closely allied contaminants from such a compound is difficult.

Since, however, the hitherto known alkaloids of ergot are quantitatively indistinguishable from one another by these pharmacological tests, the above experiments differentiate ergometrine from all of them, including the recently described alkaloids ergoclavine and sensibamine, which have been examined in Sir Henry Dale's laboratory. A paper by Dr. Vartiainen, dealing with ergoclavine and sensibamine, is now in the Press. The identity of the action of ergoclavine with that of ergotoxine has already been reported by Kreitmair.³

General Considerations

The isolation of ergometrine, without doubt the constituent to which ergot owes its introduction into medicine, will enable accurate decisions to be reached with regard to the relative values of the other clinically active alkaloids. It is already evident that ergometrine is the essential constituent of extracts intended for oral administration, while ergotoxine, ergotamine, ergoclavine, and sensibamine are relatively unimportant, and may possibly even be undesirable in such preparations. One of us (C. M.) proposes later to deal fully with the question of the usefulness of the various ergot alkaloids in obstetrical practice.

The pronouncement of the Ergot Subcommittee of the Pharmacopoeia Commission that "ergotoxine is to be regarded as the active principle for which ergot preparations are administered, and all preparations should be standardized from this point of view," appeared to be reasonable at the time when it was made, but the discovery of ergometrine destroys its scientific basis and proves it to be misleading. It seems clear that ergometrine should now be regarded as the most important active principle in any ergot preparation intended for oral administration, and the problem of the preparation of suitable extracts will have to be re-examined in the light of the knowledge now available. Whether, for example, the *B.P.* 1932 liquid extract, designed to contain the total alkaloids of the drug, is more or less desirable in clinical practice than some form of watery extract so made as to contain predominantly the ergometrine and very little of the ergotoxine-ergotamine group should be considered.

The question of standardization, too, will require examination. The colour reaction upon which the official method of assay is based is common to all the known alkaloids of ergot, including ergometrine. As at present applied it measures only the total alkaloidal content of an extract, and gives no information regarding the amount of the most important therapeutical constituent. With a knowledge of the properties of ergometrine it may be possible to devise a method for its determination in official preparations, and so put the assay of ergot extracts on a satisfactory basis in relation to their clinical efficacy.

Since this paper was written a communication by Koff⁴ has come to our notice. Using the same clinical method of testing as we have employed, he has demonstrated that the substance responsible for the characteristic clinical effect of orally administered ergot preparations is associated with the alkaloidal fraction, and he states that removal of ergotoxine from the latter does not impair its activity. These exploratory experiments are in accord with our identification of ergometrine as the active alkaloid concerned.

REFERENCES

- ¹ Moir: *British Medical Journal*, 1932, i, 1119.
- ² Idem: *Edinburgh Med. Journ.*, 1934, xli; and *Trans. Edin. Obstet. Soc.*, 93.
- ³ Kreitmair: *Arch. Exper. Path. Pharm.*, 1934, clxxvi, 171.
- ⁴ Koff: *Surg., Gynecol. and Obstet.*, 1935, lx, 190.

ENCEPHALOMYELITIS SIMULATING DIPHThERIC PARALYSIS

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The clinical picture of diphtheritic paralysis is an extremely characteristic one, and as a general rule few other conditions are likely to be mistaken for it. The main reason for this is that paralysis of the palate is hardly ever met with in childhood from any other cause. It is, however, decidedly rare, as has been emphasized by J. D. Rolleston,¹ for neuritis to occur in any but severe and well-established cases of diphtheria, though the work of Walshe in Egypt suggested that under certain conditions it might do so.

We considered that the cases here described were worth recording, because they suggest that diphtheritic paralysis is at the present moment being simulated by a disorder of an entirely different nature, and that a new significance should be attached to some of its most typical symptoms. The fact that these cases were all seen in one hospital during the course of eight weeks makes it likely that they are not rare, and it may well be that palatal paralysis may become of some value as a sign of the disorder which we believe these children to have suffered.

Case Records

The four cases were admitted to the Victoria Hospital for Children during December, 1934, and January, 1935. All of them were seen by one of us (N. H.), and all pathological examinations were carried out by the other (S. W.).

CASE I

Girl, aged 12. Admitted on December 12th, 1934, under the care of one of us (S. W.). History: slight sore throat ten days previously, followed on the next day by weakness of both legs. A throat swab had been taken and found negative to K.L.B. She was removed to a fever hospital, but further swabs were negative, and she was therefore discharged.

On admission, when seen by one of us (S. W.), she was bright and happy, sitting comfortably in bed and looking well. Cranial nerves and arms were normal; abdominal reflexes present. Both the lower limbs were very weak, but there was no localized paralysis or wasting. The knee- and ankle-jerks were absent. Muscle tone was poor. Plantar reflexes were not obtained. There was no gross sensory change.

On December 14th she had improved somewhat, but was unable to support her weight. Movements of the legs were weak and ataxic. On the 18th she could stand, and on January 3rd she walked unsteadily. On the 7th she walked quite well; the knee-jerks were just obtainable and the plantar flexor. Muscle tone was still poor. On discharge to a convalescent home, on January 24th, she had completely recovered, and both knee- and ankle-jerks were easily obtained.

CASE II

Boy, aged 3 years and 10 months. Admitted on January 11th under the care of Dr. Firth. History: a month previously he had suffered from a sore throat; a swab taken at another hospital had been negative. His elder brother had been diagnosed as suffering from diphtheria on December 28th, 1934. During the last few weeks the child's legs had gradually become weaker.

On admission there was considerable weakness of the legs, with absent knee-jerks and sluggish ankle-jerks. There was no movement of the palate on phonation. All other cranial nerves were normal. He was rather drowsy, and talked little; the voice was somewhat nasal. Faucial and nasal swabs were negative to K.L.B. Lumbar puncture showed the fluid was under considerable pressure. It was clear, and contained a few lymphocytes only. Chlorides: 772.

¹ *Proc. Roy. Soc. Med.*, 1934, xxvii, 1421.

During the next few days his condition steadily deteriorated. On the 17th he was irritable and drowsy, knee-jerks and ankle-jerks were absent, and there was general hypotonia. On the 18th he was more apathetic, and lay with open eyes. Rhonchi were present in both lungs. Lumbar puncture was again performed; the pressure was not so great as before. The fluid was not examined owing to contamination with blood. On January 20th the signs in the lungs became more advanced, and death occurred.

Post-mortem Examination.—All the internal organs appeared perfectly normal, with the exception of the lungs, each of which showed patches of consolidation at the base. Death was due to bronchopneumonia. The brain and spinal cord did not present any abnormal appearance. The meninges were healthy; the blood vessels were not engorged. On section the cerebral and cerebellar substance was normal in colour and texture. Microscopical sections were prepared from the cerebral cortex, optic thalamus, caudate nucleus, the region of the corpora quadrigemina, the pons, cerebellum, cervical cord, and upper and lower dorsal and lumbar cord. The sections were stained with haematoxylin and eosin, and with polychrome methylene-blue. At only two sites were any abnormal microscopical appearances found. In the optic thalamus and in the anterior horns of the cord in the lower dorsal region some, but not all, of the ganglion cells were swollen and globular. These, and a few others which retained their normal shape, showed tigrolysis and eccentric nuclei. The degree of damage was difficult to assess: a few of the cells may have been damaged beyond recovery, but the majority did not appear to have reached such an advanced stage, and might have completely recovered had no further injury been inflicted. Nowhere was any vascular lesion discovered. All the vessels were patent and the perivascular spaces free. There was no perivascular infiltration or oedema or haemorrhage. Nowhere was any evidence of inflammation detected. Not even in the neighbourhood of the damaged ganglion cells was there any congestion or leucocytic infiltration. The appearances were entirely different from those of encephalitis, polio-encephalitis, and poliomyelitis; but it seems beyond doubt that the incidence of encephalomyelitis is to some extent upon the ganglion cells of the base of the brain and the spinal cord, as well as on the axis cylinders. Professor Turnbull described similar changes in his account of one of Hunter and Brain's cases (*Lancet*, 1929, i, 224).

CASE III

Boy, aged 6. Admitted on December 3rd, 1934, under the care of Dr. Firth. For the past fortnight he had "seemed very weak and staggered about." He had also complained of pains in his arms and legs. There was no history of sore throat.

On admission the boy was able to walk, but reluctant to do so; he took a wide base and showed considerable ataxia. There was no movement of the palate; otherwise cranial nerves were normal. The legs were hypotonic. The knee-jerks were only occasionally obtained, and then with difficulty; the ankle-jerks were absent. There was no muscular wasting and no gross sensory change. Throat swabs taken on admission and on two subsequent occasions were negative to K.L.B. The electrical reactions of the muscles were normal, and he was treated with faradism.

He made a slow but steady improvement; power in the limbs increased and the palate showed some movement. On discharge on January 31st the knee-jerks were still very sluggish, and the ankle-jerks were not obtained. Throughout stay in hospital this case bore a very strong resemblance to diphtheritic paralysis, and he was regarded as suffering from it.

CASE IV

Girl, aged 3. Admitted under the care of one of us (N. H.) on January 31st, 1935. History: About the middle of December, 1934, she had had a severe cold and a sore throat. There had been a copious nasal discharge, with occasional streaks of blood, which persisted for several weeks. For the past three weeks she had had some difficulty in swallowing fluids, which had occasionally returned through the nose. The voice had changed recently. During the last week it had been noticed that she did not seem to close the right eye fully.

On admission the child was restless and irritable; she was able to walk, but the legs were weak and hypotonic. There was complete paralysis of the palate. In addition to this, there was right-sided facial weakness of the supranuclear

type. The weakness was slight in the orbicularis palpebrarum and considerable in voluntary movements of the lower facial muscles; emotional movements were not affected to any extent. The tongue was protruded slightly to the right, but could be deviated to the left by a conscious effort. In the lower limbs all deep reflexes were absent. Power was not greatly impaired. There were no signs of pyramidal involvement in the legs, and no loss of sensation could be detected. Owing to the length of time since the onset of the illness lumbar puncture was not performed. Faucial and nasal swabs were negative to K.L.B.

The child's condition steadily improved. The facial weakness cleared up quickly and the gait became almost normal. When last examined (January 15th) facial weakness was only just appreciable; the tongue still deviated slightly; there was nothing abnormal in the legs, except the absence of deep reflexes.

Commentary

The feature common to all four cases was absence of deep reflexes in the legs, without gross paralysis or muscular wasting—a breach of the reflex arc which was probably mainly on the afferent side. Palatal paralysis was observed in three of them, and three gave a history of affections of the throat. In one case, however, the only history of sore throat was immediately preceding the onset of the paralysis. In one case there had been a history of diphtheria in the same house after the onset of the child's symptoms.

The first three cases were clinically compatible with diphtheritic neuritis, though it is to be noted that none of them showed defect of ocular movements. The fourth combined the usual signs of diphtheritic neuritis (with the exception noted above) with others which were incompatible with it—that is, multiple lesions of the upper motor neurone, which were slight and transitory. With the exception of the child who died of bronchopneumonia, all made good progress while in hospital, and their physical signs cleared up partially or completely.

The fourth child bore a strong clinical resemblance to many cases of mild spontaneous encephalomyelitis which have been observed recently, except in that palatal paralysis has not, as far as we know, been observed hitherto in this disorder. The few post-mortem changes which were found in Case II were quite compatible with it, and to some extent suggestive of it. We believe that most probably all the four patients suffered from this affection, and we suggest that further experience may show that palatal paralysis is a symptom of a type of encephalomyelitis which is prevalent at the moment. It is to be regretted that none of these children was seen in an early stage of illness, as confirmatory evidence might have been obtained from a cellular reaction in the cerebro-spinal fluid.

We are indebted to Dr. Douglas Firth for his kind permission to examine and record his two cases.

The forty-second post-graduate course of the Faculty of Medicine of the University of Paris will be held at Easter from April 1st to 13th, and will cover the medical and hydrological treatment of vascular, renal, rheumatic, and endocrine-sympathetic disturbances in the light of recent clinical and laboratory discoveries. It will be followed by the forty-third course from May 6th to 20th, which will deal with similar conditions affecting the alimentary canal, the liver, and nutrition. Each course will be held at the Necker Hospital. From May 18th to 20th there will be a special hydrological course at Vichy. The two Paris courses will include lectures, of which summaries will be provided for those who attend, and clinical demonstrations. A certificate will be supplied to members at the end of each course. Detailed programmes and other information may be obtained on application to the Laboratory of Hydrology and Climatological Therapeutics of the Paris Faculty of Medicine. The fee for each course is 200 francs, or 300 for both.