PARALYTIC ACCIDENTS OF ANTIRABIC TREATMENT.

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Dr. P. REMLINGER, Director of the Pasteur Institute, Morocco (Tangier), has recently published a most illuminating report [1] dealing with those rare but interesting occurrences, the paralytic accidents of antirabic treatment. According to this author, three types of paralytic phenomena may occur during or shortly after the termination of a course of antirabic treatment:—

1. Paralytic rabies caused by street virus (hydrophobia).
2. Paralytic rabies caused by fixed virus (rage de laboratoire) due to the inoculation of attenuated, though living virus; this is true rabies modified by its passage through a series of rabbits.
3. The so-called paralytic accidents of antirabic treatment, the subject of this paper, concerning the etiology of which little is known, but which are generally considered not to be due to rabies virus.

DESCRIPTION OF METHODS OF PREPARATION OF ANTIRABIC VACCINE AND OF THEIR INFLUENCE ON THE INCIDENCE OF PARALYTIC ACCIDENTS.

Before proceeding further, it might be as well to explain the essential difference between the terms "street" and "fixed" virus, which are constantly referred to throughout this article.

By street virus is meant the virus responsible for hydrophobia in man, and rabies in other animals, usually due to accidental contact with a rabid animal.

By fixed virus is meant street virus which has become modified in certain particulars as a result of its passage through a series of rabbits or other animals (goats, etc., are sometimes used).

If rabbits be inoculated intradurally with an emulsion prepared from the brain or spinal cord of an animal that has died of rabies (due to so-called street virus), and if successive inoculations from the medulla of this rabbit be made into other rabbits, and so on, the virulence is increased by the successive passages, so that a stage is reached when the infected rabbits develop rabies after an incubation period of about six days, dying within ten days.

The virulence cannot be increased beyond this point, and the virus is then called fixed virus. The pathogenic power of this virus is also changed, so that it is not likely to cause rabies if injected subcutaneously.

It is from cords containing this fixed virus that the vaccine is prepared for antirabic treatment, a variety of methods for its actual manufacture being in vogue at the various institutes.
Thus, in the original Pasteur method, still adopted in many Continental institutes and in America, the spinal cord of the rabbit, which has died from fixed virus rabies on the ninth day after inoculation, is removed and dried over caustic potash at a temperature of 23°C for varying periods, from three to twenty-one days, and from these dried cords the emulsions are made. Emulsions prepared from cords dried for a relatively short period (three to five days) still contain living though attenuated virus, and it is in the forms of treatment prepared from this source that paralytic accidents are most likely to occur. (The "Hogyes" method, in which fresh virulent cord is injected, has been responsible for a large number of paralytic accidents.)

Various methods for destroying the virus (carbolic acid, Semple), (weak formaldehyde solution, Cumming), have been adopted, and, whereas authorities are by no means unanimous that these modifications are as efficacious in the prevention of hydrophobia as the older methods, there is no gainsaying the fact that patients treated by them are far less liable to paralytic accidents. Thus, at Kasauli, five cases of paralysis occurred among 8,435 persons treated with vaccine made from dried cord; whilst after the introduction of carbolized vaccine by Major Semple, R.A.M.C., the first Director of the Pasteur Institute, Kasauli, only three similar accidents occurred among 84,844 persons treated.

Bemlinger sums up the situation as follows:—"The superiority of certain methods of attenuation (methods of Semple and Calmette), the inferiority of others (dried and diluted cords), are not sufficiently marked in the statistics to render it obligatory to adopt the former and condemn the latter methods. Paralyses only constitute one side of the question of antirabic treatment. Whatever method of vaccination is used, it is essential to begin treatment with a much attenuated virus and only gradually to reach the stage of virulent cords."

Not only is the method used in the preparation of the vaccine important, but also the intensity of treatment, which varies according to the site, severity and number of wounds inflicted by the biting animal, wounds on the face and fingers being especially dangerous and requiring a prolonged and intensive course.

With these points in view, patients (in India) are now divided into four classes, the treatment given being in a rising scale of intensity from Class 1 to Class 4. The four classes are as follows:—

Class 1.—Cases not bitten, but in which the saliva of a rabid or a suspected rabid animal has come in contact with fresh cuts or abrasions.

Class 2.—Superficial, but not extensive bites on the trunk and extremities (excluding the fingers).

Class 3.—(a) All superficial bites on the fingers. (b) Superficial, extensive bites on all parts of the body except the head and neck. (c) Deep, but not extensive bites on all parts of the body except the head and neck.

Class 4.—All deep bites on all parts of the body.
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Class 4.—(a) Deep, extensive bites on all parts of the body. (b) All bites and scratches on the head and neck.

Cases in the first two categories only are treated at the Rawalpindi District Centre, carbolized vaccine being used; the more prolonged and extensive treatment for categories 3 and 4 being carried out at Kasauli.

Pathogenesis.

The pathogenesis of the accidents of treatment is at present obscure, and, while many theories as to their causation have been advanced, no very convincing proof has yet been brought forward in support of any one of them.

Amongst other theories may be mentioned the following:

1. They are due to the injection of fixed virus.
   This theory would appear to be supported by the undoubted fact that paralytic accidents are least common, following or during those treatments in which the virus has been destroyed (Semple's carbolized vaccine, etc.), and most likely to occur when virulent virus is injected (Hogyes' method).

2. Street virus, modified and attenuated, is responsible.
   That this theory is untenable in at least some cases is shown by the following facts: (a) Negri bodies have never been found in the brains of those dying from the disease. (b) Typical cases of paralysis have been recorded by Remlinger and others in which individuals who have undergone antirabic treatment have contracted one or other of the varieties of paralytic sequelae of treatment without ever having been in contact with a rabid animal; notably, the case of a school teacher who underwent the course to reassure her pupils, some of whom had been bitten; and of a young man who also undertook the treatment to encourage his fiancée, who had been bitten by a rabid dog. Both the school teacher and the young man developed typical paralysis.

3. The condition is due to rabies "toxin" elaborated by the virus, which is not itself injected (Babes).
   An attractive hypothesis, difficult to prove or disprove in the present state of our knowledge.

4. An adventitious microbial infection, incidental to the passage rabbit, injected along with the vaccine.

5. A poison of normal nerve substance (Marinesco).

6. A filtrable neurotropic virus, other than rabies, occurring in rabbits. This theory has much to recommend it, and has been advanced to account for the somewhat similar encephalomyelitis (more often a frank encephalitis) which occasionally follows vaccination against smallpox with leporine vaccine.
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(7) A dormant infection (virus or microbial), in the individual injected, is "fanned into flames" by the vaccine.

This theory was held by the recent Ministry of Health Committee on vaccination to fit in best with the encephalomyelitis that occasionally follows vaccination.

CLINICAL VARIETIES.

Whilst admitting that the "Accidents of Treatment" fall into many groupings, Dr. Remlinger was able, from a study of 329 cases presented to the International Rabies Conference held at Paris in 1927, to classify them into three main types—

(1) Landry's Ascending Type.

The most fatal of the three, with a case mortality of thirty per cent. Onset, seventh to fourteenth day of treatment, sometimes after cessation of treatment. Sometimes preceded by a history of chill. Onset sudden. Patient rapidly develops high fever, headache, vomiting, and a dorso-lumbar backache, followed rapidly by marked paresis of the legs, which rapidly become completely paralysed, retention of urine, retention of faeces, less commonly incontinence. A few hours later intense girdle pains develop in the chest and throat, followed by darting pains and tingling in the upper limbs, which may also become completely paralysed. Pain in the muscles of the face is followed by paralysis of the muscles of the neck, face and tongue, with various bulbar troubles.

The patient either dies from involvement of the higher centres in the bulb, or recovers the use of his limbs in the reverse order to that in which they were attacked. Recovery is usually complete in a few days, but weakness may persist for a much longer period.

(2) Paralysis of Dorso-Lumbar Type.

An intermediate group with a case mortality of 5 per cent. The onset is marked by slight initial fever rapidly followed by paresis, and later, paralysis, of the legs. The toes are not moved at all, or only with the greatest difficulty; subjective sensations of tingling and numbness of the legs occur early; all forms of cutaneous sensibility are much diminished; there is a plantar extensor response; early retention of urine, requiring catheterization, and of faeces are the rule; girdle pains are complained of in the chest; there is complete absence of bulbar symptoms. After a few days recovery usually commences, and is usually complete in a few weeks. Occasionally, recovery may be delayed for several months, in which case certain trophic disturbances, such as bedsores, cystitis, etc., are liable to occur.
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In some cases, much less severe, mild paresis of the lower limbs only, or combined with slight retention of urine and faeces are the sole symptoms; these mild cases tend to occur later, following cessation of treatment, than the more severe.

(3) Neuritic Types.

Mortality, nil. The peripheral nerves only are attacked. Unilateral or bilateral facial paralysis is especially likely to occur, often accompanied by oculo-motor palsy or glosso-pharyngeal weakness. Cranial nerve paralyses may be accompanied or replaced by neuritis of the radial nerve, sciatic nerve, etc., often with slight retention of urine. These peripheral nerve paralyses usually occur after completion of treatment, occasionally many weeks after.

The characteristic features of the paralyses following antirabic treatment are, according to Remlinger:

(1) The frequency of Landry's syndrome.
(2) The common involvement of bladder and rectum.
(3) Involvement of the facial nerve in many cases.
(4) The usually favourable prognosis.

Of a series of 243 instances of paralytic accidents, there were: 39 (16 per cent) cases of Landry's paralysis; 122 (50·2 per cent) cases of dorso-lumbar paralysis; 82 (33·7 per cent) cases of neuritis, the facial nerve being involved alone or with others in 67 (82 per cent) of the neuritic cases.

The percentage of the neuritic cases is probably much higher than that given, as many mild cases would have failed to report.

(Note.—The above account of the clinical varieties with statistics is copied almost verbatim from Dr. Remlinger's report.)

Pathology.

With regard to pathological findings there is little that is characteristic. According to Babes and Marinesco, who have made a careful study of the post-mortem appearances, the chief lesions are to be found in the dorso-lumbar region of the cord, the grey and white matter being attacked alike and both transformed into a pinkish grey pulp. Various changes are found in the nerve-fibres, their axis cylinders are swollen or have actually disappeared. The vessels show various changes, none of them characteristic; and, most important of all, Negri bodies have never been found in the positions characteristic of rabies or elsewhere.

Incidence.

In an analysis by Remlinger of cases from 49 Pasteur Institutes, 329 cases of paralysis were reported out of a total of 1,164,264 individuals who received antirabic treatment, or 1 in 3,538 (0·028 per cent).
The incidence varied greatly in the various institutes, some showing an incidence as low as 1 in 25,000 to 1 in 28,000, others as high as 1 in 259 to 1 in 400 per persons treated.

**OTHER ΑΕΤΙΟLOGICAL CONSIDERATIONS.**

(1) Europeans are said to be much more commonly affected (so far as India is concerned) than the native population.

Whilst this generalization may be true, it must not be forgotten that a much larger proportion of such accidents are reported in the case of Europeans, who are usually within skilled medical reach, than in the case of Indians, most of whom belong to the poorest "villager" class, returning to their villages directly the treatment is over, far out of reach of medical aid other than that afforded by the village "hakim."

(2) Young children are rarely, and children under five apparently never, the victims of paralytic accidents.

(3) Those engaged in hard intellectual work, such as authors and the professional classes, more particularly those who lead a sedentary life, are especially liable to attack.

**PROGNOSIS AND TREATMENT.**

The prognosis in these cases is usually favourable, considering the severe nature of the initial paralysis, a global mortality of 16.85 per cent being reported (Remlinger).

In only a small percentage of cases is recovery from the initial paralysis incomplete, paraplegia and distressing contractures being met with. The patient may recover from the paralysis to die later from septicæmia, the result of bedsores or of an ascending pyelitis.

Complete recovery may, however, take as long as six months. Treatment should be palliative and symptomatic. There is a natural tendency to cure, and until we are better informed as to the causation of the disease, heroic medication of any kind is out of place and may be dangerous.

**DIFFERENTIAL DIAGNOSIS.**

In most cases the only real difficulty in diagnosis lies between the symptom-complex of accidents of treatment and true hydrophobia, caused by street or fixed virus.

The symptoms may be very similar in the two diseases, the chief points of difference being:—

(1) Hydrophobia is invariably fatal, whereas a global mortality of only 16.85 per cent occurs in the case of paralytic accidents.

(2) The incubation period of hydrophobia is less constant than that of the more severe examples of paralytic accidents, being usually thirteen to fifteen days in the latter.
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(3) Mental and bulbar symptoms, often accompanied in the terminal phases by clonic spasms, are common in hydrophobia, whilst the mind is usually clear to the end in paralytic conditions.

(4) In the case of death from hydrophobia, injection of brain emulsion (from the hippocampus major or bulb) into the brain of a rabbit or other susceptible animal, will almost invariably produce rabies in the animal injected, and in a large proportion of cases (over 90 per cent) Negri bodies (small in the case of fixed virus rabies, 0·5μ or less, large in the case of street rabies, 18-23μ) will be found in its brain, at autopsy. In many cases, also, Negri bodies will be found in smears taken shortly after death from the hippocampal region of the patient's brain.

(5) Paralytic accidents are rare in children and almost unknown in those under five years of age, while hydrophobia occurs in its due proportion at all ages.

(6) Hydrophobia is most common following severe bites (especially in the head and neck regions), whilst the severity of the bite (except in so far that the treatment is more intensive) has no effect on the incidence of the paralytic accidents, which have been known to occur when the individual has not been in contact with a rabid dog.

In spite of these differences the diagnostic difficulties between the two conditions may be great, and Remlinger stresses the fact "that the history of the case, especially with regard to the gravity of the bite, likelihood of rabies in the biting animal, time elapsed since the bite, since the beginning of treatment, since the injection of the first virulent cord (if living virus be used), are more important in coming to a decision than a consideration of the symptoms which may be so alike in the two diseases."

Comparison with Other Forms of Myelitis.

In addition to the above, acute myelitis, more usually encephalomyelitis, may be met with, during the course of, or shortly after, many of the acute specific fevers, notably smallpox, measles, chickenpox, scarlet fever, diphtheria, whooping cough, and mumps.

Turnbull and McIntosh have recently reviewed the literature dealing with myelitis following smallpox, and divide their cases into three clinical groups: (1) Those with bulbar symptoms. (2) Those with bulbar symptoms and paralysis of the limbs. (3) Those with paralysis of the limbs accompanied by paralysis of the bladder and rectum.

It is this third group which resembles, clinically at any rate, the dorso-lumbar type of paralytic accident associated with antirabic treatment.

In the forms of encephalitis and encephalomyelitis following the other acute fevers, signs of meningeal involvement are common, but the cord alone may be involved, whilst in some (notably syphilis and whooping-
cough), an acute vascular lesion, haemorrhage or thrombosis, is held to be responsible.

In the variety of myelitis following mumps, meningitis, encephalitis and polyneuritis are most commonly met with.

In addition, an idiopathic variety, known as acute disseminated myelitis, has been described, and has recently received considerable attention. The possibility of this latter variety being an aberrant form of disseminated sclerosis is still under discussion.

Of recent years special attention has been drawn to the occasional occurrence of myelitis (more commonly encephalomyelitis) following vaccination with cowpox virus against smallpox. Although the symptoms commonly found in patients suffering from the two conditions (paralytic accidents of treatment and post-vaccinal encephalitis) are not identical, they have many points of similarity.

Rabbits are usually employed to “passage” the virus in both cases. In fact, in the case of post-vaccinal encephalitis or encephalo-myelitis it is only since the introduction of this method of preparation that any considerable series of cases has occurred; and some have even suggested that rabbits should cease to be used as passage animals on this account.

### TABLE I.—SOME POINTS OF SIMILARITY AND DISSIMILARITY BETWEEN POST-VACCINAL ENCEPHALITIS AND PARALYTIC ACCIDENTS OF ANTIRABIC TREATMENT.

<table>
<thead>
<tr>
<th>Post-vaccinal Encephalitis</th>
<th>Paralytic Accidents of Antirabic Treatment</th>
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<tbody>
<tr>
<td>1. Leporine vaccine used.</td>
<td>1. Leporine vaccine.</td>
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<tr>
<td>2. Incubation period—</td>
<td>2. Incubation period—</td>
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<tr>
<td>Extremes, 9-19 days</td>
<td>Extremes, 10-30 days.</td>
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<tr>
<td>Usual, 10th-12th days.</td>
<td>Usual, 13th-15th days.</td>
</tr>
<tr>
<td>3. Most common in children.</td>
<td>3. Rare in children. (Almost unknown under 5.)</td>
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<tr>
<td>(Vaccination most commonly performed at this age-period.)</td>
<td></td>
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<tr>
<td>4. Three chief clinical types—</td>
<td>4. Three chief clinical types—</td>
</tr>
<tr>
<td>b. Brain and spinal cord.</td>
<td>b. Dorso-lumbar type.</td>
</tr>
<tr>
<td>c. Spinal cord alone.</td>
<td>c. Neuritic type. (Little meningeal involvement.)</td>
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<tr>
<td>(Little meningeal involvement.)</td>
<td></td>
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<tr>
<td>5. Convulsions, trismus, etc., common.</td>
<td>5. Convulsions and trismus rare.</td>
</tr>
<tr>
<td>6. Vesical and rectal disturbances common.</td>
<td>6. Bladder and rectal symptoms the rule even in mild cases.</td>
</tr>
<tr>
<td>7. Mortality (in one large series) 58 per cent.</td>
<td>7. Global mortality 16-85 per cent. (30 per cent in Landry’s type.)</td>
</tr>
</tbody>
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### PATHOLOGICAL FINDINGS.

| 10. Both white and grey matter affected. | 10. Ditto. |
| 11. Perivascular spaces show marked infiltration with lymphocytes, plasma cells, etc. | 11. Ditto. |

1 *Editor’s Note.—According to the report of the Ministry of Health Committee on Vaccination, encephalitis is rare in young children and more common at school age and in adolescents.
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Important points of similarity are therefore:

1. The incubation period.
2. Common involvement of bladder and rectum.
3. Complete recovery in those who survive the acute stages.
4. Rapid onset.
5. Definite relationship to vaccination.
6. Leporine vaccine commonly used in both.
7. Most marked changes in dorso-lumbar region of cord.
8. "In paralysis complicating antirabic treatment, the pathological changes appear to be identical with those of post-vaccinal encephalitis." [2]

Acting on the reasonable assumption that in both post-vaccinal encephalitis and the paralytic accidents of treatment, the symptoms are due to the same or a closely-allied neurotropic virus or toxin occurring in the rabbit, it is suggested as a working hypothesis that the slightly different symptomatology in the two diseases (i.e., essentially an encephalitis or an encephalomyelitis in the one, a myelitis or neuritis in the other), may be to some extent governed by the site of introduction of the vaccine, namely, the arm in the one, the abdominal parietes in the other.

The difference in the site of injection may also determine the slightly shorter incubation period and higher mortality in the case of post-vaccinal encephalitis.

In this connection it would be interesting to know (I can find no allusion to it in the scanty literature at my disposal) if either or both affections are more likely to occur in those who suffer from a severe local or general reaction whilst under treatment.

In the only case of paralytic sequela within my experience, the patient, who was undergoing a mild "lick" course, had an unusually severe local reaction, his abdominal wall being red, raised and "lumpy" during the antirabic course (see Case 1).

Many views are held as to the pathogenesis of encephalitis following vaccination against smallpox. The recent British Committee on vaccination, after reviewing various theories, has come to the conclusion that the activation of some neurotropic virus, previously lying dormant in the individual vaccinated, by the vaccine, best fits in with all the known facts, but admits that this view is little more than a hypothesis.

It is generally concluded that the virus or viruses responsible for encephalitis lethargica and acute anterior poliomyelitis are similar but not identical with that of post-vaccinal encephalitis. Can the accidents of antirabic treatment be ascribed to a similar activation?

All the above theories have serious and obvious defects, and the pathogenesis of the whole range of "myelitic accidents" must be held for the moment not proven.

Two cases, illustrative of some of the points raised in this article, have been admitted to the British Military Hospital, Rawalpindi, during the past few months; both are considered sufficiently uncommon to warrant brief descriptions:—
**Case 1.**—Major W. was admitted on March 16, 1930, complaining of fever, pain in the back, numbness of both legs, and difficulty in micturition; he gave the following history:

He received a seven days' "lick" course (Class 1) at the antirabic centre, Rawalpindi, completing the course on March 10. During the course a severe local reaction occurred in the abdominal parietes at the site of each injection, large, raised, red and painful lumps appearing. That this unusually severe reaction was due to personal idiosyncrasy and not due to any fault in the technique of injection or preparation of the vaccine, is proved by the fact that several other individuals, including his wife, were daily receiving injections from the same "brew" and even from the same phial without any local reaction. He had undergone a previous antirabic course in 1917 at Kasauli, which was accompanied, also, by a severe local reaction but followed by no sequelae.

The patient first felt feverish on March 13 (ten days after the first injection), since when he had had an almost continuous pyrexia in the neighbourhood of 102° to 103° F., until the day of admission. Severe pain in the dorso-lumbar region of the spine, partial numbness of both legs, and difficulty in urinating were first complained of on March 15.

When examined on the morning of admission, no objective sensory loss could be detected in either leg; and their movements appeared normal; knee- and ankle-jerks were present and both plantar responses were flexor. From March 16 to 18, increasing difficulty in micturition was noted, and by the latter date complete retention of urine had set in, requiring catheterization twice daily. By this date there was almost complete paralysis of both legs, slight voluntary movement of the toes alone being possible. The knee- and ankle-jerks were absent but the plantar responses were still flexor; there was also some degree of paresthesia of both legs, a pin prick being felt but not appreciated as such. A complete transverse band of hyperesthesia had developed, enveloping the trunk from the umbilical level above to the region of Poupart's ligament below; the merest touch with a handkerchief or cotton-wool over this area caused him acute discomfort. The Wassermann reaction was negative.

For a month there was little change in his general or local condition, and a very guarded prognosis was given.

A mild degree of cystitis developed, followed by pyelitis with a swinging hectic temperature, and his cardiac condition at times gave cause for anxiety; two superficial bed-sores also appeared but rapidly healed.

Flatulence and obstinate constipation of the spastic type were disturbing and very annoying features; the latter was best treated by an injection of ½ grain of pituitrin followed 15 minutes later by a glycerine or soap-and-water enema, this assuring a satisfactory action of the bowels every other day.

An alarming feature during the first week following admission was that the hyperæsthetic area on his trunk gradually shifted upwards, suggesting
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an upward extension of the acute process, and eventually became an acute girdle pain encircling his lower costal region and causing him much discomfort and respiratory distress.

Improvement in the local and general condition set in about a month after admission, since when slow but steady progress has been maintained. At the present time a large amount of voluntary power has been regained in both legs, more advanced in the left than the right. There is slight general spasticity of the right leg with increased knee- and ankle-jerks, ankle clonus, and definite plantar extension; slight flexor and adductor spasms have worried him recently, especially at night. The general appearance and condition of the patient are now satisfactory, and his temperature has been normal for a month or more. The hyperesthetic area on the trunk has long disappeared.

Presumably, the eventual prognosis in the case of this officer is excellent, and complete recovery is to be expected.

Further interesting points in his history are that he is inclined to intellectual pursuits, is an author of some repute, and is not interested in sport. At the time the paralysis occurred he had only been married a few months.

It is interesting to note that this officer's wife, who received an antirabic course with her husband, complained of intense neuralgic pains in the head necessitating complete rest in bed, about a week after her husband developed his paralysis; whether these pains, which she describes as more intense than any she has ever had, were due to natural anxiety at her husband's condition, or were a mild form of the neuritic type of paralytic accident, it is difficult to say. In her case the symptoms, which included a quite noticeable temporary aggravation of an old Bell's palsy, subsided in a few days.

The above is, it is presumed, a fairly typical example of the dorsolumbar type of paralytic accident occurring after antirabic treatment in a man of sedentary habit engaged in intellectual pursuits.

One wonders if such accidents are more likely to occur in those who, like Major W., suffer from an unusually severe reaction during the injections.

It is interesting to conjecture how far, if at all, the previous antirabic course he had undergone played any part in the causation of the myelitis following the second course. Whether, in fact, the paralysis was part of an anaphylactic reaction, following a "summation of allergic insults" in the shape of the daily injections.

Editors' Note.—We are indebted to Major R. Priest for further particulars of the progress of this case. Under treatment by radiant heat and massage his condition continued to improve. On December 1 it was reported that he had made very good progress and could walk very much better. Sensations to light touch and pin-prick were accurate over both legs. Joint sense and vibration sense were still impaired. Bladder and bowel control had improved. The skin over the lower third of the legs was still glossy and slightly oedematous.
Case 2.—Lance-Cpl. B. was admitted on April 11, 1930, and gave the following history:—

He was bitten by a rabid dog (Negri bodies found in dog's brain at autopsy) on the cheek on March 11, 1930. He was sent to Kasauli, where he received a full "Class 4" course of antirabic treatment.

On his way back from Kasauli, on April 9, 1930, he complained of headache and fever, and was admitted to hospital on his return with the provisional diagnosis of sandfly fever, which was prevalent at the time and which his case very much resembled.

On admission, his only complaint was of slight pain at the back of the head and neck; his temperature was 104° F.; his face suffused, eyes injected and pulse rapid; blood-slides were negative as regards malaria.

By the following morning his condition was much worse, his face was markedly flushed, there was some degree of slurring dysarthria, and he had developed a very noticeable squint and complained of diplopia. There was also slight stiffness and pain in the back of the neck.

His condition rapidly deteriorated, speech became more incoherent and rambling, he developed chronic spasms of the hands and feet, commenced to froth from the mouth, and died two days after admission, four days after the onset of symptoms, and one month after being bitten; death was preceded by a sudden rise of temperature to 105-2° F., and immediately followed a short generalized convulsion, the first he had had.

Smears taken from the hippocampal region shortly after death showed no Negri bodies.

Emulsions of hippocampal tissue were injected into the brains of two rabbits, both of which developed symptoms of rabies on the sixteenth and seventeenth days respectively after inoculation.

Negri bodies (large type) were found in smears from the hippocampal region of these rabbits.

Thus, in the case of Lance-Cpl. B., we have the absolute proof by animal inoculation that he died of hydrophobia (probably street rabies, on account of the large size of the Negri bodies), and not from a severe type of "paralytic accident."

Other points, less conclusive, in the history and clinical course of this patient suggesting the diagnosis of hydrophobia rather than "paralytic accident" were:—

(1) The biting dog was proved to have been rabid (Negri bodies found in smears from brain).

(2) The patient was bitten on the cheek, an admittedly dangerous site, followed by a high proportionate mortality from rabies.

(3) The signs and symptoms did not fit into any of the three clinical groupings described by Remlinger as characteristic of paralytic accidents of antirabic treatment.

(4) Early involvement of cranial nerves, squint and diplopia, and of
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the bulb, dysarthria, with early mental symptoms, are more characteristic of rabies than of paralytic accidents.

(5) The rapid death of the patient preceded by tetanic spasms and clonic convulsions characteristic of hydrophobia.

In conclusion, my thanks are due to Major A. C. Craighead, I.M.S, Officiating Director of the Pasteur Institute of India, Kasauli, to whose kind offices I am indebted for the loan of the monograph by Dr. Remlinger dealing with the accidents of antirabic treatment; he also materially aided my inquiry by successfully inoculating rabbits with portions of brain tissue from Lance-Cpl. B. sent to him in glycerinated solution, and afterwards demonstrated the presence of Negri bodies in smears from the brains of these rabbits. My thanks are also due to Major C. H. K. Smith M.C., R.A.M.C., D.A.D.P., Rawalpindi District, who carried out the autopsy on Lance-Cpl. B., and who also successfully inoculated rabbits with rabies virus from his brain; and last, but not least, I owe a debt of gratitude to Dr. Remlinger, Director of the Pasteur Institute, Morocco (Tangier), without the constant help of whose excellent report this article would never have been written.

REFERENCES.
