quick perception, a ready judgement and a delicate susceptibility. It is not the strength needed by the man who wields a bludgeon, but rather that which guides the deft hand of the fencer.

All knowledge is of value in the making of a successful practitioner and the mass of all that is to be known in the science of medicine is colossal to contemplate. It must not be assumed that the education of the physician can be founded exclusively upon textbooks and treatises, even when it is supported by work in the laboratory and at the bedside. A man may possess all the learning that a well equipped library may contain and all the erudition attentive observation in the wards may bestow and yet be short of complete success as a practitioner of his art. Absolute efficiency cannot be gauged by academic distinction nor can it be discovered by the touchstone of the examination table. In the accomplishments of the most learned physician there may be one thing lacking the need of which may stand between him and the fullest equipment for success, and that one thing is a tactful and a sympathetic knowledge of his fellow man. It is possible that a doctor may be acquainted with all that is to be known of the diseases of man and yet know too little of the man himself. Indeed, it is not too much to say that the highest qualifications of the practitioner of medicine are not to be represented by any university degree nor discovered by any system of inquisition.

In the treatment of the sick a certain profession of dogmatism is essential. The sick man will allow of no hesitancy in the recognition of his disease. He blindly demands that the appearance of knowledge shall be absolute, however shadowy and unsubstantial may be the bases of it. Moreover, the sick man in his weakness looks to his doctor for the supporting hand and the strong arm; he is moving in the dark and he needs to be led; he is haunted by apprehension and his fears must be allayed.

It is this succouring of the weak, this guiding of the feeble, which represents that which is best in the profession of medicine. This great privilege, this kindly power, is the heritage of all who embrace the healing art, and it is the possession, of all others, upon which the influence of the physician is based.

The second need in the equipment of the medical man is absolute fidelity. All those who profess to attend upon the sick undertake a solemn trust which needs to be observed with punctilious care. The sick man must place implicit faith in his doctor or no faith at all. The fullness and simplicity of this confidence are the measure of the scrupulous honesty with which it must be received. In accepting this trust every physician takes upon himself a grave responsibility, and he who is the most exact in the right observance of this confidence has the greatest claim to be worthy of his calling. The burden of such a trust is little appreciated beyond the confines of the medical profession, and every physician of any experience has had to learn with some bitterness how much self-denial and self-effacement this trust implies, how little the responsibility of it is appreciated, and how much injustice to the doctor its honest acceptance may involve.

The public are apt to talk glibly of "medical etiquette" and to assume that it is founded upon some special code of ethics, and based upon a system of morals especially constructed for the advantage of the medical profession. Such criticism is unjust, as criticism usually is which is based upon imperfect knowledge. It is needless to say that there is no precept in "medical etiquette" which is other than the outcome of the simplest justice, the simplest right doing, and above all the truest care for the interests of the patient.

The third article in such part of the *Religio Medici* as bears upon the qualifications of the physician is this. He must be kind. He must needs be a man of wide sympathies, and possessed of that rare qualification which enables him to put himself in the patient's place. There need be little art in this. Genuine sympathy cannot be assumed, or if assumed, its artificiality is too apparent to deceive even a child.

In the mere treatment of the sick a simple kindness of heart is an essential factor, and it can never be replaced by any assumption of manner, however elaborate, or however precisely mimicked.

In conclusion, therefore, I would say that those who are about to enter upon the arduous career of medicine can keep no better motto before their eyes than this:

"FORTITER, FIDELITER, FELICITER."

SCIENTIFIC GRANTS COMMITTEE

OF THE

British Medical Association.

REPORT LXXII.

ON EXALTATION OF BACTERIAL VIRULENCE BY PASSAGE OUTSIDE THE ANIMAL BODY.

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(From the Gordon Laboratory, Guy's Hospital, and the Pathological
Laboratory, Oxford.)

THE virulence of a bacterium for a particular species of animal is in general heightened by its growth in the tissues of an animal of that species. Accordingly the usual method employed for heightening virulence is that of "passage" through a succession of animals.

Now the virulence of a bacterium for any given animal depends upon its power of living and multiplying and of forming harmful substances within the tissues of the animal in question; and the resistance of the animal depends upon its faculty of forming "antibodies"—both such as neutralize these harmful substances, and such as assist the bacteriolytic action of the normal "complement"—as well as on its power of forming lysogenetic complement by a proliferation of its leucocytes. And the increase in virulence of the bacterium within the tissues of a living animal is the outcome of the struggle which is carried on between these two opposing tendencies. For leaving aside the question of toxins and antitoxins, the survival of bacteria in the animal body depends exclusively upon their power of resistance to the bacteriolytic action brought to bear upon them.

Two substances are necessary to bacteriolytic action—namely, the immune body which is formed by the proliferation of certain "side chains" which are pre-existent in the normal animal, and, indeed, probably situated in its leucocytic tissues;¹ and the complement or leucocytic ferment which dissolves the bacteria after their saturation with the immune body. And it has been shown, more especially in the analogous experiments on haemolysis, that once a saturation with the immune body has occurred, the complement inevitably completes the lysogenesis. Accordingly the virulence of a bacterium must be dependent on its relative resistance to such saturation by the immune body; that is to say, upon the quantity of immune body which is needed to produce its saturation, or, in other words, the number of receptor² groups for immune body which are present in it. And hence increase of virulence apparently implies increased formation of such receptors by the bacterium concerned; that is, immunization of the bacterium against immune body.

In support of this position I have already offered evidence from the results of growing the bacillus typhosus in specific immune serum.³ The bacterium in question slowly acquired an increased virulence, and since the immune serum was without bacteriolytic action, this was apparently attributable to a reaction of the bacterium to the immune body present. That immune body was taken up from the serum or neutralized by the bacterial receptors was evidenced by the diminution of its protective power for guinea-pigs which was observed after the bacillus had been grown in it.

¹ Deutsch, *Annales de l'Institut Pasteur*, 1899, vol. xiii, p. 689. Bulloch, *Trans. Path. Soc. Lond.*, 1901, vol. lli, p. 242.

² The term receptor was introduced by Ehrlich to designate the hypothetical side chains of protoplasmic molecules by which they are enabled to take up and incorporate appropriate atom groups from their surroundings.

³ *Journal of Pathology and Bacteriology*, 1902, vol. viii, p. 34.

I have now examined the question from a somewhat different standpoint by growing a particular variety of typhoid through fresh (bacteriolytic) normal rabbit's blood for nearly thirty passages, and noting the effect upon its virulence.

Description of the "Passages" in Vitro.

An old laboratory culture of the bacillus typhosus was selected, and from it two subcultures were made on ordinary agar. The first of these was used for the first inoculation into blood, the second being reinoculated daily in successive subcultures on agar throughout the duration of the experiments, and used for comparison with the cultures of the same organism after its growth in blood.

Passage through blood was arranged and carried out as follows. A small quantity of blood was taken aseptically from a rabbit's ear and diluted 1 in 10 with culture broth. This mixture was inoculated with a loopful of a broth emulsion of the typhoid culture, and incubated for three hours at 37° C. A sample of the fluid was then plated on agar. The plate was examined on the following day, and a subculture from a colony made on agar. This constituted the first passage of the organism through fresh blood. From the subculture a broth emulsion was prepared, and from this a second sample of fresh dilute blood inoculated to constitute the second passage, and exactly the same procedure was repeated as before for this and the succeeding passages. In all 26 such passages through blood were made, occupying a period of between three and four months, with an average of about two passages per week. On two occasions only were the plates from the blood cultures found to be contaminated; these were rejected, and a return was made to the subculture from the preceding passage. The original culture was designated Typhoid 1, and the cultures after passage Typhoid 2, 3, 4 ... 27 respectively.

Observations on the Cultures after Passage.

In order to discover whether the procedure which has been described was producing any modification of the organism, a number of the cultures were examined on several occasions as regards their susceptibility to the bacteriolytic action of fresh rabbit's blood. This test was carried out as follows:—A series of tubes containing equal volumes (0.5 c.cm.) of fresh normal rabbit's blood diluted 1 in 10 with culture broth were inoculated respectively with one loopful of an eighteen hours' old broth culture of each of the typhoid cultures under examination. The tubes were then incubated for three hours at 37° C., and subsequently two loopfuls of each transferred to a series of melted gelatine tubes and plated. Colonies were counted on the third day after plating. The results of one such observation are given below.

Designation of Culture.	Quantity of Diluted Normal Blood.	Colonies in Plates.
Typhoid 1 (before passage) ...	0.5 c.cm.	1,800
" 8 (after 7 passages) ...	"	6,480
" 14 " 13 " ...	"	10,800
" 19 " 18 " ...	"	14,120
" 23 " 22 " ...	"	19,440

Such observations showed that the resistance of the organism to the bacteriolytic action of fresh blood became progressively increased. The total change in this respect which was affected by the passages is shown in the following observation for which I took two tubes, each containing 1 c.cm. of fresh (six hours old) normal rabbit's serum, and inoculated them respectively with two loopfuls of a two days' old broth culture of Typhoid 1, and the same quantity of a similar culture of Typhoid 27. The tubes were incubated for three hours at 37° C., and then a tube of melted culture gelatine was added to each, and the whole plated, with the result below.

Thus only 4 bacilli of the two loopfuls of Typhoid 1 survived the bacteriolytic action of the serum, while 66 of Typhoid 27 remained resistant. Evidently the organ had be-

come considerably more resistant to the bacteriolytic action of fresh blood or serum as the result of the passages through blood.

Designation of Culture.	Quantity of Normal Rabbit's Serum Six Hours Old.	Colonies in Plates.
Typhoid 1	1 c.cm.	4
" 27	"	66

Animal Experiments.

I now proceeded to test the virulence of these two cultures, Typhoid 1 and Typhoid 27, for guinea-pigs and for rabbits. For this purpose agar cultures forty-eight hours old, and so inoculated that the whole agar surface was well grown over, were employed. The culture tubes were carefully chosen of the same size; they contained the same amount of agar medium, and they were sloped to the same height in order to obtain a surface of approximately constant area. For injection, the growth was washed off and emulsified with ordinary culture broth. The doses used are given in terms of fractions of an agar culture per 100 grams of the weight of the animal employed. They were administered intraperitoneally by means of a hypodermic syringe. The following table shows the guinea-pig determinations, the letters M. L. D. standing for minimal lethal dose.

Determinations of M. L. D. for Guinea-pigs.

Typhoid 1.				Typhoid 27.			
Guinea-pig.	Weight of Animal in Grams.	Amount of Culture per 100 Grams.	Result.	Guinea-pig.	Weight of Animal in Grams.	Amount of Culture per 100 Grams.	Result.
1	175	$\frac{1}{10}$	Nil after 24 hours; died in 40 hours.	1	150	$\frac{1}{10}$	Dead in 18 hours.
2	145	$\frac{1}{10}$	Lived	2	190	$\frac{1}{10}$	"
3	190	$\frac{1}{10}$	"	3	200	$\frac{1}{10}$	Dead in 24 hours.
4	250	$\frac{1}{10}$	Ill after 24 hours; recovered.	4	238	$\frac{1}{10}$	Ill after 24 hours; recovered.
5	200	$\frac{1}{10}$	Dead in 30 hours.	5	230	$\frac{1}{10}$	Ill after 24 hours; died in 30 hours.
6	250	$\frac{1}{10}$	Ill after 24 hours; died in 1 week.	—	—	—	—

M. L. D. not less than $\frac{1}{10}$ of a culture.

M. L. D. somewhere near $\frac{1}{10}$ of a culture.

From this table it follows that the virulence of the organism for guinea-pigs was at least doubled by twenty-six passages through fresh rabbit's blood.

The determination of virulence for rabbits was next attempted. These rabbit inoculations were carried out during my summer vacation in the Pathological Laboratory at Oxford by the kind permission of my friend Dr. Ritchie. Similar means were taken as before to ensure a uniformity in the bacterial content of the cultures. The doses used are not, however, strictly comparable with those employed for the guinea-pigs in the previous table, seeing that the Oxford cultures were made in tubes of a slightly different size and on a different batch of agar from that used for the guinea-pig inoculations. The results are given below:

The M. L. D. of the organism for rabbits had therefore been diminished from about $\frac{1}{10}$ to about $\frac{1}{100}$ of a culture per 100 grams of body weight; that is to say, the virulence had been more than doubled (multiplied about $2\frac{1}{2}$ times) for these animals by passage through fresh blood of the same species of animal.

Passage of the bacillus typhosus through fresh (actively bacteriolytic) rabbit's blood accordingly produced an increase of its virulence. And considering that the total length of its residence in the bacteriolytic fluid was only about three days

(twenty-six times three hours), the increase observed may be regarded as considerable, and, indeed, quite comparable with that produced by passage through the living animal. As concerns the bacterium itself, the experiments afford a good example of the principle of the survival of the fittest in the struggle for existence.

Determinations of M. L. D. for Rabbits.

Typhoid 1.				Typhoid 27.			
Rabbit.	Weight of Animals in Grams.	Amount of Culture per 100 Grams.	Result.	Rabbit.	Weight of Animals in Grams.	Amount of Culture per 100 Grams.	Result.
1	—	—	—	1	1,083	$\frac{1}{10}$ +	Dead in 24 hours.
2	1,388	$\frac{1}{10}$ +	Dead in 24 hours.	2	1,027	$\frac{1}{10}$	"
3	1,203	$\frac{1}{10}$	Lived.	3	1,290	$\frac{1}{10}$	"
4	1,162	$\frac{1}{10}$	Dead in 24 hours.	4	915	$\frac{1}{10}$	Lived.
5	1,350	$\frac{1}{10}$	"	5	1,378	$\frac{1}{10}$	Dead in 24 hours.
6	1,433	$\frac{1}{10}$	Lived.	6	1,615	$\frac{1}{10}$	Very ill after 24 hours; recovered.
7	1,540	$\frac{1}{10}$ +	Ill after 24 hours; recovered.	7	1,410	$\frac{1}{10}$	Dead in 24 hours.
8	1,410	$\frac{1}{10}$	Lived.	8	1,570	$\frac{1}{10}$	"

M. L. D. about $\frac{1}{10}$ of a culture.

M. L. D. about $\frac{1}{10}$ of a culture.

NOTE.

The following precautions were observed in these experiments:

1. Necropsies were performed on all the animals which died.

2. The bacillus (Typhoid 27) was examined microscopically and culturally at the termination of the series of passages, and was found to possess the characters which are regarded as distinctive of the bacillus typhosus, including Durham's reaction.⁴

And (3) a comparison was made of the relative numbers of the bacilli in emulsions of Typhoid 1 and Typhoid 27 similar to those employed for the animal inoculations. Such emulsions appeared of similar density to the naked eye, and showed approximately the same number of colonies in plates prepared from equal volumes of the two emulsions for enumeration.

CONCLUSIONS.

1. The virulence of a bacterium may be increased by "passage" through a bacteriolytic fluid *in vitro*. The practical bearing of this observation and its relation to certain of the problems of infection and immunity are apparent.

2. The increase of bacterial virulence, which may be brought about by "passage" through the body of a living animal, is probably attributable to the effect of the successful resistance of the surviving micro-organisms to the bacteriolytic action of the living tissues.

[The expenses of this work were defrayed from grants received from the Scientific Grants Committee of the Royal Society and from the British Medical Association.]

MEDICAL MAGISTRATE.—Dr. Fulton, of Eston, R.S.O., Yorkshire, has, by the direction of the Lord Chancellor, been made a justice of the peace of the North Riding of Yorkshire.

THE LIGHT TREATMENT IN THE BRADFORD ROYAL INFIRMARY.—A new department for the light treatment of lupus, including a Roentgen-ray apparatus, was formally opened in the Bradford Royal Infirmary on October 10th by the Mayor of Bradford. The installation, which has cost about £180, has been presented to the infirmary by Mr. William Parkinson, of Allerton.

A memorial to the late Dr. Alwin von Coler, Surgeon-General of the German army, subscribed for by officers of the corps, was unveiled on August 26th, the first anniversary of his death.

⁴ Frequently spoken of as Widal's reaction.

SEVENTIETH ANNUAL MEETING

OF THE

British Medical Association.

Held at Manchester, July 29th, 30th, 31st, and August 1st, 1902.

PROCEEDINGS OF SECTIONS.

SECTION OF PSYCHOLOGICAL
MEDICINE.

GEORGE W. MOULD, M.R.C.S., L.S.A., President.

PRESIDENT'S ADDRESS.

RECENT PROGRESS IN THE HOUSING OF THE
INSANE.

THE PRESIDENT said: I do not propose to take up your time from the active business of the Section by any long address of my own, but simply to offer to you a few words of warm and sincere welcome to the City of Manchester in the name of the Lancashire and Cheshire Branch of the British Medical Association as one of its oldest members. It is now twenty-five years since the city had the honour of receiving and entertaining you, and since that time many honoured and distinguished men in our speciality have passed away, but fortunately have left behind them the legacy of great work they did in their lives, and their names will always be honoured and their work held in the highest esteem and regard not only by all of us who personally knew them, but by all students of psychological medicine who will profit for all time by their recorded work. Two of the men who held so high a place at the time of our last meeting were Drs. Bucknill and Hack Tuke, names honoured during life and venerated after death. The former was President of this Section at the time of our meeting here, and ably and well filled the office, and the latter was ever to the front with all the wonderful kindness of his nature and his active and ready sympathy in the work he loved so well and wrought so ably in. I am sure I may say that the joint work of these two men is the solid foundation on which has been built the works of their successors in authorship, such as Maudsley, Clouston, Blandford, Crichton-Browne, Clifford Allbutt, James Ross, Bevan Lewis, Savage, and other standard authors whose amplified and extended works are now our guides in psychological medicine.

At this meeting we are unusually fortunate in having here such distinguished men to open the discussions in our Section as Sir John Sibbald, Dr. Clifford Allbutt and Dr. Mott, each one a master in the special subject to which his life has been and still is devoted.

Professor Charcot was a very prominent figure at our last meeting here, and imparted in his own brilliant way that store of knowledge of nervous diseases which did so much to aid in the recognition and treatment of the grave and serious diseases of the nervous system which we have to battle with.

Professor Virchow was another prominent figure at our last meeting here; a giant then in pathological research, and, if not the founder, certainly the great stimulator, of the work that is now being carried out in most of our great asylums by able and distinguished men, one of whom—Dr. Mott—we have the good fortune to have amongst us to-day; and it is not too much to say that the results of the labours of these workers in the pathological laboratories have revolutionized the treatment of nervous diseases, with their grave mental disturbance.

Going back to the year 1858, when I first entered into our speciality as medical officer, and for a time manager, of the Droitwich Asylum, of which Sir Charles Hastings, the founder of the British Medical Association, was the proprietor, and afterwards at the Birmingham Borough Asylum and the Lancashire County Asylum at Preston, the whole course of medical and physical treatment has materially changed. Restraint, though not altogether disused, was but little employed, and constant outdoor exercise was the rule. Still