in action, the combination ought to be of service in the treatment of trypanosomiasis in man.

REFERENCES.

- ¹ J. E. Dutton, Thompson-Yates Laboratories Report, 1902, vol. iv, Part II, p. 455. ² Royal Society, Reports of the Sleeping Sickness Commission, 1903. ³ Laveran, *Ann. Inst. Pasteur*, t. xvi, p. 792. ⁴ E. J. Moore, *Lancet*, 1904, vol. ii, p. 15. ⁵ C. R. Chichester, *Journ. Trop. Med.*, 1904, vol. viii, p. 195. ⁶ Broden, *Bull. de la Soc. d'Etudes Colon.*, Février, 1904. ⁷ P. Ehrlich and K. Shiga, *Berl. klin. Woch.*, March 4th and April 4th, 1904. ⁸ H. Wendelstadt, *Deut. med. Woch.*, 1904, xxx, p. 1711. ⁹ H. W. Thomas and S. F. Linton, *Lancet*, 1904, vol. i, No. 20, p. 1336.

A CASE OF CEREBRO-SPINAL MENINGITIS : LUMBAR PUNCTURE: RECOVERY.

By JAMES DONELAN, M.B.,

Chevalier of the Crown of Italy; Physician, Italian Hospital, London.

IN view of the increasingly-frequent occurrence during the last few weeks of cases of cerebro-spinal meningitis the following instance seems worthy of record, especially in view of the immediate improvement that followed the surgical intervention.

The patient, an English architect, aged 50, who had met with reverses of fortune, was found comatose in his lodgings on October 25th, 1904, and removed to the Holborn Infirmary, where in an interval of consciousness he was able to communicate with his friends, and was transferred to the Italian Hospital on October 26th. From his own subsequent account he was in his usual good health until October 23rd, when he was seized with shivering, violent headache, and severe pain in his neck and back. He became unconscious, and must have been in that state for nearly two days before he was found. In the hospital he lay semicomatose, but roused when spoken to and complained of intense occipital pain extending along his neck and spine. The neck was rigidly extended owing to clonic spasm of the muscles, and there was some opisthotonos, though not in a marked degree. Kernig's sign was easily elicited both in the sitting and recumbent postures. The conjunctivae were suffused and the pupils widely dilated, but reacted to light and for accommodation. There was a petechial rash all over the body, especially on the lower extremities, while the skin generally was hyperaesthetic. He was perspiring moderately, and the sweat had the peculiar odour usually associated with typhus. There was some coryza, with muco-purulent discharge from the nostrils; no bacteriological examination of this secretion was, however, made. The bowels were constipated and the breath extremely foul, partly owing, no doubt, to the neglected state of his teeth and the existence of an extensive pyorrhoea alveolaris. The temperature on admission was 100.3° F. and the pulse 108. The blood count showed leucocytosis, 26,000 per c.mm. There were no pulmonary or other symptoms than those already given.

In view of the coryza, the case was at first regarded as one of influenzal cerebro-spinal meningitis; still, the possibility of it being a sporadic example of epidemic cerebro-spinal meningitis was considered, and the patient was isolated. He was given a calomel purge followed by an enema, and ice was applied to the head and along the spine. A mixture containing 20 minims of the ammoniated tincture of quinine and 5 minims of glycerine of carbolic acid in cinnamon water was given every four hours, and 20 gr. of bromide of potassium on the first two evenings. He was put on milk diet without alcohol.

On the 28th—that is, the fifth day from the seizure and within forty-eight hours of his admission—the leucocytosis having advanced to 36,000, the temperature to 101° F., and no improvement in the other symptoms having taken place, but, on the contrary, a slight degree of aphasia having presented itself, it was decided to employ the lumbar puncture. This was performed under strict aseptic conditions by Mr. G. Lenthal Cheatle, surgeon to the hospital. The fluid, about 4 oz., rushed out with considerable force, and was slightly turbid when held to the light. Its withdrawal appeared to have an immediately beneficial effect, as the patient became quite conscious in a few hours, and the pain, muscular spasm, and aphasia gradually disappeared in about two days. On the day following the puncture the temperature fell to 99°, and he said he felt quite well but weak. Next day the temperature rose to 101.6°, but fell after the bowels were relieved by an enema.

In view of the great improvement in his condition it was

not thought necessary to repeat the lumbar puncture; the cutaneous hyperaesthesia, however, persisted, but disappeared at the end of the first week. He made an uninterrupted recovery in two weeks. He remained in the hospital, however, until he could be sent to a convalescent home, and was transferred to the care of the dental surgeon, Mr. McKay, who successfully treated his pyorrhoea.

A portion of the fluid removed through the lumbar puncture was examined by Mr. Cheatle at King's College, and was found to contain numerous polynuclear leucocytes, some of which enclosed the diplococcus intracellularis. A similar result was obtained from the specimen examined in the hospital laboratory by Dr. V. Pereira, Resident Medical Officer. It is perhaps to be regretted that a bacteriological examination was not made of the coryzal discharge or of the thick spongy incrustation on the teeth, as it may have thrown some light on the path of invasion.

I think it may be fairly claimed that in this case its remarkably favourable termination was due to the early employment of the lumbar puncture. The therapeutic value of this procedure has been much disputed, but it has always had a strong advocate in Netter, who advises early and repeated lumbar puncture. The value of any remedy is proverbially enhanced by its speedy employment. *Cito, bene, et recte*, and the withdrawal of the fluid at the earliest possible moment seems to be imperatively called for in cerebro-spinal meningitis. Properly carried out it can do no harm, while it is of the utmost importance to relieve tension on such essentially vital parts of the human organism. By so doing one has the best chance of avoiding pus formation, which will almost inevitably take place if the patient continues to live and the tension is not relieved.

Those who, like the writer, remember something of the Dublin epidemics of twenty years ago and over will recall the fact that patients who died on the second or third day had their meninges only congested, and the subarachnoid space more or less distended with a clear or slightly milky fluid. On the other hand, in those who did not die for a week or more the fluid varied from a yellowish creamy exudate to green pus. Had Quincke's suggestion been in vogue in those days and the tension been relieved by early lumbar puncture it is probable there would have been far fewer opportunities of viewing the last two stages of the inflammation *post mortem*. It may, perhaps, be said that patients have recovered without lumbar puncture, and that many died after several weeks in whom after death the fluid was found clear or nearly so. This, however, seems to point rather to greater resistance to probably a small initial dose of the diplococcus or one of less intense virulence. It cannot possibly be thought that the disease is in any sense self-limited, or that the adoption of measures to relieve tension as early as possible is other than imperatively necessary.

BIBLIOGRAPHY.

- Weichselbaum, *Fortschritte d. Med.*, 1887, v, pp. 573 to 620. Rolleston and Allingham, *Lancet*, 1899, i, p. 889. Osler, article in *Encyclopaedia Medica*. Osler, *Lancet*, 1899, i, p. 1699. Jaeger, *Deut. med. Woch.*, 1899, July 20th. Saundby, On the Etiology of Non-Tuberculous Meningitis, *Brit. Med. Rev.*, 1900, xlviii, 269 to 281. Netter, Meningites Aiguës Non-Tuberculeuses, *Rev. Mens. d. Maladies de l'Enfance*, Paris, 1900, xviii. Netter, article in *Twentieth Century Practice*. Cipollina e Maragliano, Del valore diagnostico del Segno di Kernig, *Bollet. del R. Accad. Med. Genoa*, 1900, xv, 17. V. Griffo, Cyto-diagnostic des Meningites, *Comptes Rendus Soc. de Biol.*, Paris, 1901, lili, 11 to 12. H. Thursfield, Post-basis Meningitis, *Lancet*, 1901, i, 459. Landau, Ein Fall von Meningitis Siderans, *Munch. med. Woch.*, 1901, xlviii, 442. J. Fim, Kernig's Sign Associated with Remarkable and Unusual Symptoms, *BRITISH MEDICAL JOURNAL*, 1901, 396.

THE SODIUM SALTS OF THE COUMARIC ACIDS AS THERAPEUTIC AGENTS.

By GILBERT T. MORGAN, D.Sc.LOND., F.I.C.,

Royal College of Science, South Kensington.

THE hypodermic application of sodium cinnamate in aqueous solutions (hetol) or dissolved in glycerine, as recommended by the author in the *Lancet*, July 12th, 1902, p. 66, still continues to receive considerable attention, and among the more recent developments of the treatment based on the use of this therapeutic agent may be mentioned the serum obtained by the firm of Kalle and Co., of Biebrich-am-Rhein, from tuberculous horses after repeated injections of the cinnamate (German patent No. 147,470).

Another point of interest bearing on the connexion between the chemical structure of cinnamic acid and its physiological action is the discovery that phenylpropionic acid

in the form of an aqueous solution of its sodium salt (thermiol) also has a marked action in the development of leucocytosis, and can likewise be applied to the treatment of tuberculosis. Both these acids contain an unsaturated carbon chain attached to a benzene nucleus, the former acid having a double linking and the latter a treble bond, as indicated by the following formulae:

Since these substances are far more active physiologically than benzoic acid, $\text{C}_6\text{H}_5\text{CO}_2\text{H}$, which does not contain the unsaturated group, one may assume as a working hypothesis that this action is in some way connected with the presence in the molecule of the double or treble linking, this junction being known to be a point of great chemical reactivity.

In the course of a series of clinical investigations carried out by Dr. Lovell Drage with the glycerinum sodii cinnamatis a demand arose for a drug having a more pronounced action, and the author was thereby led to consider in what way the physiological activity of cinnamic acid might be enhanced.

The employment of benzene derivatives as therapeutic agents has amply demonstrated the fact that the presence of an amino- (NH_2) or a hydroxy- (OH) group in the aromatic nucleus greatly increases the physiological action of the parent hydrocarbon, and it therefore seemed likely that the use of a substituted cinnamic acid containing one of these groups might bring about the desired effect. Since the employment of amino-compounds of the antifebrin type is often attended by unpleasant secondary effects, the author was in the first place led to employ a hydroxy-derivative, and to recommend the use of sodium ortho-coumarate, a substance having the structure of cinnamic acid, with a hydroxyl (OH) substituent:

A glance at the foregoing formulae will show that ortho-coumaric acid is likewise somewhat similar in constitution to salicylic acid, these two acids standing in the same relationship to each other that cinnamic acid does to benzoic acid. This likeness to salicylic acid was also a determining factor in the choice of ortho-coumaric acid for medicinal purposes, bearing in mind the beneficial action of the salicylates in certain pathological conditions.

For hypodermic injections the author prepares a 22 per cent. aqueous solution of the sodium ortho-coumarate containing a slight excess of the free ortho-coumaric acid. The dichroic solution is quite limpid and stable, and as the salt is extremely soluble in cold water, even a higher concentration may be employed if necessary.

In all the cases hitherto studied the solution has induced a rapid physiological action, the leucocytosis being well marked and resembling that effected by the cinnamate.

Experiments have also been instituted on the sodium salts of the two isomeric coumaric acids with the view of ascertaining whether the change in the relative positions of the active groups brings about any appreciable differences in their physiological effect.

Sodium para-coumarate, prepared by the Perkin-Fittig synthesis from para-hydroxybenzaldehyde, is a much less soluble salt than the ortho-compound and accordingly an 8 per cent. aqueous solution was employed. The results obtained with equivalent quantities seemed to show that the action was of a similar nature, but rather less intense than that produced by the ortho-salt.

Sodium meta-coumarate which was employed in 20 per cent. aqueous solution had a very marked physiological action, being apparently even more active than the ortho-compound. The meta-coumaric acid required for this preparation was produced synthetically from meta-nitrobenzaldehyde.

From a chemical point of view the action of the meta-

acid is of special interest. It is well known that benzenoid ortho-compounds and para-compounds in general often resemble one another in their chemical and physical properties, whereas they frequently both differ markedly from their isomerides of the meta-series. In the case of the ortho-coumaric and para-coumaric acids the groups (OH) and ($\text{CH:CH.CO}_2\text{H}$) are in sympathetic positions, and might accordingly be supposed to act conjointly, but in the meta-compound these groups are in apathetic positions with respect to each other, so that the meta-acid might be expected to exhibit the dual properties of a phenol and a cinnamic acid, each substituent producing its physiological effect to some extent independently.

The three isomeric coumaric acids are certainly physiologically active, but it must be left for further experiments to decide which of these is likely to prove to be the most serviceable therapeutic agent. The investigation is being extended to other compounds of a similar type, and it is hoped that it may become possible to correlate the physiological action of these substances with their chemical constitution (compare Drage, BRITISH MEDICAL JOURNAL, April 29th, 1905).

TWO CASES OF UNILATERAL CONVULSIONS AND PARALYSIS IN YOUNG SUBJECTS ASSOCIATED WITH EXUDATIVE ERYTHEMA.

By T. K. MONRO, M.A., M.D., F.F.P.S.G.,

Physician to the Glasgow Royal Infirmary and Professor of Medicine in St. Mungo's College, Glasgow.

THE following cases deserve to be recorded, both because the combination of the non-embolic hemiplegia of early life with exudative erythema seems to have escaped notice by previous writers, and because all new facts ought to be published which may help to throw a sidelight on the pathology of that variety of paralysis. The remarks on the cases will come in most appropriately after the latter have been described.

CASE I.

Severe Gastro-enteritis in a Boy of 12 years; Right-sided Convulsions and Hemiplegia with Aphasia; Bedsores; Striae Atrophicæ; Erythema Nodosum; Conjunctivitis; Alveolar Inflammation.

J. T., sent by Dr. McCallum of Tarbolton, was brought to me on October 2nd. As it was afterwards found that he was making very slow progress at home, it was arranged that he should come into my wards in the Royal Infirmary, and he was admitted on November 3rd. Dr. McCallum informed me that the boy had, on several occasions, had rheumatism in subacute form, and that he was an inveterate cigarette smoker. He never, however, had scarlet fever, measles, whooping-cough, or, indeed—apart from rheumatism—any illness until June 12th, 1903. On that day, possibly as a result of prolonged bathing, he began to suffer from pain and stiffness in his joints. These symptoms subsided after a few days, and were followed, in the course of a few days more, by severe pain, vomiting, and diarrhoea, which continued for a fortnight and caused such wasting and exhaustion that the patient became almost comatose. At this time convulsions began. They involved the right angle of the mouth, the right arm, and the right leg simultaneously, and were strictly confined to the one side. The attacks recurred frequently throughout the first two days, and then became fewer and less severe, until they finally ceased, a fortnight after they began. The patient was insensible for about five days, and spoke no word for three weeks from the time when the convulsions began. During this period the evacuations were passed into the bed, a bed sore developed in the sacral region, and linear atrophy of the skin took place in numerous areas about the knees and thighs. So far as was observed, the temperature was subnormal throughout. A trace of albumen was recognizable in the urine for a time after the convulsions set in, but not before. There was no headache or vomiting. The right hemiplegia and aphasia dated from the convulsive seizures. Sensation was not affected. Before his illness patient was in the fifth standard at school, and was regarded as a smart boy.

Three weeks after the convulsions began, he first uttered the words "aye, aye," and since then he has regained a considerable amount of language. Even at the time of his original visit, on October 2nd, his mother stated that he understood everything that he heard, and this is certainly the case at present. He cannot, however, name all the letters of the alphabet, though he recognizes some words. His writing of letters is very bad, particularly when he uses the right hand.

There is still some paresis of the right side of the face. The power of the right upper limb is still defective, the dynamometer registering scarcely 5 kilos with the right hand, as against 13 with the left. There is slight contracture in the flexors of the elbow. There is some wasting of the muscles of the right forearm, and this atrophy is associated with slight tenderness, but no wasting is recognizable in the hand. The leg is scarcely affected, so that the gait is normal. The two calves are alike in girth.

The heart, lungs and urine are normal. Ophthalmoscopic examination reveals no morbid change in the fundi. Apart from the tenderness