What I do wish to say is that nothing has impressed me so forcibly or so favourably as the qualities of many of the younger surgeons on whom has rested the chief stress of the actual treatment of the wounded. There is not a medical school in Great Britain or Ireland that has not reason to be proud of its pupils, and the work of the surgeons has been equalled and supported by that of their pathological colleagues.

I do not know whether to admire most the energy and keenness which has enabled the staffs to work days and nights without adequate rest, or the technical surgical skill in complicated and difficult operations on the abdomen and limbs alike which has been so conspicuous a quality in so many officers. The care and zeal and patience displayed in efforts to save limbs and life have been no less praiseworthy than operative dexterity.

The Royal College of Surgeons has influenced and guided the teaching of surgery during many years, and all who have shared in this responsibility may feel a legitimate pride in the splendid work now being done by its pupils. "The tree is known by its fruit," and the future of British surgery is in safe keeping, for many of the best brains and hands which guide its course are yet young.

ON THE BACTERICIDAL EFFECT EXERTED
IN VITRO BY ETHYLHYDROCUPREINE
(OPTOCHIN) HYDROCHLORIDE ON
A FÆCAL STREPTOCOCCUS
OBTAINED FROM WOUNDS.

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(A Report to the Medical Research Committee.)

Ethylhydrocupreine (optochin) is an alkaloid derived from cuprea bark. It is the methyl derivative of quinine which has been reduced by the introduction of a further two hydrogen groups. Its chemical formula is $C_{21}H_{29}N_2O_2$. The hydrochloride is a white crystalline powder, is soluble 1 in 10 of water, the diluted solution showing a bluish fluorescence. It is neutral to litmus and has an intensely bitter taste. It can be administered by the mouth or subcutaneously in doses of 1 to 2 grammes (15 to 30 grains) daily. In view of the fact that cases of amaurosis and amblyopia have been reported after administration of the drug these doses should not be exceeded. It was studied by Morgenroth in 1911 as a pharmacotherapeutic agent in experimental pneumococcal septicæmia in mice. It was shown to possess very considerable bactericidal powers and was able to protect over 90 per cent. of artificially inoculated animals against infection by the pneumococcus.

In 1912 Sir A. E. Wright¹ carried out a number of *in vitro* experiments with optochin hydrochloride in connexion with work on pneumonia, and was able to demonstrate that it retained its bactericidal effect on the pneumococcus in the presence of blood and serum when diluted two million-fold. In view of these very striking bactericidal results and owing to the general resemblance of the fæcal streptococcus (enterococcus) which is recoverable

from most infected wounds in the present war, Sir A. E. Wright suggested to me the advisability of investigating the bactericidal power of optochin in the case of the enterococcus. The bacterial emulsion used in all the following experiments was a dilution of a 20 hours' broth culture of a fæcal streptococcus recovered from pus from a recently infected wound.

In freshly prepared aqueous solution, left in contact with the microbes for 20 hours at 37° C., optochin kills the enterococcus in two million-fold dilution, as is shown in the following experiment.

Experiment 1.

Streptococcus emulsion.	Optochin hydrochloride.	Water.	Colonies after 37° C., 24 hours.
1 loopful.	10 c.mm. 1/200	—	0
Ditto.	10 c.mm. 1/2000	—	0
Ditto.	10 c.mm. 1/20,000	—	0
Ditto.	10 c.mm. 1/200,000	—	0
Ditto.	10 c.mm. 1/400,000	—	0
Ditto.	10 c.mm. 1/1,000,000	—	1
Ditto.	10 c.mm. 1/2,000,000	—	10
Ditto.	—	10 c.mm.	∞

Contact 37° C., 20 hours.

It is necessary to emphasise the words "freshly prepared," for it was found that exposure to light soon diminished the bactericidal activity of the solution, as may be seen in the following experiment.

Experiment 2.

Streptococcus emulsion.	Optochin hydrochloride.	Sterile water.	Colonies after contact 20 hours.		
			Solution kept in the dark.	Solution exposed to light 4 hours.	Three days old.
1 loopful	10 c.mm. 1/20	—	0	0	0
Ditto.	10 c.mm. 1/200	—	0	0	0
Ditto.	10 c.mm. 1/2000	—	0	0	0
Ditto.	10 c.mm. 1/20,000	—	0	0	∞
Ditto.	10 c.mm. 1/200,000	—	0	0	∞
Ditto.	10 c.mm. 1/400,000	—	0	10	∞
Ditto.	10 c.mm. 1/1000,000	—	1	∞	∞
Ditto.	10 c.mm. 1/2,000,000	—	10	∞	∞
Ditto.	—	10 c.mm.	∞	∞	∞

In human serum optochin kills the enterococcus in a concentration of 1 in 400,000. Further—and this is additional evidence that its activity is not quenched by serum—the action of the drug becomes more evident the longer it is allowed to remain in contact with serum and bacteria. These points will be appreciated by reference to Experiments 3, 4, and 5

Experiment 3.

Streptococcus emulsion.	Human serum.	Optochin hydrochloride.	NaCl 0.85 %	Colonies after 37° C., 15 hours.
1 c.mm.	10 c.mm.	10 c.mm. 1/20	—	0
1 c.mm.	10 c.mm.	10 c.mm. 1/200	—	0
1 c.mm.	10 c.mm.	10 c.mm. 1/2000	—	69
1 c.mm.	10 c.mm.	10 c.mm. 1/20,000	—	207
1 c.mm.	10 c.mm.	10 c.mm. 1/200,000	—	∞
1 c.mm.	10 c.mm.	10 c.mm. 1/2,000,000	—	∞
1 c.mm.	10 c.mm.	—	10 c.mm.	∞

Contact 5 hours, 37° C.

¹ THE LANCET, Dec. 14th, 1912, p. 1633.

Experiment 4.

Strepto- coccus emulsion.	Human serum.	Optochin hydrochloride.	NaCl 0·85 %	Colonies after 37° C., 20 hours.
1 c.mm.	10 c.mm.	10 c.mm. 1/20	—	0
1 c.mm.	10 c.mm.	10 c.mm. 1/200	—	0
1 c.mm.	10 c.mm.	10 c.mm. 1/2000	—	0
1 c.mm.	10 c.mm.	10 c.mm. 1/20,000	—	0
1 c.mm.	10 c.mm.	10 c.mm. 1/200,000	—	0
1 c.mm.	10 c.mm.	—	10 c.mm.	4680

Contact 20 hours, 37° C.

Experiment 5.

Strepto- coccus emulsion.	Human serum.	Optochin hydrochloride.	NaCl 0·85 %	Colonies after contact 37° C. for—			
				Not incubated.	1 hour.	3 hours.	16 hours.
1 c.mm.	10 c.mm.	10 c.mm. 1/20	—	—	0	0	0
1 c.mm.	10 c.mm.	10 c.mm. 1/200	—	—	0	0	0
1 c.mm.	10 c.mm.	10 c.mm. 1/2000	—	—	640	207	0
1 c.mm.	10 c.mm.	10 c.mm. 1/20,000	—	—	1340	210	78
1 c.mm.	10 c.mm.	10 c.mm. 1/200,000	—	—	ca. 1500	2414	582
1 c.mm.	10 c.mm.	10 c.mm. 1/1,000,000	—	—	—	3480	∞
1 c.mm.	10 c.mm.	—	10 c.mm.	1972	—	4920	∞

Experiments have shown that in dilutions which are effective against microbes optochin does not interfere with phagocytosis or with the emigration of leucocytes. Its close congener quinine also possesses bactericidal properties for the enterococcus, though to a much smaller degree, as is shown in Experiment 6.

Experiment 6.

Strepto- coccus emulsion.	Human serum.	Quinine hydro- chloride.	NaCl 0·85 %	Colonies after contact 37° C. for—			
				Not incubated.	1 hour.	3 hours.	16 hours.
1 loopful.	10 c.mm.	10 c.mm. 1/20	—	—	0	0	0
Ditto.	10 c.mm.	10 c.mm. 1/200	—	—	0	0	0
Ditto.	10 c.mm.	10 c.mm. 1/2000	—	—	444	1700	0
Ditto.	10 c.mm.	10 c.mm. 1/20,000	—	—	800	4800	∞
Ditto.	10 c.mm.	10 c.mm. 1/200,000	—	—	ca. 850	ca. 5000	∞
Ditto.	10 c.mm.	10 c.mm. 1/2,000,000	—	—	—	—	∞
Ditto.	10 c.mm.	—	10 c.mm.	118	—	—	∞

Optochin has very limited powers of penetration, as was demonstrated by superimposing a 1 in 1000 solution on an infected column of clotted centrifuged blood in an emigration tube. After 10 hours the solution had only succeeded in penetrating to a depth of 1/5 millimetre. Below this depth the microbes had grown with undiminished vigour. This fact would seriously limit its efficacy in the treatment of bacterial infections, for it would be unable to diffuse into and exert its influence in abscess cavities, infiltrated tissues (such as would be found in croupous pneumonia and wound infections), and other dead spaces. It would appear that it might find its useful sphere of application

in cases of streptococcal bacteraemia. But opportunity for putting this to the test has not yet offered.

In conclusion, it is a pleasant duty to acknowledge my indebtedness to Colonel Sir A. E. Wright and to the Medical Research Committee under whose auspices this work was carried out.

FUNCTIONAL NERVE DISEASE AND THE SHOCK OF BATTLE.

A STUDY OF THE SO-CALLED TRAUMATIC NEUROSES ARISING IN CONNEXION WITH THE WAR.

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THE nervous effects of intense emotional strain involving the risk of death first received medical recognition in 1875, when Erichsen, the London surgeon, published an account¹ of a number of cases of obscure injuries of the nervous system resulting from railway collisions. But his cases, as can now be discriminated, are a heterogeneous collection, some functional, others organic nervous (such as locomotor ataxy), and others, again, fracture-dislocations of the spine. Moreover, his conjecture that the symptoms are "dependent on molecular changes in the cord itself" was long ago refuted by H. W. Page.² Nevertheless, the term "spinal concussion," for all its misleading inaccuracy, was slow to be discarded, though Dana in 1884³ claimed that the cases thus designated were really instances of traumatic neurasthenia, hysteria, and hypochondria; and only in 1889, on the publication of Oppenheim's monograph⁴ recording some 40 cases met with in Berlin over a period of several years, did the term "traumatic neurosis" pass into general use.

But Oppenheim, while recognising traumatic neurasthenia and traumatic hysteria, went so far as to describe a neurosis specifically caused by injury; and to this he gave the name of "traumatic neurosis." On this cardinal point opinion was not reconciled for some 20 years; but according to the modern view as summed up in 1908 by Pearce Bailey, of New York,⁵ "the theory of a special traumatic neurosis lacks clinical foundation, and has been generally abandoned."⁶ Some of these cases, adds Bailey, "are mixtures of hysteria and neurasthenia."⁷

If opinion has seemed unduly slow in reaching this conclusion it has been even more backward in finding answers to many important questions bearing on these cases. Why, for example, do only some and not all the men and women exposed to railway collisions, big fires, electric shocks, shipwrecks, &c., develop neuroses? Why do the symptoms vary so widely, and what determines their form in any given case? Are they influenced by the patient's state of mind at the moment of the accident, or by his personal temperament, gradually formed in the course of many years? What is the treatment of these cases? Are they, like other neuroses, susceptible

¹ On Concussion of the Spine, by J. Eric Erichsen, London, 1875.

² Injuries of the Spine and Spinal Cord, and Nervous Shock, by Herbert W. Page, M.A., M.C. Camb., London, 1883.

³ Concussion of the Spine and its Relation to Neurasthenia and Hysteria, New York Medical Record, Dec. 6th, 1884.

⁴ Die Traumatischen Neurosen, Berlin, 1889.

⁵ Diseases of the Nervous System resulting from Accident and Injury, by Pearce Bailey, A.M., M.D., second edition, New York, 1908.

⁶ Loc. cit., p. 361.

⁷ Loc. cit., p. 362.