the fever ceased within the same period of time. The immediate results of the injection of the cinchonine salts were thus very satisfactory, and will be found to compare favourably, especially as regards the more serious malignant tertian variety, with those of administering quinine by various methods in the army in England as reported by J. W. W. Stephens and his colleagues.⁴

With regard to relapses the patients could not be kept in hospital long enough to furnish complete data. Four were discharged free from relapses on from the fifth to the twenty-fourth day, while in other cases after from one to four injections relapses were recorded from between the sixth to the thirty-third days, very much in the same way as in the army cases after similar quinine treatment. I did not use the cinchonine salts with the object of or expectation of preventing relapses by a few injections, but in order to rapidly control the fever and cause the parasites to disappear from the blood, after which a prolonged course of oral administration of quinine is indicated to prevent a recurrence of the fever.

The following recent case will serve to illustrate the value of preliminary intramuscular injections of cinchonine salts in cases of malaria in which oral administration cannot safely or conveniently be relied on.

A lady consulted me for what was obviously a benign tertian malaria, from which she had suffered on and off for over a year. Recently the attacks had become more frequent and severe, and she had to go to bed every other day during them; while, when she took quinine, she vomited, and it failed to control the fever. The blood showed benign tertian parasites in every field of an oil immersion lens, indicating a severe infection, not without danger if unchecked. I injected $7\frac{1}{2}$ grains of cinchonine bihydrochloride into the deltoid muscle on the day before an attack was due, and warned the patient that this could not be expected to stop completely the attack due the next day. Twenty-four hours later she felt quite well, and her blood was quite free from parasites, and, as a matter of fact, she had no attack. Three more 10-grain doses were given at daily intervals, after which she could take quinine by the mouth without trouble. On inquiry regarding the amount of discomfort after the injections, she said it was so little that she could with difficulty locate the spot the day after the injection. There was some cinchonism after the 10-grain doses.

CONCLUSION.

Cinchonine bihydrochloride in a 1 in 2 solution carefully sterilized in an autoclave is so rapidly absorbed that I consider it to be almost as quick and effective in its action in severe malaria as quinine or cinchonine salts intravenously, without the inconveniences and possible dangers of the latter, although in such rare extreme infections as that which I reported last year⁵ intravenous injections are advisable. In severe cases of malaria and during the prevalence of pernicious cases, as well as in patients who vomit orally administered quinine, I suggest the further trial of intramuscular injections of $7\frac{1}{2}$, 10, and in adult males up to 15 grains of cinchonine bihydrochloride (or in less severe cases, if preferred, the cinchonine acid hydrobromide, which produces less cinchonism) during the first few days of an attack of malaria, to rapidly control the fever and the infection, to be followed by a full course of quinine orally to prevent relapses.

REFERENCES.

¹ BRITISH MEDICAL JOURNAL, September 22nd, 1917. ² *Ind. Journ. Med. Research*, January, 1918, p. 463. ³ *Ibid.*, vol. 3, No. 1, p. 1, 1915. ⁴ *Ann. Trop. Med. and Parasit.*, vol. xi. ⁵ *Ind. Med. Gaz.*, November, 1917, p. 385.

EPIDEMIC ENCEPHALITIS.*

BY

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IN the early part of the year an epidemic appeared in this country. Its nature was from the first somewhat obscure. Those who saw the earlier cases were faced with a similar difficulty to that which faced the courtiers in the story of Cinderella. They could not find amongst the diseases of their acquaintance a foot which would go into this newly found glass slipper. A search was therefore made amongst diseases which, so to say, did not move in Court circles, and were not personally known to the seekers. Amongst these it was at first thought that the owner of the slipper had been found, and that her name was Botulism. After

many painstaking efforts to force her foot into the slipper, it was found to be impossible, and the attempt was abandoned. Botulism was not Cinderella.

The botulism episode is, however, not without its bearing on this discussion. It emphasizes the inability of early observers to recognize in this epidemic a familiar known disease, and it reminds us of a fact which cannot be entirely ignored—namely, the alteration in quantity and quality of our foodstuffs under the present war conditions.

In dealing with the clinical aspects of the epidemic I propose to give an account of my own experiences rather than to attempt a review of the epidemic as a whole from the incomplete data as yet at our disposal. From the cases I have had the privilege of seeing in other districts, and from the excellent records which have appeared in the press, I think that the epidemic as seen in Sheffield and district may be taken as a fair sample of the whole. In one respect this is not true—there was not one fatal case throughout.

Sixteen undoubted cases came under my immediate observation. One of these was under my colleague Major Yates, in the Royal Infirmary. Besides these cases I have heard of some half-dozen other undoubted cases in the area, and I am satisfied that there have been several mild or abortive cases which passed unrecognized at the time.

List of Cases.

No., Sex, Age.	Date of Onset.	Lethargy.	Asthenia.	Ophthalmoplegia.	Paralysis Seventh Nerve.	Fever.	Remarks.
1. M. 15	1918. ?Mar. 7	+	+++	+	R. L.	?	Myasthenia gravis-like.
2. F. 23	Mar. 11	++	++	++	+	++	Like tuberculous meningitis.
3. F. 26	Mar. 17	-	-	-	++	+	
4. M. 26	Mar. 17	++	++	++	+	++	Like tuberculous meningitis.
5. M. 37	Mar. 25	+++	+++	++	+	+	Polyneuritic symptoms.
6. F. 56	Mar. 21	-	++	-	+	?	Severe tremor; Parkinson mask.
7. F. 70	Mar. 30	++	+++	+	-	-	Sudden onset, like stroke.
8. F. 17	?Mar. 7	++	++	++	-	?	Meningitis suspected.
9. M. 55	Mar. 25	++	++	+	+	+	Speech hurried.
10. F. 9	Mar. 31	+++	++	+	-	++	Katatonias, type of Batten and Still.
11. F. 16	Mar. 29	+++	++	+	-	+	Slept 48 hours on end.
12. M. 50	Apr. 15	+++	++	++	+	+	Very ill whilst in hospital.
13. F. 65	Apr. 16	+++	++	++	+	++	Left ptosis for a long time.
14. M. 12	May 2	++	++	++	-	+	Considerable delirium.
15. F. 5	May 13	+++	++	++	-	++	
16. M. 44	May 1	?	+++	+	+	+	Polyneuritic symptoms.

+ , Present; ++, marked; +++, very marked; -, absent.

The cases included persons of each decade up to seventy years. Only two were under ten. The sexes were about equally represented. The epidemic began early in March, and was practically over by the end of April.

MODE OF ONSET.

This varied considerably. In most of the cases the date of onset could be fixed quite easily. In five the onset was sudden, in the rest it may be described as gradual.

SYMPTOMS AND SIGNS.

The three cardinal signs in a typical case are lethargy, general asthenia, and cranial nerve palsies. From the combination of these three a clinical picture arises which is characteristic. It is difficult to say to which of the cardinal signs the picture is due, but as a rule it is chiefly to the asthenia and lethargy. The clinical picture, as a whole, is one of immobility. In my early paper I used the expression, "lying like a log." The attitude in bed suggests an effigy on a tomb; the immobile head and face a mask. This mask-like appearance is increased where there is facial diplegia, but a definite facial palsy is not necessary to produce it.

* Contribution to a discussion at the Royal Society of Medicine on October 22nd.

One or even two of the three cardinal signs may be slight or absent. In the first case that I saw lethargy was not present to any extent. The boy had been rather drowsy at first, but when I saw him three weeks after the onset it had passed off entirely. In spite of that the general asthenia was so extreme that he gave a typical picture of immobility, and at the time reminded me of myasthenia gravis. The actual cranial palsies were only slight and limited to a slight ophthalmoplegia. When watching me or answering questions the head was kept perfectly still. He could barely move his arms or legs from the bed. He could not turn over in bed. I could not form any opinion as to what he was suffering from, and admitted him to hospital for observation.

Curiously enough, another of my early cases (No. 3) had only one of the three cardinal signs. She was a young married woman. On March 17th she had pain over the left eye, and within twenty-four hours had an almost complete facial diplegia. There was no lethargy or asthenia throughout. In a sense her face was also like a mask, but it was a different mask.

At the time that I saw these two cases there was no knowledge of an epidemic in the district and I did not in any way connect them together. Meanwhile, one of our hospital nurses (Case 2), was in my wards, suffering from what appeared to be tuberculous meningitis, and within the same week I saw, in consultation, a youth (Case 4), in whom I made the same diagnosis. Both these cases had stupor, with intervals of delirium, pyrexia, and cranial palsies. Both were wanting in various important points of diagnosis. When, however, the nurse developed facial diplegia, it struck me that it was rather extraordinary to see two facial diplegias in a week. When, further, the nurse began to recover instead of dying, and I was informed that the youth had similarly deceived our expectations, I began to suspect that there might be some connexion between all four cases. From that time onwards the cases followed one another so quickly that the existence of a local epidemic of some kind became certain.

I have recalled these early personal experiences in order to emphasize what I think is of importance—namely, that the three cardinal signs must be considered as a whole in considering the clinical entity of these cases. Any one of them may predominate, or may be slight or absent. In most cases the cranial nerve palsies form but a small part of the whole symptom-complex.

Prodromal Period.

In most cases there is a distinct interval between onset of illness and appearance of characteristic symptoms. This varies rather widely. It is often difficult to fix exactly. In most cases one must be content with "a short time" or "a few days." I have referred to the four cases in which the onset was sudden, and the prodromal period less than one day. In three cases with rather long prodromal periods the patients were under observation throughout.

Of these the hospital nurse (Case 2) began with severe neuralgia of the right side of the face on March 11th. On the 19th there was vertigo and tinnitus on the left. On the 21st some stiffness of the right face, but no paralysis was noticed. She remained on duty until the 22nd, when the vertigo and tinnitus became much more severe. Temperature 103.2°. She was admitted to the ward as a patient. Lethargy was noticed on the 23rd and meningitis suspected on the 25th. Actual facial diplegia was not noticed until the 26th, but from her own account it is evident that it was beginning on the 21st. Her prodromal period was not less than ten days.

Case 4 called at his doctor's surgery on March 17th, complaining of vertigo. He received some medicine and was able to go about until the 27th, when he became drowsy and took to bed. Delirium began on the night of the 29th, and on the next day he had unequal pupils, strabismus, right facial palsy. Temperature 101°. Here again the prodromal period was not less than ten days.

Similar variations in the length of the prodromal period have, I believe, been observed in the epidemic as a whole. Speaking generally, it is usually a few days, say one to four or five.

The onset of the cardinal signs may be sudden, but it is usually ingravescent. This is particularly true of the cranial palsies. They take some time to develop fully, and

may vary in amount and extent from day to day. The general asthenia tends to make the facial palsies less obvious than usual.

Ophthalmoplegias.

Strabismus of variable extent, inequality of pupils, and nystagmus were commonly present. The last named was sometimes of an irregular inco-ordinate kind.

Fever.

This was noted in many cases. Possibly it was present in all, but of that there is no proof. Sometimes it was severe and prolonged, as in Case 2, the nurse, in whom it lasted till the fifth week. On the other hand, in Case 5, a soldier who was in hospital for gas poisoning when the encephalitis began, it never rose above 99°, and that only on the first and eighth days. Yet his attack was severe and very prolonged.

Lethargy.

This was, perhaps, the most striking feature of most of the cases. It was not true sleep. Often the patient was surprisingly awake to what was going on. Many patients who were stuporose all day became delirious at night, returning to stupor next day. Sometimes the delirium was of a foolish kind, and suggested hysteria. One of my cases, a girl aged 9, showed the type of stupor, with katonias, described by Batten and Still.

Tremors.

In one case (No. 6), a woman aged 56, tremors with asthenia were the chief symptoms. When I saw her the tremor had almost gone, after lasting several days. Only the asthenia, and the face like that of paralysis agitans, remained.

Speech.

During the lethargic period this was often affected. The words were imperfectly muttered, as though it were too much trouble to speak at all. In one case (No. 9), a middle-aged man, there was a distinct hurried or festinating speech, such as is sometimes observed in cases of paralysis agitans.

RESULTS.

All the sixteen cases are still alive. Within the last few days I have seen most of them, and where that has been impossible I have received reports from their medical men. I have divided them into three groups, as follows:

Group A. Recovery complete and absolute. Seven cases (Nos. 1, 3, 4, 6, 12, 13, 14).

Group B. Recovery practically complete. Some slight trace of illness left behind. Six cases (Nos. 2, 8, 9, 10, 11, 15).

Group C. Recovery incomplete. Three cases (Nos. 5, 7, 16).

Group B.

Case 2.—The nurse is back at duty. She feels perfectly well. When tired there is slight left facial paresis, with unequal pupils and slight diplopia.

Case 8.—This woman is at work. Slight photophobia and headache.

Case 9.—This man is at work. His wife says he has changed mentally since his illness. I have reason to think that this dates from an earlier period.

Case 10.—This child is at school again. She has developed a nervous shrugging of the shoulders. Osler has, I think, observed a similar sequela.

Case 11.—A girl of 16. The doctor reports that there is marked ptosis of the right eye, some strabismus and diplopia.

Case 15.—This little child of 5 is in excellent health. She still has a very slight strabismus. The doctor who sends me the report underlines "very."

Group C.

These three cases are, after six months, still far from complete recovery. It is worth noting that in each case the present incapacity is due to the trunk and limb muscles generally, and that the cranial palsies have disappeared completely, or almost so.

Case 7.—The old lady of 70 began rather suddenly, with general weakness and tingling in the hands and feet. Lethargy was pronounced, ocular palsies slight. Her doctor reports that she is still very weak, and that she tires very quickly after the slightest muscular effort. The eye symptoms have disappeared.

Case 5.—The soldier with gas poisoning. From the first his asthenia was profound, lethargy deep and prolonged, cranial palsies multiple and bilateral. From the first he complained of numbness and tingling in the hands and feet, and in the

latter there was impaired sensation up to the knees. His knee-jerks were absent. His progress has been very slow, and at the present time he is unable to sit up without support. There is foot-drop on both sides; some oedema of the feet. He is improving daily; the knee-jerks have returned. All his trunk and leg muscles react to faradism. Above the waist he has recovered completely.

Case 16 (Major Yates's case).—This patient is at present in a very similar condition to the preceding. He still has some nystagmus, right facial paresis. There is weakness in both arms, the left more than the right, but it does not prevent him from using them fairly well. He can walk by himself, but there is double foot-drop and a stepping gait. The knee jerks are still absent, and the muscles are generally flabby and wasted. The muscles below the knees do not respond to faradism, with the exception of the peronei in the right leg.

I do not propose to refer in detail to the results of a very large number of examinations of cerebro-spinal fluids, bloods, excreta, etc., which were made by my colleague Professor Douglas from these cases. But I should like to express my thanks for his valued help on the pathological side, and for his extensive investigations of various food-stuffs during the Botuline era.

CONCLUSIONS.

The points for discussion may be summed up as follows: Is this, or is it not, an epidemic of poliomyelitis? If it is not, then it may be either an entirely new disease, or one that until recent times has not been observed in epidemic form.

The clinical resemblances, such as there are, between these cases and poliomyelitis were recognized from the first. In my paper I called attention to the absence of cases of "localized limb paralysis commonly seen in acute poliomyelitis."

The clinical differences, however, have been so recently stated by Kinnier Wilson with such clearness that I need not do more than mention them. Lethargy and asthenia, so severe and prolonged in most of the cases of encephalitis, are not recorded as occurring in typical cases of poliomyelitis, either sporadic or epidemic.

I cannot think that any one would consider the term "sleeping sickness" descriptive of poliomyelitis in general and yet it would not be an inappropriate name for this epidemic. In fact, if one takes away the palsies from these cases of encephalitis, little remains which is common to them and to poliomyelitis. Even the palsies present striking differences in the two diseases in their mode of onset, situation, and results.

In poliomyelitis the onset tends to be rapid and maximal; the regions affected are usually those innervated from the spinal cord; the distribution often unilateral. They frequently leave permanent residual effects of greater or less extent in the area first attacked. In the recent epidemic, the paralyzes are typically of gradual ingravescent onset; they almost always affect regions innervated by cranial nerves, and are often bilateral. So far as our evidence goes at present, they usually leave no permanent residual effects in the area first affected.

We know that many nerve poisons, for example, diphtheria, *B. botulinus*, lead, alcohol, etc., show a peculiar predilection for certain particular parts of the nervous system. In these cases of epidemic encephalitis there seems to be such a definite selective action at work.

It has been said that the commonly held view of poliomyelitis as essentially a cord disease is based too much on sporadic cases, and that in its epidemic form it is characterized by the multififormity of sites affected. This line of argument rather accentuates the clinical difference between poliomyelitis and the cases in the recent epidemic. The latter were notable for the uniformity of the sites affected.

As regards the possibility of this being an old disease which has only recently been recorded in epidemic form I have no proofs to bring forward. We know that a similar epidemic appeared about the same time of year in 1917, as recorded by Economo in Vienna, and that Netter has recorded similar cases in Paris. Possibly, in the course of time, records of sporadic cases of a similar type may be found stowed away in the pigeon-holes of other disease—poliomyelitis, influenza, etc.—where they have been regarded as abnormal or exceptional varieties. Such a line of inquiry seems worth consideration. Not until these alternatives have been set aside can we speak of it as a new disease; and, in any case, the final decision must rest with the pathologist.

QUININE PROPHYLAXIS IN MALARIA.

BY

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THE importance of arriving at some definite conclusion as to the usefulness, or otherwise, of routine quinine giving as a preventive of malaria requires no emphasizing. The strictures of Dr. Treadgold, in the *BRITISH MEDICAL JOURNAL* of May 11th, 1918, are thoroughly deserved.

The opportunity of making controlled experiments on the subject must have occurred times innumerable, yet the whole literature of the subject provides hardly anything worth the name of statistics. The reason for this is, partly, the apathy which attacks Europeans in the tropics, and from which medical men are by no means immune. It is, however, much more largely to be accounted for by the preconceptions and prejudices of those in official positions who are able to impose their will over large areas; the effect is very often to inhibit useful research activity. It is one of the dangers that will have to be guarded against in the schemes now proposed to establish a national medical service.

The following experiment will be better understood if I give a short explanation of the two categories of rubber estate labour with which it deals.

Tappers are those coolies whose work consists in paring off the thin shaving of bark from the tree, and so starting the flow of latex from which rubber is produced. His day's work consists in carrying out this operation on from 300 to 400 trees each morning, and collecting the resultant latex in two buckets which he then carries to the factory. It is light work, and the tapper is usually finished for the day by noon, having begun from 5.30 to 6 a.m. Weeders are all the rest of the labour force; the name explains their chief duty, but they are used in many other ways, for road and drain making, pruning, attending to pests, diseases, etc. On the whole their work is harder, and their day is from 6 a.m. till 2 p.m. Among the weeders there is a much higher proportion of women and children, and elderly coolies, than amongst tappers, who are chiefly men from 15 to 40 years of age.

It will be noted that the tapping force is that on which the daily output directly depends, and its maintenance at full strength is one of the chief cares of the management. The experiment here recorded owed its inception to the anxiety of the manager to keep his tapping force up to strength.

It was decided to give each tapper 10 gr. of quinine each day at the factory. It was given when the man brought in his latex pails, so that the giving was rigorously performed. This was maintained for the whole of the year 1917, and during that same period no prophylactic quinine was issued to the weeding coolies.

The following figures give the result stated in percentage per month admissions to hospital:

	Tappers.	Weeders.
Average monthly labour force of each class	140.83	252.03
Average number of cases per month admitted to hospital for malaria	20.16 = 14.31% per month	33.25 = 13.19% per month.

When it is remembered that the tappers are of superior physique, better paid and have lighter work, it must be admitted that all the valuable quinine which has been swallowed by this large number of men during a whole year gave no protection whatsoever against malaria.

This report entirely relates to Indian Tamils, both tappers and weeders being of this race, and both living under identical conditions and in the same sets of buildings.

THE alliance between Columbia University and the Presbyterian Hospital, New York, which was made in 1911 with the object of forming a great medical centre in that city, has been dissolved. The university was unable to get the money needed for its share of the buildings and rejected the plans proposed as the condition of an endowment offered by the Rockefeller Foundation.