and the purpuric petechiae and swelling of the right hand and arm were much less. Similarly, the only adult male whose condition gave rise to anxiety was bitten in the early spring by a hibernating viper.

### Reproduction

Pairing takes place in April and May, and the young, 5 to 20 in number, are born in August and September. The young, on releasing themselves from the transparent membrane in which they are enclosed at birth, measure 6 to 8 in. (15 to 20 cm.) in length and feed on insects and worms.

### Natural Enemies

Owing to the dearth of rabbits since the onset of myxomatosis the buzzards in Cornwall have been seen killing adders by flying upwards with the adder in their talons and dropping it from a height of about 150 ft. (46 m.). The water bailiff at the reservoir assures me that he has seen this on at least three occasions. The stunned snake is then torn to pieces and eaten by the buzzard.

**Mortality Rate from Adder-bites in the U.K.**

Walker (1945), in his summary of the accounts of 50 cases reported to him, states that there had been seven deaths from adder-bite in England and Wales up to the year 1945. He was able to trace five of these fatal cases. The particulars of these are as follows:

No.	Sex	Age (Years)	Previous Health	Duration (Hours)	Mode of Death
1	M	11	Delicate	12	Collapse: cardio-respiratory failure; conscious
2	M	4½	Healthy	60	Circulatory collapse; unconscious
3	F	3	"	6	" "
4	F	6	"	36	" "
5	M	51	Delicate Insane. W.R. +	26	Unconscious, with T. 102° F (38.9° C.), bounding pulse and stertorous breathing

The Registrar-General for Scotland informs me that no deaths from viper-bites occurred in Scotland during 1950-8. The Registrar-General for England and Wales informs me that the most recent deaths assigned to snake-bite occurred in two males in 1941.

In 1957 a boy of 14 collapsed and died a few minutes after he had been given antivenin serum as treatment for an adder-bite. Death was attributed to cardiovascular collapse from anaphylaxis due to the serum (*Lancet*, 1957).

We are faced with the anomaly that so far as England and Wales is concerned the only death reported from adder-bite for the last 18 years was due to anaphylaxis from the antivenin given. On the other hand, the deaths due to adder-bite collected by Walker had received no antivenin and at that time no antihistamine preparations were available. It is therefore probable that the present reduction in the mortality rate is due to the more general use of antihistamine drugs and antivenin. Dr. S. Campbell, of St. Just, who has treated numerous cases of adder-bite, relies on "piriton" and rarely finds it necessary to give antivenin.

A feasible explanation for a death occurring in an adult is the fortuitous puncture of a vein by the poison fang—quite a likely event in a middle-aged person with extensive varicosities about the ankle.

**The Victim**

The ages of those bitten varied from 5 to 45 years. There were no fatalities, and in only four cases were there marked general symptoms in which hospital treatment was imperative. All the bites were on the extremities—nine the hand and three the ankle.

Sir Philip Manson-Bahr (1957) states that the venom of the adder in this country is of low toxicity. It rarely, if ever, kills adult humans and is dangerous only to small children. He wisely points out that the main danger to life arises much more from the heroic and often obsolete methods of treatment so often applied than from the viper venom itself.

Up to the year 1957 I could not have agreed more with this expert opinion, but in 1958 I encountered three cases of adder-bite of unusual severity which proved how effective intramuscular or subcutaneous specific anti-viper serum can be. The serum available is the Pasteur Institute E.R. serum in ampoules of 10 ml. for neutralizing the venom of vipers in France (*Vipera berus* and *Vipera aspis*). There they recommend subcutaneous injection locally if possible and

warn one against anaphylactic reactions, especially in subjects allergic to horse serum. Serum-sickness occurs in a large proportion of cases, usually about the seventh to tenth day. Analysis of the antivenin shows specific gravity, 1028; total proteins, 7.2 g./100 ml. (albumin 0.8 g., globulin 6.4 g.).

The results of an adder-bite are completely unpredictable, as they depend on the amount of venom injected and the age and constitution of the patient. The effects are local and general; the former are constant but variable in intensity, the latter may be negligible in adults.

**Local Reaction**

A sharp pain is felt at the time of the bite, which an intelligent girl described to me as being like a jab with a red-hot needle. This is followed by oedema, eventually showing haemorrhagic discoloration and spreading usually up to the groin or axilla in the case of the limbs. It reaches its maximum intensity in from 6 to 24 hours. In addition, petechiae may develop in the vicinity of the bite and occasionally spread up the lymphatics, and the adjacent lymph nodes may become swollen and tender. Occasionally, in a bite on the finger or toe, haemorrhagic blisters develop in 48 hours; this occurred only once in our series. In a girl of 17 who was bitten on the wrist the whole arm and shoulder became very oedematous and went completely canary yellow within 14 hours. A similar reaction was reported by Goddard (1951) in an adult male.

**General Reaction**

Reactions vary greatly in intensity from mild to profound collapse. Giddiness associated with sweating may develop some 20 minutes after the bite. This may pass off in mild cases, but in many others persistent and severe vomiting occurs, together with marked cardiovascular collapse which may go on to drowsiness and semi-consciousness, especially in young children. These general symptoms usually develop within the hour, and our experience has been that if they have not developed by the end of two hours after the bite the case will be mild and no antivenin is necessary. It is usually at least two hours before patients arrive at the Royal Cornwall Infirmary, so that it is easy to decide if antivenin is really required or if antihistamines, rest, and reassurance are all that are necessary; at times it is difficult to convince relatives and practitioners that this is sound advice.

The earlier the onset of general symptoms the greater the shock and vomiting and the local reaction to the bite. Our patients recovered completely from their general symptoms in from 2 to 12 hours after admission to hospital, but the oedema persisted in one case for over four weeks and was associated with discomfort on walking for much longer; eventually a complete recovery was made with no residual after-effects. Curiously enough, this was the only case which received immediate local treatment. The patient was bitten on her ankle while walking near the Lizard. A passer-by applied a tight bandage above the bite and within 20 minutes she was given antivenin locally around the bite. The local practitioner who treated her always keeps antivenin in his refrigerator, as he has seen several adders in his garden and is naturally apprehensive about his young children. (Pasteur Institute E.R. serum was given.)

### Circumstances Under Which the Victims Were Bitten

These circumstances varied from the ridiculous to the bizarre.

A party of young children found a hibernating adder in March. They sat in a circle prodding it with twigs until the snake awoke from its torpor and bit the main aggressor, aged 5, on the hand.

A man on holiday from the Midlands chased and captured an adder by the tail. On being asked why he did this he said he wanted to crack its head off like cracking a whip. On inquiring why he wanted to do this he replied that he had seen a cowboy do this in a strip cartoon. He was bitten on the thumb and was admitted slightly shocked and sweating; his hand and thumb were considerably swollen. He was given 10 ml. of serum subcutaneously and detained for the night. Apart from slight residual swelling he was none the worse for his cowboy exploit, of which he was more proud than ashamed.

There were only four instances out of the 16 bites in which the victim was not to blame.

A naval airman was climbing the cliffs near Mullion and, in reaching for a hand grip above his head, inadvertently placed his hand on a viper which was lying torpid in the sun. It says much for the stoicism of the Senior Service that he did not relinquish his hold and fall backwards over the cliff. He was bitten on the dorsal surface of the middle phalanx of his right thumb. His general condition was excellent, and as he gave a very bad history of asthma and hay-fever no antivenin was given. The thumb was grossly swollen to about three times its normal size compared with the left thumb, and two fang marks were clearly visible. No local or general treatment was given, and he never vomited or showed any signs of shock. His hand was still swollen to a less extent next day, but no petechiae developed and he returned to his unit at his own request. This was the mildest case of adder-bite encountered.

### Two Severe Cases

A sea scout aged 11, in camp near the Lizard, stated that his scoutmaster picked up a snake by the neck and demonstrated it to the boys as a harmless grass snake; he then put it down on the ground and the boy picked it up with both hands and was bitten first on the index finger of his left hand and then on the index finger of his right hand. He promptly threw the snake away. He was admitted two hours later very shocked and vomiting bile-stained fluid. The middle phalanx of the left index finger showed two fang punctures and was tense and very swollen; the middle phalanx of the right index finger showed two similar fang marks but was only slightly swollen. He was given 10 ml. of antivenin intramuscularly into each buttock and vomiting ceased an hour later. Considerable swelling of both arms followed and two large haemorrhagic bullae appeared on his left index finger 48 hours later, together with some small purpuric patches on the dorsum of the hand. His general condition was excellent after 15 hours, but gross swelling of both arms persisted for four days and necessitated his being fed. It was possible to discharge him back to his camp at the end of 10 days. He later had to be readmitted to a small local hospital with marked serum sickness in spite of having been on a prophylactic dose of promethazine all the time he was in hospital.

A girl of 17 on holiday, living in a caravan near a wood, sat down and felt a sharp prick on her left arm, and on looking down saw two drops of blood on her left wrist but saw no snake, wasp, or hornet. The undergrowth where she was sitting was a tangled mass of vegetation. She returned to her caravan and called to her neighbour, as she began to feel very nauseated. She was brought to the hospital in a state of collapse and vomiting bile-stained fluid, and was grossly confused mentally. She was given glucose-

saline intravenously, but no local treatment was attempted, as the casualty officer thought it was an allergic reaction to a wasp-sting and she was too collapsed to give a history. Her left arm was grossly swollen to the elbow, and, on being asked to see her, I decided to give her 20 ml. of antivenin; she then slowly recovered from her shock. The next morning the left arm was swollen from the hand to the shoulder and was a bright canary yellow in colour; her general condition was excellent. On examining the arm at the end of four days, when the gross swelling was beginning to subside, two puncture marks 1 cm. apart could be made out. She was treated with promethazine hydrochloride 24 mg. t.i.d., and her condition gave no further cause for anxiety. Liver-function tests on August 26 were perfectly normal. A blood count on August 22 showed: clotting-time, 1 minute 30 seconds; bleeding-time, 1 minute 48 seconds; haemoglobin, 113%; red blood cells, 5,200,000/c.mm.; total white count, 11,600/c.mm. (polymorphonuclears 81%, lymphocytes 17%, monocytes 2%). Her arm was still very swollen and canary yellow on discharge on August 28. Her general practitioner informed me that her arm was still swollen and yellow on September 1. She continued taking promethazine until September 8, by which time the swelling had almost subsided and no serum sickness or urticarial rash had developed.

### Discussion

"There are nine-and-sixty ways of constructing tribal lays. And every single one of them is right," says Kipling. Alas, this does not apply to the treatment of adder-bites.

The various methods of treatment advocated for snake-bite are legion; many are obsolete and dangerous, giving rise to considerable sloughing of tissues and damage of important structures—for example, median and ulnar nerves. It is obvious that, short of animal experiment on a large scale, using known quantities of dried *Vipera berus* venom, it is impossible to assess the value of cortisone and antihistamine drugs; this applies even more to the numerous undesirable tissue-damaging local measures advocated, such as tourniquet, incision, and suction, rubbing in potassium permanganate crystals, infiltration with 5% carbolic soap solutions, etc. The only remedy which has stood up to the test of time is specific antivenin given early and in adequate dosage; and here the question of allergy and serum sickness must be weighed in the balance in every case of adder-bite in England.

In my very limited experience in the treatment of viper-bites due to *Cerastes cornutus* in Iraq I was impressed with the efficacy of the specific antivenin injected locally at the site of the bite, preferably through the fang punctures where the anatomical site allowed and the case was seen very early. In cases where tourniquet, incision, and potassium permanganate crystals or injections had been given by others I was distressed to see the gross destruction of tissue, even leading to sloughing of tendons and consequent serious disability.

Treatment by the tourniquet, incision of the bites, followed by the rubbing in of potassium permanganate crystals into the wound has no place when dealing with adder-bites in England and cannot be too strongly condemned; it is now obsolete in modern practice in the tropics (Reid, 1956, 1957a, 1957b, 1957c).

The application of a tight bandage above the bitten part followed by "cut and suck" immediately after the bite in an attempt to remove as much of the venom as possible is logically sound, but is extremely dangerous in lay hands and is certainly strongly contradicted as

a first-aid measure for a bite from *Vipera berus* in the United Kingdom.

Viper venom is absorbed by the lymphatics, and the best first-aid treatment is to immobilize the part by splinting or bandaging and to keep the patient at complete rest in a recumbent position. The general reaction after the bite usually ensues within one hour, and this depends on the dose of venom injected and the size and constitution of the patient.

All young children should be brought into hospital as soon as possible, and, if the case is seen very early and the site of the bite permits, 1–2 ml. of antivenin should be injected through the fang marks and the remaining 8 ml. given subcutaneously or intramuscularly into the buttocks, mixed with hyaluronidase. It is wise to give antihistamine prior to the serum.

In the case of adults or children from 10 upwards, if there are no severe general symptoms at the end of two hours from the time of the bite no antivenin is necessary, and all that is required is rest and reassurance and the administration of antihistamine drugs such as promethazine or chlorpheniramine ("piriton").

In severe cases in adults with marked collapse and vomiting the contents of two ampoules (10 ml. in each) of antivenin mixed with hyaluronidase are injected into the buttocks intramuscularly. If the case is seen very early and the site allows—for example, calf—2–3 ml. of antivenin is injected locally through the fang marks and the rest of the antivenin used as indicated above. We have never had to exceed a total dose of 20 ml. of antivenin in any case. The symptoms of collapse and vomiting have always disappeared in two to three hours after giving antivenin. Our cases are always put on promethazine as a precaution against serum sickness and for its therapeutic effect.

If no antivenin is available and the patient's condition is critical intravenous plasma (Goddard, 1951) has been strongly recommended pending the arrival of antivenin. Ariff (1955) recommended cortisone for viper-bites, but I have had no personal experience of its efficacy.

To summarize, far more harm is done by obsolete heroic methods of treatment than by masterly inactivity and immobility together with antihistamine drugs, holding a watching brief ready to give antivenin if the general condition warrants it.

*Prevention.*—This should take the form of public propaganda by press, through television, and in schools, with the advice to leave all snakes in this country well alone; they are useful and harmless scavengers, and even the dreaded adder will bite only if handled or trodden on.

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## FIRST INTERNATIONAL CONFERENCE ON CONGENITAL MALFORMATIONS

LONDON, JULY 18–22

[FROM SPECIAL CORRESPONDENTS]

An International Conference on Congenital Malformations, sponsored by the National Foundation (U.S.A.), was held at Church House, Westminster, from July 18–22, under the joint honorary presidency of Mr. BASIL O'CONNOR (U.S.A.) and Sir GEOFFREY MARSHALL (United Kingdom). Professor J. D. BOYD (Cambridge) was the general chairman, and Dr. G. W. CORNER, of the Rockefeller Institute, New York, gave the theme address. The conference was in eight sessions.

### I.—Incidence of Malformations

The first session was on the incidence of congenital malformations. Mr. CARL L. ERHARDT (New York), whose paper was read by Dr. LOUIS HELLMAN, discussed "Pitfalls in Investigations of Aetiology." The same inciting event, he said, might result in quite different defects; yet similar defects might derive from widely varying causes. A given factor did not invariably produce the effect that was expected, and some embryos affected by a specific type of insult might die and be aborted, while others proceeded to delivery at term. Different malformations became manifest at widely different ages, and the situation was further complicated by the interplay of genetics and environment. For example, some malformations resulted from a defective gene which expressed itself only under certain environmental conditions, while acquired defects might simulate inherited defects with great exactness. Descriptive and analytical studies were both dogged by difficulties of definition and diagnosis. One of the major problems was the large number of observations required to demonstrate an association convincingly.

Professor MAURICE LAMY (Paris) said it seemed that the overall incidence of major malformations visible at birth or recognizable by anatomical examination of stillborn infants or infants who die during the neonatal period was close to 1.5%. The incidence of major malformations for all infants born after the 28th week of pregnancy and with an observation period of one year after birth would seem to be around 4–5%. This by no means represented the totality of malformations, as some only became manifest later in life. It was safe to say that the overall incidence of major malformations was higher than 5%. In countries where death due to infection and deficiency states had declined most, the mortality due to congenital malformations represented 15–20% of infant mortality as a whole. Anomalies of the cardiovascular, alimentary, and urogenital systems were more frequent in males, whereas there was a definitely increased prevalence of monstrosities, spina bifida, and meningocele among females. Hydrocephalus showed a varying sex-prevalence in different countries.

Professor T. MCKEOWN (Birmingham) restricted his discussion of the sources of variation in the incidence of malformations to five indices: maternal age; birth order; season of birth; social class; and secular variation. There were fairly well defined trends in the incidence of many malformations, reflected in an increase associated with primogeniture and increasing maternal age. There would also appear to be a distinct seasonal fluctuation in the incidence of certain malformations, and this was not related to the seasonal variation in incidence of rubella. Anencephalus was the only malformation whose incidence had been shown to be associated with social circumstances, in Scotland the incidence being remarkably higher in births to parents in the unskilled-worker class than to parents in professional and related classes. No such relation was, however, observed in Birmingham data.