With the same dose of chloral as chloralamide a very different effect was obtained (Fig. 4). The operation could not be commenced until after an hour had passed, and then the animal was not so deeply under as was the case with chloral hydrate. The pressure in this case was little below the normal level when the carotid was joined to the manometer, and although it subsequently fell, it rose again and was well maintained $6\frac{1}{2}$ hours after the drug had been given. The explanation of so marked a difference is undoubtedly to be found mainly in the much slower absorption of chloralamide as compared with chloral hydrate; but this is not the whole explanation. In order to obtain a result with chloral hydrate more comparable to that of chloralamide, 0.5 gram per kg. was injected into the stomach of a rabbit, but as this proved insufficient another 0.5 gram per kg. was given half an hour later. Although the animal did not seem to be more deeply narcotised than the chloralamide rabbit, the blood pressure was distinctly lower. Furthermore, in this case the respiration soon began to fail, and the animal was allowed to die.

In order to overcome the variability in absorption intravenous medication was resorted to. The tracings are shown in Figs. 5 and 6. The pressure in the chloral hydrate tracing, although of a larger rabbit, is seen to be lower than that of the chloralamide one, but the subsequent fall is not proportionately greater. The respiration in the case of the chloral hydrate is seen to be more markedly influenced than with chloralamide, and this effect seems to be constant. It bears out the view that first suggested the use of chloralamide as a hypnotic, that the amide radical would probably act as a respiratory stimulant.

We therefore conclude that although when injected rapidly into the circulation, chloralamide and chloral hydrate produce the same initial fall of blood pressure when given by the stomach or in any way in which the circulation is slowly reached, the depressing effects of chloralamide on the heart and blood vessels are less marked than those of chloral hydrate. The respiration also is not influenced to the same extent. The formamide group cannot therefore be inactive; it plays a part in counteracting the depressant action of the molecule quite apart from its influence in diminishing the solubility.

From what I have said with regard to the vascular effects and the solubility of chloralamide, we shall not be surprised to find that its toxicity is less than that of chloral hydrate. A dose of the latter corresponding to 1 gram per kg. body-weight of anhydrous chloral is invariably fatal to rabbits within twenty-four hours, but these animals always recover from a similar dose given as chloralamide.

NOTE AND REFERENCES.

¹ I speak of these as my own experiments, but I ought to mention that they were performed for me by my late assistant, Mr. C. R. Marshall, now Professor of Materia Medica in the University of St. Andrews, who has rendered me much valuable help in the preparation of these lectures. ² *Recherches Expér. sur la Puissance Toxiques des Alcoôls*, 1899; *Bull. Gén. de Ther.*, September 30th, 1884, p. 251. ³ *Compt. Rendus*, cxxiv, p. 829, 1897. ⁴ *Zeit. f. Phys. Chem.*, ix. ⁵ *Zeit. f. klin. Med.*, xxiv, 374, 1894. ⁶ *Arch. f. Exp. Path. u. Pharm.*, Band xlii, 1899. ⁷ Paschakis and Obermayer, *Pharmacol. Unter. ueber Ketone u. Acetozime*, Leipzig, 1892. ⁸ *Arch. di Farm. e Terap.*, iv, 12, 1896. ⁹ *Arch. de Pharmacodynamie*, I, p. 1, 1895. ¹⁰ *Arch. f. Exp. Path. u. Pharm.*, xxi, 137. ¹¹ *Journ. of Physiol.*, xxii, p. 38.

SEQUEL TO A CASE OF ACUTE TETANUS TREATED BY INTRACEREBRAL INJECTIONS OF ANTITOXIN.

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As the method of administering the tetanus antitoxin by intracerebral injection is at present on its trial, I communicated the above case, which appeared recently in this JOURNAL¹ at the earliest opportunity, when convalescence was apparently well established. Unfortunately, after the disappearance of all symptoms of tetanus, the patient again became seriously ill and died on May 5th, more than eight weeks after the last intracerebral injection. The results of the *post-mortem* examination leave but little doubt that the fatal termination of the case was directly due to the particular method of injection employed. The following are the clinical notes of his fatal illness.

April 6th, 1899, the patient was obviously gaining strength, and was able to be out of bed a short time daily.

April 8th. He complained of headache, chiefly frontal, with vomiting. The temperature was normal. As it was considered that these symptoms were perhaps due to rather obstinate constipation, repeated doses of calomel, gr. iij, followed by seidlitz power, were given. In eight days there was complete relief of the headache and vomiting (April 16th). From this date he improved steadily for nine days, when he appeared again to be convalescent, and was able to be out of bed on two occasions.

On April 28th the headache and vomiting recurred, and on the 29th there was a slight rigor.

On May 3rd he seemed better. On the 4th he became for a short time collapsed and unconscious; on partially recovering he shrieked several times. There was for a brief interval spasm of the right arm and hand, and of the left leg and foot, with opisthotonos. Common sensation in the right leg varied remarkably; at one time pinching produced no response, at another the leg was withdrawn. Twitching of left fingers, hand, and arm, and of the left leg, occurred, on one occasion. Double optic neuritis was observed. A consultation was held to decide as to the advisability of operation; this was negatived. The boy remained quiet, and for the most part unconscious, and died at 8 A.M. on May 5th, 1899.

The following is an account of the *post-mortem* examination of the head made by Dr. Joshua Ferguson:

"The calvarium was easily separated. In the region of the frontal eminence, on each side, the tracks of the recent punctures, now occluded by healthy granulation tissue, were noted. On the external aspect of the dura mater, at a site corresponding on each side with the punctures, a few minute buds of healthy granulation tissue were observed, otherwise the membrane was normal in appearance. On its deep surface, it was slightly adherent throughout to the surface of the cerebrum; no visible exudation was present, the subdural space being notably dry. On the right side, at the site of puncture, the dura was attached to the brain by a minute tuft of healthy organised adhesions. On the left side it was free.

"The convexity of the hemispheres presented a normal appearance over the posterior and middle lobes. The frontal lobes on both sides, but more markedly on the left, showed distinct bulging, with flattening of the convolutions and partial obliteration of the sulci. On section of the brain substance abscess cavities were revealed on each side, situated deeply in the centre of each lobe. That on the left was about the size of a hen's egg and contained about 2 oz. of thick yellow pus. This cavity was in communication with the left lateral ventricle, into which pus had passed; it also communicated through the great transverse fissure with the cerebellar fossæ. The cerebellum was bathed in pus, which had also passed into the perimedullary spaces. The abscess cavity proper was surrounded by a zone of deeply congested cerebral tissue, which could be traced posteriorly backwards and downwards toward the internal capsule. On the right side the abscess cavity was about half the size of that on the left, and its walls showed less evidence of acute inflammation. It contained about 1 oz. of pus. The brain seemed otherwise normal.

"*Bacteriological Examination of the Pus.*—Cover-glass specimens of the pus were stained with gentian violet and Loeffler's blue, and examined microscopically. Cocci were present in considerable numbers, singly and in groups. No chain cocci, diplococci, or bacilli were seen. Gelatine plates and tubes were inoculated and kept at room temperature. Agar-agar capsules and tubes were also inoculated and kept at 37° C. In every case pure cultures were obtained possessing the characteristic appearances of *staphylococcus pyogenes aureus*."

REMARKS.

Every care was taken to secure asepsis while drilling the skull and injecting the serum; the drill and needle were always boiled before use, and as sepsis was not at any time observed clinically, it seems to me difficult to believe that the source of infection was introduced with the serum; but whatever may have been the exciting cause of sepsis, damage to the brain from the repeated injections would unquestionably predispose to it. In this case repeated injections were risked on account of the excessive severity of the symptoms; probably, however, it is unsafe to venture a repetition of the process in any one case.

REFERENCE.

¹ April 15th, 1899, p. 895.

THE Caledonian and the North British Railway Companies have each issued a *Guide and Handbook* of seaside, farmhouse, and country lodgings, boarding-houses and hotels on their several systems. Each volume is provided with a map and is illustrated. Both are published by Messrs. Fairbairn, 10A, George Street, Edinburgh, and will be sent post free for 5d.