out. In no instance have we noted any slowing of the pulse. In only three cases have we seen any unpleasant effects upon the circulation following an operation or examination under eucaïne, and in each of these there was sufficient reason to otherwise account for the trouble without attributing it to the drug. We have judged it best to relate briefly these three occurrences.

CASE XV.—J. W., aged 25, male, has been suffering from chronic suppurative otitis media for twenty years. A warm 8 per cent. solution of eucaïne was introduced into both ears and retained for ten minutes to allow of an examination with the probe. The anaesthesia was complete, but on touching a small granulation on the inner wall of the left tympanum the patient fell from the chair in a swoon, his face becoming livid, his lips blue, and his pulse small and irregular. He revived as soon as he was laid upon the floor, and then broke out into a profuse cold sweat. Later he stated that with the swooning sensation he experienced one of intense nausea, and thought he would vomit. He had experienced similar sensations before, while syringing the left ear. The unpleasant symptoms in this case were undoubtedly due to the combined cardiac and gastric aural reflexes.

CASE XVI.—A. C., aged 70, female, suffering from a large new growth in the right nostril. A piece was removed for microscopic examination after being swabbed with 8 per cent. eucaïne. The pulse was 72, and remained unchanged in rate or character throughout. The local anaesthesia was complete. After the operation the patient complained of feeling faint. She had, however, been suffering from attacks of profuse epistaxis for five months, and was also the subject of aortic insufficiency.

CASE XXV.—A. A., aged 28, female.¹ A nasal polypus was removed from this patient under an 8 per cent. solution of eucaïne. Immediately after the operation she became faint, but did not lose consciousness. Pulse 108. This patient was in a very low state of health, having active syphilitic ulceration of the soft palate, and active tuberculous deposit at both apices, while she was also suffering from anaemia and debility consequent upon a recent miscarriage.

b. Local.—Our observations upon the local effects of eucaïne on the circulation are at present incomplete, several points having arisen requiring further consideration. We have not, however, found it to cause hyperaemia of the turbinate bodies, in fact in several cases it has induced slight ischaemia. In two cases it has been noted that a turbinate body which before the application was in contact with the septum was not touching it in any part when anaesthesia was established. Of course, any ischaemia observed was not to be compared to that caused by cocaine. This is a point upon which we hope to make further observations in the future. In no case has there been the hæmorrhage after an operation which so often forms an unpleasant feature of cocaine anaesthesia. We would here wish to mention an apparent effect upon the salivary secretion. In the first case (xxvii), in which an 8 per cent. solution was used to anaesthetise the uvula for laryngoscopy, a considerable increase of saliva was noted. On another occasion, when a 2 per cent. solution was used, this feature was absent. A similar increased salivation was noted in Case xxxii under the 2 per cent. In Case xxix (posterior rhinoscopy) the saliva was not increased. Out of four tonsillotomies, in only one was increased salivation noted. This is an important point for decision by future observation, as its upholding will establish another point of difference from cocaine (which decreases the salivary secretion), and may detract from the usefulness of eucaïne in operations upon the oral cavity.

4. After-effects.—With the exception of Cases xv, xvi, and xxv, we have not noted a single instance of what might be construed as an unpleasant after-effect; the 3 excepted cases have been already related and explained. We have alluded to 6 cases as having experienced the effects of cocaine. In the first of these (Case iii) a female, aged 55, the use of cocaine for the removal of a nasal spur had caused such alarming syncope as to necessitate the employment of ether and amyl nitrite. This case has since been three times under eucaïne without the least discomfort. The 5 remaining cases all declared that, whilst cocaine had caused unpleasant sensations in the mouth and throat (variously described as "contracting," "freezing," and "numbing"), lasting for some hours, eucaïne on the contrary rendered them anaesthetic to the operation without causing any after-effect greater than (in one case) an unpleasant taste lasting half an hour.

Several points remain for further experience to decide, but we consider that our results so far justify us in continuing the investigation. Eucaïne cannot, however, wholly replace cocaine, since the effect of the latter in reducing the size of the turbinate bodies gives it a value as an aid to diagnosis which eucaïne does not appear to possess.

THE TREATMENT OF PHTHISIS BY GUAIACOLATE OF PIPERIDINE.

BY

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THE success which has attended the treatment of phthisis by creasote and its derivatives, especially in the earlier stages, has led us to try a newly synthesised body, piperidine guaiacolate, which not only contains an antiseptic moiety, but also a constituent which possesses a nervine and vascular tonic action. In order to put our results with this substance as succinctly as possible, we shall divide this paper into three parts—(I) Chemistry, (II) Pharmacology, (III) Therapeutics.

I. CHEMISTRY.

Piperidine guaiacolate has been prepared by Dr. Schidrowitz, and for its chemistry we are indebted to him.¹ It is a compound formed by the action of piperidine on guaiacol in a suitable solvent, such as benzol or petroleic ether, and it must be regarded as a guaiacolate of piperidine, having the formula $C_8H_{11}NC_7H_5O_2$. Its exact chemical composition is still under investigation. It crystallises in prismatic needles or plates. It is soluble to the extent of 3.5 per cent. in water; it is also easily soluble in most organic solvents. It melts at 79.81° C. It is decomposed into its constituents by mineral acids and alkalis. The chemical property which from a pharmaceutical standpoint is most worthy of note is the relative solubility of this salt. When the insolubility of the carbonate of guaiacol is borne in mind this becomes emphasised. The solubility is such that gr. x can be administered in an ounce draught of simple water, or if the specific gravity of the medium be raised by the addition of a little glycerine or mucilage, a dose of gr. xx to xxx can be given.

II. PHARMACOLOGY.

The pharmacology of the guaiacolate of piperidine resolves itself into the pharmacology of guaiacol and piperidine, for it is into these substances that the salt is decomposed, probably not in the acid medium of the stomach, but in the alkaline one of the duodenum. The reason for this assumption is that large doses—3j—can be given without the slightest eructation of guaiacol. The action of guaiacol is too well known to be discussed here; it acts in the intestine as an antiseptic, in the structures through which it is excreted, for example, the respiratory mucous membrane, it acts also as an antiseptic. We will only give here a brief summary of the pharmacology of piperidine, as this subject forms part of a research to be published elsewhere by one of us (Tunncliffe) in conjunction with Dr. Lauder Brunton. When hydrochlorate of piperidine, suitably diluted, is injected into the circulation in doses of 0.05 g. pro kilo body weight, the heart is slowed and the vessels contracted, a considerable rise of blood pressure taking place. When injected under the skin in doses of from 1 to 2 cg. pro kilo, an increase in reflex excitability occurs, so that if the drug is pushed convulsions may develop. Thus in suitable doses piperidine must be regarded as a cardio-vascular tonic and spinal stimulant.

III. THERAPEUTICS.

During the last three months an inquiry as to the value of piperidine guaiacolate in the treatment of pulmonary tuberculosis has been carried out at the City of London Hospital for Diseases of the Chest. The patients to whom the drug was given were subjected to close observation, and the effects of the medicine were from time to time noted. In all, 14 cases were placed under observation, of which 8 were out-patients and 6 in-patients. The duration of the observations varied, but as a general statement it may be said that six weeks was the average. In order to test efficiently the value of the drug, cases were chosen more or less haphazard, some being early

¹ *Proc. Laryng. Soc. Lond.*, vol. iv, I. p. 14

¹ The manufacturers are Messrs. Joseph Turner and Co., Queensferry, Flintshire

cases in which improvement might be expected under appropriate treatment, others being more advanced, while yet others were in such a stage as to make it improbable that much good from any form of treatment would accrue. In all cases the dose to begin with was fixed at 5 gr. three times a day, and this was gradually increased until 20, and in one case 25 gr. were given for a dose. So far as could be gathered from questioning patients and personal observation, no unpleasant effects were noticed. All of them stated that the medicine had agreed with them. Pains were taken to ascertain if the drugs produced any gastric or intestinal irritation, but in no case could it be determined that the processes of digestion were in any way interfered with by the medicine. We think this worthy of special stress, because experience has so often taught us that when other derivatives of creasote, such as crude guaiacol, are given over a lengthened period, their use has to be discontinued from time to time, owing to the gastric and intestinal disturbances caused by them. But in these cases no such untoward event happened.

With regard to the varied symptoms of phthisis it is difficult to say with certainty that the guaiacolate of piperidine had any distinct effect upon them. For in all cases of phthisis it is so frequently found that improved hygienic conditions (good food, rest and attention), such as residence in a hospital affords, play a large part in the restoration of the patient's health. This much may, however, be said that in many instances the cough appreciably improved while the treatment was in progress. The temperature was in no case affected adversely by the drug; in most cases it receded to normal. The appetite, for the most part, was maintained, and very often patients expressed the belief that the medicine improved it; indeed, in some cases it seemed that it had a markedly good effect upon the appetite. Some patients gained in weight while the treatment was going on, and in two instances it was thought that more flesh was put on than would have been the case had ordinary remedies been tried. The expectoration in most cases decreased while the drug was being taken. Among the out-patients especially there was a general improvement in strength and vitality. In the case of out-patients it must be remembered that improved hygienic conditions do not come into operation to the advantage of the patient as they do in in-patient practice.

Coming now to speak of the changes noted in the physical signs, it must be admitted that discussion of this subject is full of difficulty, for it so often happens that, although considerable improvement takes place in the general condition of the patient, yet no marked change occurs in the physical signs. Some of the cases (out-patients) whose condition was found to be improving were examined week by week to see if any change could be found in the physical signs. Consolidation and excavation were of course unaffected, but in not a few instances the lungs were noticed to become drier with less moist crepitant *râles*. This change was attributed to the fact that the area of simple inflammation around the tuberculous infiltration itself had passed from an active to a more quiescent condition. It must be admitted, however, that the same improvement in physical signs could not be seen in most of the cases under treatment as in-patients. Two out-patients considered that the medicine relieved their dyspnoea, and, to judge from the lung signs, which were under the treatment improving rapidly, it might very well be the case.

GENERAL CONCLUSIONS.

In stating the effects of any new drug upon a given disease, the physician must always guard himself against "over enthusiasm," so often it happens that a new medicine has been reputed to be successful in some affection, and upon fuller trial its effects are found to be trifling, or even *nil*. Of piperidine guaiacolate it may be generally stated:

1. That experience has shown that it is a perfectly safe drug in doses from 5 to 30 gr. three times a day.
2. That it causes no unpleasant effects.
3. That it is exceedingly well borne by the stomach, and in this respect it is equal to any other derivative of creasote.
4. That patients while under its influence improved in appetite and general strength.

TWO CASES OF TRIGEMINAL NEURALGIA AND TRISMUS ASSOCIATED WITH LOSS OF TEETH.

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Two patients lately under my care have presented some points of interests which it may be worth while shortly to record. Both were suffering from severe facial neuralgia, starting from and radiating about the temporo-maxillary articulation. For the sake of clearness it will be well to consider the general characteristics of both cases.

1. *Deficiency in Number of Teeth.*—Both patients were entirely edentulous as regards the upper jaw, and had but three or four teeth in the incisor region of the lower jaw; of the latter, in one case, one, and in the other, two, were carious, and were extracted by me. I would point out, as an important factor in causation, the absence of grinding teeth in both cases.

2. *The Nature of the Attacks of Pain.*—The pain in both cases was paroxysmal, the patients keeping the mouth closed in order to avoid excitation of pain and spasm. In the patient whose case is first described removal of her artificial teeth had this effect. Attempts at mastication had a like result in Case II, but after wide separation of the jaws, while the patient was anaesthetised for the purpose of examination, as recorded later, the symptoms were materially reduced in intensity, for some days, occurring only under greatly increased stimulation.

3. *The area of the distribution of the pain* in each case presented marked features of similarity. It was partly local, but radiated over the area supplied by the auriculo-temporal nerve, that is to say, over a skin area including the front of the ear and temple, the point of maximum intensity lying in front of the ear along the upper border of the zygomatic process. In one case the pain appeared to be more extensive, though in a minor degree of severity, as it was clearly described as passing down the alveolar margins of both jaws unilaterally. Attention is called to the fact that branches of the auriculo-temporal nerve supply sensory filaments to the temporo-maxillary articulation.

4. *The Condition of Facial Spasm and Trismus.*—This facial spasm was probably of a reflex irritative character, comparable to that seen in other conditions, as, for instance, in tic douloureux, where twitching of the eyelids becomes a marked symptom. It may be noted that the fifth and seventh cranial nerves are intimately associated; their cerebral origins are in close proximity, and communicating branches pass between the nerves themselves and between their exit from the skull and their termination, where the intercommunication is extensive. The jaw muscles were thrown into tetanic spasm during the attacks of pain, producing a temporary trismus.

5. *The atrophic condition of the masseters and temporal muscles* was due to disuse in both cases, and was so marked as to produce sinking in of the temporal region. This is no uncommon senile condition.

6. *Injection of the conjunctiva and increase of lachrymation* was noted in both cases on the affected side, and is also probably a reflex condition, due to the same causes as that already described above when referring to facial spasm.

7. *Absence of disease of the temporo-maxillary joint* was ascertained under an anaesthetic.

8. *No obvious disease of the teeth, gums, or alveoli* was detected sufficient to account for the symptoms.

CASE I.—A lady of about 60 years of age, looking older, owing probably to her extremely neurotic temperament, was sent to me by Dr. Ferrier. She had suffered for some considerable time—it was impossible to ascertain quite how long—from neuralgia referred generally to the alveolar borders of the jaws, and particularly to the left side of the face and head. On inspection of the mouth it was found that the patient was almost edentulous, having but four remaining teeth, all in the lower jaw (first premolars and the canines of either side). She was wearing dentures which fitted badly. Further investigation elicited the fact that she never voluntarily withdrew more than one of the plates from the mouth, as shortly after removal of both plates spasm of the facial muscles ensued, and violent neuralgic pains, radiating from the temporo-maxillary joint as a focus, occurred. The upper plate was a complete denture bearing incisor, canine, premolar, and molar teeth; the lower similar in character, but having spaces in lieu of teeth where her own remained. It may be mentioned that the necks—the junction of tooth and gum—of these remaining teeth were highly sensitive to mechanical irritation or changes