

far upon the composition of the blood plasma, need not now be considered.

2. Mental temperament is inborn, and but little susceptible of being altered. A person is born with a certain temperament for which he is no more responsible than for the shape of his nose, and this inborn temperament tends to remain fundamentally the same throughout life, resisting almost completely all attempts, educational or psycho-therapeutical, to modify it. No doubt some of his emotional disposition can be modified by training—an artistic aptitude can be developed by constant exercise, a bad temper bettered by systematic control—yet the native temperament remains, fundamentally unchanged. A person's temperament never in fact, undergoes a decided change except as the result of the normal cyclical changes, such as puberty and senility, or in consequence of disease, such as Graves's disease, myxœdema, or actual insanity. We meet a man we have not seen for years, and when we come to speak to him it is as if we were carrying on a conversation of yesterday, so conscious are we of his unaltered temperament; and it is this which constitutes the essence of the man, or, as we say, his personality. There are the same old gestures, the same old tricks of speech, the same old play of facial expression, all indicative of the same temperament. Contact with the world, his successes, his failures, his troubles, have no doubt left their impress. Youthful ardour may have been damped; the optimist may have lost some of his hopefulness; the shy man may have grown bolder; the genial man may have become somewhat soured, the cheery nature more subdued; but all such changes are on the surface only. When we come to probe below the surface we shall find that the temperament remains fundamentally the same: the very sensitive, the very shy, the very timid, the irrepressibly self-confident, remain sensitive, shy, timid, self-confident to the end of the chapter.

Now if the foregoing propositions are sound—if a congenitally morbid mental temperament constitutes the basis of classical psychasthenia, and if temperament is all but insusceptible of being changed—the limitations of psychotherapy in psychasthenia are apparent. If we cannot alter feeling tone, strike at the foundation upon which the whole superstructure of psychasthenia is built up, we cannot cure the affection. In my experience the congenital psychasthenic remains psychasthenic to the end. I am far from saying that psychic treatment is wholly useless for these patients. Much can be done to establish a sane habit of thought and to discipline morbid feeling tone, even though this remains essentially the same.

As to the legitimacy of the conclusions Dr. Rivers draws from his case I am somewhat doubtful. His patient, one judges from the description, appears to be a congenital psychasthenic with a bent towards claustrophobia. It is, of course, conceivable that but for the early claustrophobic incident the specific fear of closed spaces would never have displayed itself; but everything must have a beginning, and I judge that the experience with the dog happened to be the first opportunity for the display of the specific fear. Thereafter it showed itself on several occasions, and I suggest that these later manifestations would have occurred even in the absence of the initial incident.

My experience of claustrophobia leads me to doubt whether the mere resuscitation of a forgotten experience is capable of dispersing the fear. May not the cure (?) in Dr. Rivers's case be an instance of faith-healing? Do we sufficiently realise the tremendous power of *absolute* belief? If we could convince a person that by jumping off the Monument in a particular way he would plane gently down and alight unhurt below, he would have no kind of hesitation in attempting the experiment. Similarly, if we succeed in implanting the belief that the revival of a forgotten fearful experience will for ever prevent the recurrence of a similar fear, we shall go far to prevent its recurrence. The crucial test would be to observe the effect of the revival without letting the patient know that a cure was expected from it.

**SOCIETY FOR THE STUDY OF INEBRIETY.**—The seventh Norman Kerr lecture will be delivered by Major W. McAdam Eccles, M.S., M.B., F.R.C.S., R.A.M.C. (T.), on Tuesday, Oct. 9th, at 5.30 P.M., in the Robert Barnes Hall, 1, Wimpole-street, Cavendish-square, London, W., on the subject of "War and Alcohol." The honorary secretary of the society is Dr. T. N. Kelynack, 139, Harley-street, W. 1, to whom acceptances of invitations should be addressed.

## Correspondence.

"Audi alteram partem."

### THE PHYSIOLOGICAL AND ANTISEPTIC PROPERTIES OF FLAVINE.

To the Editor of THE LANCET.

SIR,—The tone of Dr. C. H. Browning's letter in your issue of Sept. 15th is an unfortunate one. It seems to be more an expression of his wounded feelings than argument against my findings.

He congratulates himself that in his second paper on flavine, which appeared in the *British Medical Journal* on July 21st last, he forestalled me in a number of my experiments. In this matter he may certainly congratulate himself, as my article was in the hands of the censorship authorities weeks before his paper appeared. His experiments, however, were not carried far enough. In connexion with the toxic power of flavine on the leucocytes, he still used as the maximum time of exposure two hours, which is altogether too short to bring out the full toxic effect on the leucocytes, just as it fails to show the maximum bactericidal power. In his first paper he found that flavine 1 in 500 was the highest dilution which in 20 minutes caused marked inhibition of phagocytosis. In his second paper he states that in two hours flavine 1 in 10,000 had little effect on the phagocytic power. I have found that in five hours flavine 1 in 256,000 gives marked inhibition of phagocytosis, while in 24 hours the leucocytes are completely destroyed by a 1 in 2,000,000 dilution.

I have shown in my article that a 1 in 2000 dilution of flavine completely inhibits emigration of the leucocytes. However, in a septic wound treated with flavine 1 in 1000 there is still a more or less purulent exudate. This is capable of two explanations: either the *in vitro* experiment does not represent what happens in the body or the flavine does not come into contact with the leucocytes in the walls of the wound in sufficient strength to prevent their emigration. As we shall see the latter is the more likely explanation.

Experiments cited in my paper show that the purulent discharges from a wound are very potent in "quenching" flavine. The bared surfaces of the wound also have a great affinity for flavine. The following observation illustrates this point. A patient had a cup-shaped wound in the front of his leg following a fracture of the tibia. This depression was about  $2 \times 1 \times 1$  cm. and held about  $1\frac{1}{2}$  c.c. of fluid. It was lined with granulation tissue. The hole was carefully swabbed out and washed with normal saline solution until the washings were clear. In the next two hours it had four changes of flavine (1 in 1000) and then it was filled with flavine (1 in 1000) which was allowed to remain for two hours, after which it was removed. The strength of the flavine removed as measured by the colour intensity was 1 in 3500. We see, then, that the granulation tissue-walls of this wound extracted in two hours most of the flavine from the solution applied, and that even after they had been well dyed with four changes of 1 in 1000 flavine during the previous two hours.

The same wound, immediately after I had removed the above-mentioned two-hour sample of flavine, was filled with a fresh supply of flavine 1 in 1000 and left for 15 hours. At the end of that time the walls of the wound were covered with a mucous-like coating which I take to be the same that the distinguished surgeon (name unknown) has commended as "coagulated lymph." On examination this appeared to consist almost entirely of disintegrated leucocytes, a finding quite in keeping with the test-tube experiments on the powerful leucocidal action of flavine.

The original instructions sent out with flavine by the Medical Research Committee, and presumably drawn up by Dr. Browning, stated that it might be employed in conjunction with any of the various techniques recently advocated in wound treatment. In his second paper on flavine Dr. Browning mentions that unsatisfactory results have followed the two-hourly flushing with flavine after the method of Carrel, and he recommends that it be applied on gauze and only the minimum of water should be introduced so that

the discharges of the wound might not be unduly diluted, as the antiseptic acts better in a serous medium. Here, as elsewhere, Dr. Browning seems to assume that in a septic wound the discharge consists only of serum and bacteria. In connexion with the application of flavine on gauze it is of some interest to note the quenching effect of ordinary surgical gauze on flavine. A piece of gauze was taken measuring 11 × 9 centimetres, 16-ply thick, and weighing 5 grammes. This was placed in a small dish and 20 c.c. of flavine, 1 in 1000, was poured on. The gauze was kneaded for a few seconds to distribute the fluid in its interstices and then 12 c.c. of fluid was squeezed out. The colour of this corresponded with a 1 in 5000 dilution of flavine. The fluid was poured back on the gauze and left two hours, after which, on being expressed, it gave a colour corresponding with flavine 1 in 10,000. A similar experiment was done with flavine 1 in 4000 (using the same weight of gauze and the same volume of fluid), and after being in contact with the gauze for five minutes the expressed fluid corresponded in colour to flavine 1 in 128,000. These observations show clearly that the gauze dressing has a very powerful affinity for flavine, and that if gauze is wetted with a solution of flavine and applied to a wound the concentration of the dye which comes out of the gauze is very much less than that which went in. Another very simple method of demonstrating the great affinity of cotton tissues for flavine is to half fill a small test-tube with flavine 1 in 1000 and to press down slowly into it a tight-fitting cotton-wool plug. The first fluid which exudes above the cotton wool will have absolutely none of the yellow colour of flavine. It may be done also by packing tightly a little wool or gauze into a piece of glass tubing and allowing a 1 in 1000 solution of flavine to percolate through it. The first fluid which comes through will have no yellow colour. Using this method, and packing a piece of gauze weighing 0.38 gm. into a tube of a calibre of 6 mm., from a solution of 1 in 1000 flavine 1.3 c.c. of colourless fluid percolated through before any trace of the yellow colour of flavine was noticed. It may be that this action of gauze in reducing the effective concentration of flavine is the cause of the difference between the unsatisfactory results which have followed the application of flavine by irrigation after the method of Carrel and the more favourable results which have followed its application on gauze. Dr. Browning has stated that too frequent applications of flavine may lead to "undesirable cumulative effects on the tissues locally," and in this way he explains the failure of flavine used by Carrel's method. The absorptive action of the gauze would certainly seem to prevent this.

Dr. Browning states: "It appeared to be a hard enough task to demand of an antiseptic that it should not be quenched in a serous medium," and he appears to resent the suggestion that anything further should be asked of an antiseptic. The production of an antiseptic the power of which is enhanced by serum is a very fine achievement, but in the case of flavine this seems to be more than counterbalanced by the ease with which the dye is absorbed by the walls of the wound, by the purulent discharges, and by the dressings.

Dr. Browning objects to my interpretation of the "therapeutic coefficient" as a comparison of the toxicity of a substance to leucocytes with its toxicity to bacteria (acting in serum). Although there can be no doubt from the text of his original article that this was the sense in which he used the term, he insists that it should be applied only to the ratio between the concentration which inhibits phagocytosis by 50 per cent. acting for 20 minutes in 25 per cent. serum, and the lethal concentration to bacteria acting for 24 hours in 80 per cent. serum. If the term is to be applied only in this limited sense, then "Browning's coefficient" would be an appropriate name; but "therapeutic coefficient" is altogether too ambitious, and implies that the numeral arrived at has some real value in therapeutics.

When I started working with flavine I hoped that I should be able to convince myself that at last we had a really efficient antiseptic for use in septic wounds, and it was with great regret that I found my experimental results could lead me to no other conclusions than the unfavourable ones mentioned in my article.

I am, Sir, yours faithfully,

ALEXANDER FLEMING.

Sept. 24th, 1917.

## PURULENT BRONCHITIS:

ITS INFLUENZAL AND PNEUMOCOCCAL BACTERIOLOGY.

To the Editor of THE LANCET.

SIR,—I have read with considerable interest the article as above entitled by Captain Adolphe Abrahams, Captain N. F. Hallows, Dr. J. W. H. Eyre, and Major H. French in your issue of Sept. 8th; nevertheless, in fairness to myself, I should like to have the opportunity of pointing out that their observations contain little that is new and not contained in my "Bacterial Diseases of Respiration."<sup>1</sup> Therein I pointed out (1) how atypical and unlike anything described in the standard text-books of medicine are the majority of cases of bacterial infections of the lower respiratory tract; and (2) how rare it was in my experience for cases of lobar pneumonia to have a sudden onset, or occur, as it were, spontaneously, but that, on the other hand, they were either due to an awakening of a dormant focus of infection in the lung, or to the rapid extension into the chest of an acute nasal or tracheal catarrh, especially when the *B. influenzae* is associated with the pneumococcus (pp. 103, 104). I also pointed out (p. 105) that

"The pneumonia supervening on an attack of so-called 'influenza,' this latter being much more frequently a pure pneumococcal or a combined pneumococcal and influenzal infection, is commonly regarded as a fresh superimposed infection by the pneumococcus; this is an utterly erroneous view in the great majority of cases."

On the other hand, when there has been a dormant pneumococcal focus in the lung—parenthetically I may remark that needling of the lung has shown me that sometimes the pneumococcus and *B. influenzae* are associated at these foci—

"the factor which above all probably decides the lighting into virulence of the dormant pneumococcus is the incidence of a fresh infection by some other catarrhal micro-organism. Chief among these is undoubtedly the *B. influenzae*, and it is owing to this fact that an epidemic of influenza is nearly always attended by a greatly raised mortality due to acute pneumonia. At the same time, it must be admitted that a pure invasion of any part of the respiratory tract by the *B. influenzae* is comparatively rare; there is nearly always some other associated microbe, and this is usually the pneumococcus" (p. 107).

The conclusion of the authors, and also of Lieutenant J. A. B. Hammond, Captain W. Rolland, and Lieutenant T. H. G. Shore,<sup>2</sup> that—

"the primary invasion of the lung tissues is by the *B. influenzae*, and that pneumococci, present at the same time, are at first of low virulence; that the earlier symptoms seem to be attributable to a *B. influenzae* toxæmia; and that exaltations of the virulence of the pneumococci by symbiotic growth with the *B. influenzae* would appear to follow"—

is therefore a misconception of the process and only a partial statement of the truth, especially in view of the experiments I adduced (p. 32) to show how potent is the effect of the presence of other bacterial toxins (pneumococcal, staphylococcal, streptococcal) upon the rate of multiplication of the *B. influenzae*. At the same time, I am prepared to admit that the *B. influenzae* may be a potent factor in raising the virulence of the pneumococcus.

I have been studying closely for nearly 15 years both the clinical aspects and bacteriology of the respiratory tract, and have been much struck by the gradual increase, especially during the last four years, in the severity of these bronchitic and pneumonic attacks, and I can assure the authors that the condition they describe has not been confined to the Aldershot military area nor even to the military as apart from the civilian population. I have had large experience of it in private practice and among the New Zealand troops at Codford and Hornchurch. So certain was I that a culmination would be reached last winter that I strongly advised the D.D.M.S., N.Z.E.F. in England that a special chest hospital should be established, and predicted a very high rate of incidence among our troops at Codford, which he subsequently informed me had been exceeded. The mortality rate at Aldershot was, I believe, exceeded among the New Zealand troops at Codford. The severe epidemics of pneumonia which have ravaged Guatemala city for years (p. 104) have, I am informed, a mortality rate of 40 per cent. It is highly probable that the grouping together of large numbers of men in huts and marquees tends both to raise the rate of incidence and mortality

<sup>1</sup> Bacterial Diseases of Respiration and Vaccines in their Treatment. 1913. H. K. Lewis.

<sup>2</sup> THE LANCET, July 14th, 1917 (p. 44).