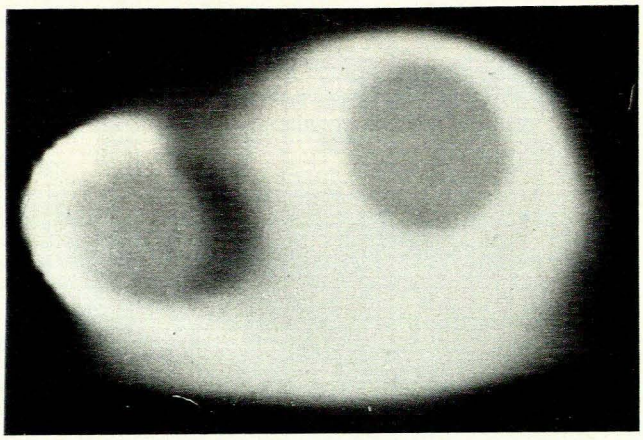

Fig. 11. Slice through the bases of the second and third fingers of the glove, producing a combination of 'cystic' and 'solid' images. In this case the 'solid' appearance is due to partial-volume averaging.

The same principles of partial-volume averaging of the wall of the capsule apply to a craniopharyngioma. To illustrate this point, a simple experiment was carried out. A surgical glove was distended with water and inserted into a similar glove, with a thin layer of diluted barium sulphate between the layers. Care was taken to use only the minimum amount necessary to spread the barium evenly between the two gloves. The fingers of the gloves were tied to prevent the inner glove from slipping out, since barium sulphate acts as a lubricant between two rubber surfaces. A slice through the palm of the glove shows thickening of one side due to partial-volume averaging. This is similar to the apparent thickening of the skull vault in slices near the vertex. A slice through the bases of the second and third fingers resembles a padlock (or double padlock), which proves that the nodular enhancement is in fact caused by partial-volume averaging (Fig. 11).

Conclusions

1. Slice thickness and level determine the appearance of a cystic lesion.
2. The CT appearances of various conditions are similar.
3. The padlock sign is not specific for any lesion.
4. The padlock sign may be caused by cavitation in a solid lesion or partial-volume averaging in a cystic lesion.

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Snakebite and the use of antivenom in southern Africa

P. A. CHRISTENSEN

Summary

Information contained in 2553 completed questionnaires on snakebite victims in southern Africa from 1953 to 1979 confirmed that most bites occur in the summer months. Of the patients, 1950 were recorded as Black and 588 as White. There was only a slight predominance of males among the Blacks, whereas White males outnumbered females by 3:1. The median age for both groups was about 20 years. The incidence was highest in Blacks aged 10-14 years and in Whites of 15-19 years; there were many bites on the hand (42%) in young White males who needlessly expose themselves by handling snakes. Most offending snakes were vipers, with puff adders heading the list, followed by night adders and burrowing adders. The ringhals, followed by the Black mamba and the spitting cobras, were the most frequently identified elapid snakes. There were 52 fatalities. Elapid snakes caused 41 of these, and vipers, presumably always the puff adder, 11. The death rate in children aged 10 years or younger (5,1%) was significantly higher than that for older persons (1,4%), and the death rate for the Black group as a whole (2,5%) was significantly higher than that for Whites (0,5%), probably owing to a longer delay in treatment and a tendency to use less serum.

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With the introduction of a pepsin-treated anti-snakebite serum in 1948, it was decided to seek information about snakebite in southern Africa and to investigate the efficacy of the new antivenom by means of questionnaires, and a questionnaire has accompanied each ampoule of serum issued by the South African Institute for Medical Research since then. Some of the serum has been used to treat animals, some patients have received more than one vial, and much has been stored 'just in case' and been

discarded when outdated but, even so, the response has been disappointing. Until the end of 1979 only about 3 300 questionnaires dealing with human beings had been returned. Furthermore, the information obtained in this way is restricted to serum-treated victims and cannot reveal the overall incidence and mortality of snakebite. Nor can the questionnaires give satisfactory information about the clinical aspects of snakebite, but they can indicate how serum is being used and also yield some epidemiological information of value, if it is accepted that they cover a random sample of snakebite victims.

Material

The questionnaires returned during the first 5 years from 1948 to 1952 were evaluated earlier,[1] and the data presented here are based on 2 553 questionnaires returned to the SAIMR from 1953 until the end of 1979 from the Republic of South Africa and the bordering territories of South West Africa, Botswana, Zimbabwe, Mozambique, Swaziland and Lesotho. About 75% of the questionnaires came from parts of the RSA itself: 42% came from Transvaal, 30% from Natal, 24% from the Cape Province and only 4% from the more thinly populated Orange Free State. About one-half of the 'foreign' questionnaires came from Zimbabwe (Rhodesia), where the serum has been readily available. The return was lower than expected from Natal, where the incidence of snakebite is assumed to be fairly high and the treatment facilities are good.[2]

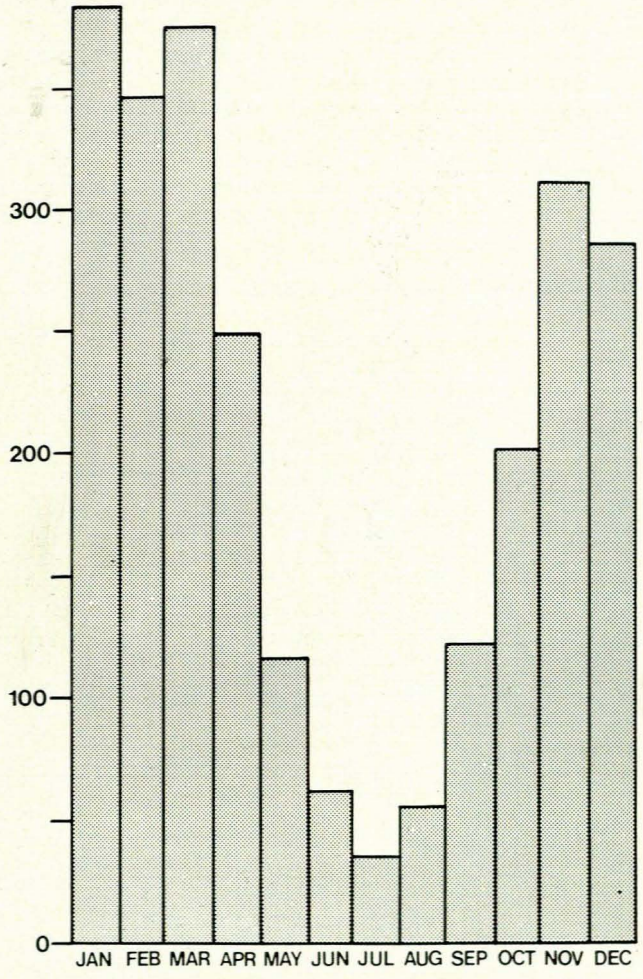

Fig. 1. Monthly incidence of serum-treated snakebite, based on reports received from 1953 to 1979, inclusive.

Results and discussion

The monthly incidence, recorded in Fig. 1, confirmed that bites are few during the cold and in most parts dry winter months of June, July and August, and reach their highest number in the warmth of January. The equally large number in the usually cooler month of March may be explained by an increased activity of snakes before hibernation, as suggested by Visser and Chapman,[2] who recorded a distinct peak for this month.

Fifteen of the 2 553 questionnaires failed to indicate the patient's race, but 1 950 involved Blacks, 1 074 males and 876 females, suggesting that the sexes in this race group are about equally exposed to snakebite, whereas in the White group of 588 the males outnumbered the females by 437 to 151. Ten Indians, 7 males and 3 females, and an uncertain number of persons of mixed race were included in the White group. The proportion of Indians would undoubtedly have been greater had there been a better response from Natal, where most of them live.

The age distribution (Fig. 2) is based on 2 412 questionnaires which gave relevant information. It is essentially the same for Blacks and Whites irrespective of sex, the median age being

Fig. 2. Age distribution of serum-treated snakebite cases according to race and sex.

about 20 years. The incidence was highest in Blacks aged 10-14 years and in Whites of 15-19 years. This slight difference in distribution may be due to the fact that many young Whites expose themselves needlessly to snakebite, resulting in many bites on the hand, as mentioned below.

The frequency with which different parts of the body were bitten was calculated from the information contained in 2 538 questionnaires and recorded in Table I. The distribution agrees with that noted in the earlier series,[1] but the 23,6% involvement of the upper limb differs somewhat from the 9,4% recorded by Visser and Chapman.[2] The reasons became apparent when the frequency with which both sexes of the two race groups were bitten on a hand was calculated with the result shown in Table II. The remarkably high figure of 42% for White males accounts for the difference between the distribution according to body site recorded here, and that observed for an exclusively Black and Indian population in Natal.[2] Many young White South African males have unfortunately a morbid interest in venomous snakes, and it is not surprising that 2 of every 3 bites involving those aged between 15 and 30 years were inflicted on a hand.

TABLE I. BODY SITE INVOLVED AS A PERCENTAGE OF 2 538 BITES

Foot	41,7	52,7	72,7	74,4
Ankle	11,0			
Lower leg	20,0			
Upper leg	1,7			
Hand	18,7	23,6		
Arm	4,9			
Trunk	0,7	2,0		
Neck and head	1,3			

TABLE II. RACE AND SEX DISTRIBUTION OF BITES ON A HAND

Race	Sex	Bites: Total	Bites: On hand	%
Black	**M**	**1 074**	**165**	**15**
	F	**876**	**108**	**12**
White	**M**	**437**	**183**	**42**
	F	**151**	**16**	**11**
Total		**2 538**	**472**	**19**

Snakes involved

The snakes responsible for the bites are listed in Table III. More than half (62%) could not be named and were entered in the table either as 'unknown' or as 'unknown viper' or 'unknown elapid', if this was indicated in the questionnaire and considered to be a reasonable assumption, but it should be remembered that the clinical findings may be similar in bites from puff adders and spitting cobras.[3]

Table III confirms not only that most offending snakes remain unidentified, but also that many victims (here 19%) suffer no harm except maybe some pain, which has been ignored for the purpose of the table. It further confirms that bites are caused mostly by vipers, mainly puff adders, followed by night adders, and that only the former endanger life. But puff adders are apparently not, as is sometimes assumed, responsible for most of the snakebite fatalities in the region. Fifty-two of the questionnaires reported the patient's death. Elapid snakes caused 41 of these fatalities, and vipers, presumably in all instances *Bitis arietans*, only 11.

Dysphagia was the only sign of neurological involvement recorded in 3 of the 36 cases of *Atractaspis* bite, and there was no indication that the presynaptic neurotoxin in *B. caudalis* venom described by Lee *et al.*[4] was active in any of the 35 bites caused by this snake. *B. atropos* venom is known to contain a heat-stable but not dialysable neurotoxin,[5] and 4 of the 9 persons bitten exhibited mild ophthalmoplegia. The local reaction was in no case as severe as that described recently in an atypical case of berg adder bite, where there were no eye disturbances.[6]

Hemachatus haemachatus, the common ringhals, is the most frequently identified elapid snake. It is not usually considered a

TABLE III. SPECIES RESPONSIBLE FOR SNAKEBITES AND THE EFFECTS

Snake	No. of bites	Effect: None*	Severe local	Systemic	Death
Unknown	**1265**	**288**	**73**		
Unknown viper	**173**	**29**	**25**	**8**	**7**
Puff adder (*Bitis arietans*)	**401**	**43**	**50**	**9**	**4**
Night adder (*Causus rhombeatus*)	**146**	**31**	**7**		
Burrowing adder (*Atractaspis bibronii*)	**36**	**3**	**3**		
Horned adder (*Bitis caudalis*)	**35**	**4**	**8**		
Berg adder (*Bitis atropos*)	**9**	**2**	**3**	**4†**	
Unknown elapid	**150**	**30**	**1**	**69**	**17**
Ringhals (*Hemachatus haemachatus*)	**141**	**27**		**14**	**1**
Black mamba (*Dendroaspis polylepis*)	**75**	**5**		**63**	**21**
Green mamba (*Dendroaspis angusticeps*)	**17**	**6**		**10**	
Spitting cobra					
Naja mossambica	**59**	**17**	**6**	**2**	**1**
Naja nigricollis nigricincta	**4**		**2**		
Cape cobra (*Naja nivea*)	**17**	**4**		**7**	
Egyptian cobra (*Naja haje*)	**5**			**5**	**1**
Garter snake (*Elapsoidea sundevallii*)	**4**				
Shield-nosed snake (*Aspidelaps scutatus*)	**1**				
Miscellaneous‡	**15**				
Total	**2553**	**489**	**178**	**191**	**52**

* Pain ignored.
† Ophthalmoplegia.
‡ Six back-fanged and one harmless species (see text).

threat to life, yet 1 patient died. This was a 7-month-old Black girl, who was gravely ill and given 40 ml of antivenom intravenously when first seen, 7 hours after being bitten.

Years ago, the mambas were considered to be variants of the same species, *Dendroaspis angusticeps*, but their venoms are quite distinct, which was known even before systematists separated the two. The green mamba (*D. angusticeps*) is not a particularly dangerous snake, but the black mamba (*D. polylepis*) most certainly is. The entries for this snake in Table III indicate a case mortality of 28% for serum-treated persons, but the information presented here goes back to 1953, and the serum issued by the SAIMR before 1962 had no effect on any mamba venom. From then on a specific mamba antivenom became available in addition to the usual polyvalent serum, and these two preparations were replaced by a single fully polyvalent antivenom in 1971. Most of those completing the questionnaires had entered the lot number of the injected serum, and it was possible to account for the type of antivenom used in the 21 fatal cases, as follows: specific serum 5 deaths/38 cases; nonspecific serum 15 deaths/35 cases; serum of doubtful specificity 1 death/2 cases. To avoid prejudice, the death in the doubtful serum group was allocated to the specific group, and the survivor to the nonspecific group, so that the ratios became 6/39 for the specific and 15/36 for the nonspecific serum. The persons receiving specific serum had obviously fared better than the others ($\chi^2 = 5{,}2$).

The local effects recorded here in cases of bites by the spitting cobra, *Naja mossambica*, were not severe, but it is known (G. H. D'Alton — personal communication) that the tissue destruction caused by bites by the South West African spitting cobra, *N. nigricollis nigricincta* (zebra snake), can be as devastating as that seen in cases of bites by the type species in Nigeria.[3]

Bites by the small snakes of the genera *Aspidelaps* and *Elapsoidea* are not considered medically important, and those recorded here produced no noteworthy signs of poisoning. One of the 15 snakes included in Table III under the heading 'Miscellaneous' was a harmless *Philothamnus semivariegatus*, identified after the patient had been treated with (the wrong) serum for a boomslang bite. The other miscellaneous snakes were the following back-fanged species (number of bites in brackets): *Dispholidus typus* (5), *Thelotornis capensis* (1), *Psammophylax* species (5), *Psammophis sibilans* (1), *Telescopus semiannulatus* (1) and *Crotaphopeltis hotamboiea* (1). Bites by the two first-named species, the boomslang and the bird snake, can be fatal, but pain and swelling were the only complaints recorded here.

Mortality

The seriousness of bites in the very young was clearly demonstrated. A total of 412 children aged 10 years or younger were bitten and 21 died, i.e. a death rate of 5,1% against 1,4% for the 2 141 older children and adults ($\chi^2 = 21{,}6$). The death rates according to race, age and sex are shown in Table IV. They do not disclose any difference between the sexes, but the death rates of 2,5% for Blacks and 0,5% for Whites are significantly different ($\chi^2 = 8{,}1$).

In discussing the different death rates in the two population groups it is important to bear in mind that the data presented here deal with cases of serum-treated snakebite, and not with snakebite in general. It is very probable that many Black victims go untreated, either because they do not seek help or because they place their trust in traditional cures, and that the death rate therefore would be high, but the difference noted here for Black and White serum-treated patients was not expected. There may or may not be racial differences in susceptibility to venom, but the material was scrutinized for other explanations.

One possible explanation could be that Blacks are especially exposed to bites by dangerous species, but the percentage frequencies for bites by such snakes in Blacks and Whites were comparable. They were, respectively, for puff adders 15,5 and 16,4, for black mambas 3,1 and 2,4, and for unknown elapid snakes 5,4 and 7,3.

One important factor in the higher mortality rate among Blacks was a longer time lapse between the bite and the initiation of serum treatment. This is illustrated by the graphs in Fig. 3, which records the cumulative percentage for each race group of patients having received serum at different times. This correlation between treatment time and case mortality for the two race groups must strengthen the belief in the preventive value of antivenom, and the even longer delay in the treatment of those of either race who died (Fig. 3) serves further to stress the urgency of serum treatment.

Antivenom treatment

To be used to best advantage the serum should be injected intravenously and the dose should be adequate. The volume used and the route of injection were noted in 2 532 questionnaires and the information has been summarized in Table V, which also shows the percentage of cases in which a doctor was in attendance. It is seen that an equal proportion, about two-thirds, of the two race groups had received medical attention, and, irrespective of race, only about 20% of the patients had received some or all of the serum intravenously. Only 25% of the doctors had used this route, and only 18 of 51 of the patients who died were given serum intravenously.

Serious snakebite poisoning requires large doses of antivenom, yet only 2% of all the patients received 50 ml or more, and 65% received only 10 ml, the contents of a single ampoule. Furthermore, the injected volume was noted in 42 of the fatal cases, and only 12 of these patients received more than 20 ml. Obviously, too little serum was too often given by the wrong route.

The difference in the percentages of Black and White victims given only 10 ml or less of antivenom is more than 3 times the standard deviation, and it must be accepted that the Blacks as a whole had not only been treated later but had also received less serum than their White counterparts. The obvious suggestion that Whites received privileged treatment is not acceptable to

TABLE IV. SNAKEBITE DEATH RATES ACCORDING TO RACE, SEX AND AGE

				Persons older than 10 years						Children aged 10 years, or younger					
	Total			Males			Females			Males			Females		
Race	Bites	Deaths	%	Bites	Deaths	%	Bites	Deaths	%	Bites	Deaths	%	Bites	Deaths	%
Black	**1961**	**49***	**2,5**	**921 (6)**	**19**	**2,1**	**730 (5)**	**10**	**1,4**	**159**	**12**	**7,5**	**151**	**8**	**5,3**
White	**592**	**3***	**0,5**	**367 (3)**	**2**	**0,5**	**123 (1)**	**0**		**73**	**1**	**1,4**	**29**	**0**	
Total	**2553†**	**52**	**2,1**	**1288**	**21**	**1,6**	**853**	**10**	**1,2**	**232**	**13**	**5,6**	**180**	**8**	**4,4**

*$\chi^2 = 8$.
† Fifteen surviving victims, whose race, sex and age were not recorded, were assumed to be older than 10 years and proportionally allocated as indicated in brackets.

TABLE V. PERCENTAGE OF PATIENTS TREATED WITH ANTIVENOM: BY A DOCTOR, INTRAVENOUSLY, AND GIVEN THE VOLUMES INDICATED

Race	No.	Treated by doctor	Serum given IV	Volume (ml) 10	20	30	40	≥ 50
Black	**1946**	**64,6**	**18,9**	**67,0***	**25,3**	**4,6**	**1,4**	**1,6**
White	**586**	**67,7**	**20,6**	**59,5***	**28,2**	**5,6**	**4,4**	**2,9**
Total	**2532**	**65,3†**	**19,3**	**65,1**	**25,9**	**4,9**	**2,2**	**2,0**

* SD = 2,2%.
† One-quarter received serum intravenously.

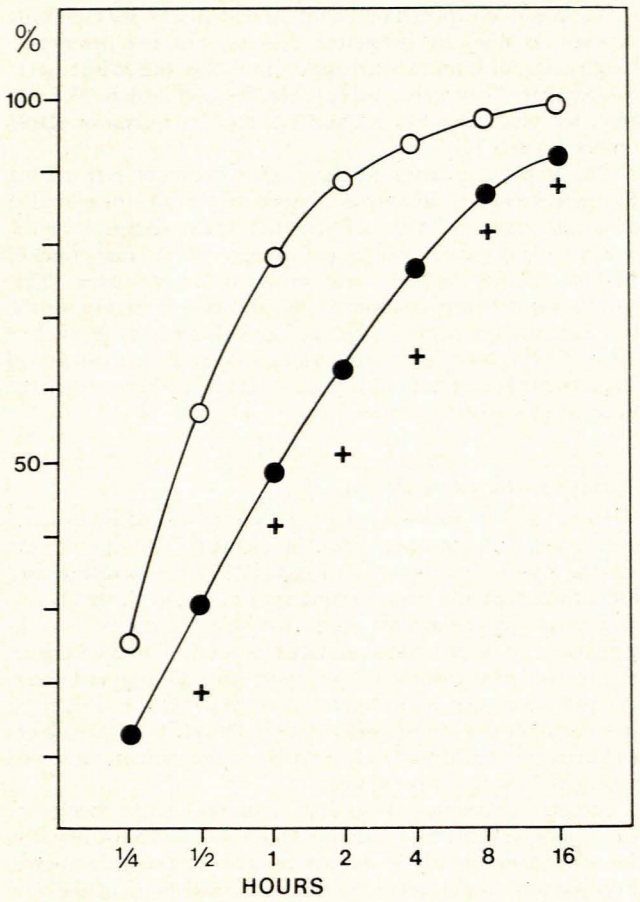

Fig. 3. Relationship between treatment time and the cumulative percentage of serum-treated snakebite victims (● Black persons, o White persons, + fatal bites, both race groups).

one well acquainted with local conditions, but the Blacks are undoubtedly at a disadvantage. Most laymen called upon to treat with serum have exaggerated ideas about its efficacy and take the contents of a single ampoule to be enough; others do not inject more because they lack confidence altogether and may fear adverse reactions. Such misconceptions, linked with transport diffculties and possible local serum shortages, are particularly likely to affect those living in remote rural areas, and they are in this country predominantly Blacks.

It saddens one to know that some of those who died might have been saved if more serum had been given in time, but it is gratifying to note that even small doses injected by a route other than the intravenous one can have a demonstrable beneficial effect, a point which has always been in doubt. In this connection it might be mentioned that it was generously suggested in many questionnaires that the serum had prevented the occurrence of any signs of poisoning, a possibility that cannot be denied, although it may be hard to believe that a little serum given under the skin is that effective.

In how many cases was the serum injection unnecessary? Few night-adder bites would justify its use, and laboratory experiments indicate that it would be useless in the treatment of bites by any of the other three small vipers listed in Table III, and in the treatment of bites by *Elapsoidea* and *Aspidelaps* species and back-fanged snakes. These snakes were responsible for 246, or 10%, of the total number of bites. Furthermore, if black mamba bites are treated as the exception, and if there are no signs of poisoning, it may possibly be right not to inject serum in cases of bite by most of the other snakes listed in Table III: 449, or 18%, of the bites belonged in this category. Thus in all about a quarter of the injections may have been given needlessly, and many more would have been superfluous if Visser and Chapman[2] were correct in believing that serum has little or no place in the treatment of puff adder bite. But this is probably an underestimation of its value, as pointed out by Warrell,[7] who has reason to maintain that local necrosis may be prevented by antivenom given within several hours of a bite.

Serum reactions

Some adverse serum reactions are to be expected occasionally. Most are of the delayed type and are usually readily overcome, but acute sensitivity reactions complicate the early treatment of snakebite, and may be fatal. Visser and Chapman[2] treated 712 patients with serum prepared at the SAIMR and recorded 5 early reactions (0,7%), which were corrected with an anti-histaminic, and cannot therefore have been very serious. Warrell[7] finds this incidence inexplicably low in view of observations made in Nigeria with antivenom of the same manufacture.[8,9] Pooling of the data recorded in the two Nigerian studies, and excluding 5 pyrogen reactions, indicates that the South African *Echis* antivenom caused immediate reactions in 13 of the 71 patients treated. To the manufacturer this is an alarmingly high incidence, which must be due to unfortunate but unknown properties of this particular antivenom, not shared by the polyvalent serum.

Information about serum reactions is requested in the questionnaires, and those examined in the present study together with 384 considered earlier, 338 from other parts of Africa, and 23 questionnaires dealing with eye injuries caused by spitting snakes and (wrongly) treated with serum given parenterally, add up to almost 3 300 cases of serum injection. An immediate serum sensitivity reaction was recorded in only 10 (0,3%) of the questionnaires, a low incidence, and in keeping with Visser and Chapman's observation.[2] A total of 81 fatalities was reported; anaphylaxis was the obvious cause of one of these and could not be absolutely excluded in two others. Chapman[2] treated 712 patients with South African antivenom without loss of life due to serum sensitivity, and it is fair to conclude that the risk of death from snakebite is greater than that attached to the injection of antivenom.

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