Observations

ON

THE CONTROL OF TRACHOMA.*

BY

N. BISHOP HARMAN, M.A., LL.D., F.R.C.S.,
SENIOR OPHTHALMIC SURGEON TO THE WEST LONDON HOSPITAL;
OPHTHALMOLOGIST TO THE EDUCATION DEPARTMENT
OF THE LONDON COUNTY COUNCIL.

TRACHOMA is practically extinct in England. It is still prevalent in some parts of the British Empire. It is rampant in some Eastern countries. Trachoma was at one time common in England. The conditions that have conduced to its virtual extinction are worth investigation. They may point the way to measures calculated to secure a similar result elsewhere.

The necessity for control of a disease depends upon the measure of the damage done by it. To obtain this measure there would be needed a census of the eye conditions of the population. This is manifestly impossible. But we can fairly compare figures drawn from the examination of sections of the population. These, although not national maps, may be fair average samples. Hospital figures cannot be considered such samples, for they are obtained from selected portions of the population. The most desirable figures are to be obtained from the schools, and from the examination of recruits for military service.

Van Millingen,¹ in 1895, collected figures for eighteen countries. Clemow,² in 1903, supplemented these figures. They showed the wide spread of the disease, and the unequal incidence in the several countries. I have collected some later figures, and these show that whereas in some countries there is an effective control of trachoma, in others the problem is still of great magnitude. From these figures we may judge the vast amount of suffering and loss of economic efficiency caused by the disease in countries where it is rife.

Egypt still heads the list of afflicted countries. In the last report³ of the Ministry of the Interior of Egypt there are some astounding figures of the prevalence of trachoma among school children. An ophthalmic survey was carried out among all the pupils of the primary schools in certain capital towns of the provinces in which there were ophthalmic hospitals. There were seventeen schools with 8,045 pupils; "91 per cent. of all pupils were found to be infected with the various stages of trachoma, whilst 23 per cent. of the total were found attacked with the serious stages of trachoma." The figures are so amazing that one might ask whether the diagnosis of trachoma in so great a proportion of the children could be justified, and whether perhaps some other follicular condition might not have accounted for many. But there are available the series of reports of this department when the work was under the direction of A. F. MacCallan which fully bear out the high incidence. Also, there is Lister's⁴ record of the examination of the Egyptian members of the Labour Corps employed in France by the British authorities in the great war—"at a low estimate 45 per cent. were either suffering from or had had trachoma."

China runs Egypt close. Some 25 per cent. of the population appears to be affected. In the dramatic story of Professor Harvey Howard's captivity by Chinese brigands⁵ there is this passage:

"Famines, floods and disease are rampant in China, but it is common knowledge that the most devastating of these three is disease. And of all the disease, the one that is the cause of the most misery and economic distress is probably trachoma. It is found all over China; it affects nearly every home, and all classes of society. From statistics I had gathered, I had come to the conclusion that fully one hundred millions of Chinese people have trachoma, and that probably five million new cases, mostly children, develop each year. I had estimated that not less than one million Chinese are blind in both eyes, and that three or four millions more are blind in one eye; further, that not far from twenty millions have had their vision so much

impaired by inflammation and the formation of scar tissue, due to trachoma, that they are able to eke out only the barest kind of existence."

The situation in India is better. Members of the Indian Medical Service have told me that although there is much trachoma it is less severe than in other Eastern countries, and is less important as a cause of blindness. The reports of the Madras Government Ophthalmic Hospital⁷ for the six years from 1923 to 1928 show that of an average of 21,000 new patients each year about 4.5 per cent. were suffering from trachoma.

There are two recent reports for European countries in the papers of the League of Nations. In Italy, Lutraria⁸ reports that trachoma is met with in almost all parts, but it is most common in the islands of Sardinia and Sicily. The army figures of 1913 show that of 502,221 conscripts, 3,543, or 0.7 per cent., were rejected for chronic conjunctivitis believed to be trachoma. In some of the islands the proportion of rejections was four times as high.

In Holland, Josephus Jitta⁹ reports that trachoma is found only in Amsterdam, mostly among the poorer Jews. A commission of inquiry sitting in 1914-17 reported the existence of 3,300 cases. Of 66,418 Christian children 2,396, or 0.6 per cent., and of 7,062 Jewish children 625, or 8.8 per cent., had trachoma. He is of opinion that trachoma is not endemic in the country, but that it was imported from Poland and Russia. He states that it is above all a family disease. Children are affected at an early age either by their parents or by older children.

In the British Isles, Ireland shows most trachoma. Story¹⁰ reported that there was a decrease towards the end of the century, but that in later years it has increased.

"Most of the credit for this increase is to be given to the American doctors, who inspected all immigrants to the United States at the Irish ports, and remorselessly refused embarkation to any with even doubtful signs of trachoma. Consequently, large numbers of most undesirable aliens were left stranded in Ireland—whole families, perhaps, from far regions of Eastern Europe, and trachoma accordingly became more prevalent in this country."

In England the figures collected in 1922 by the Committee on Blindness¹¹ were informative, but to my mind the best picture of present conditions is given by the figures of the London school children. London is a vast area; it includes every variety of social condition and a considerable alien community. For the children in the elementary schools there is a regular medical inspection, and there can be no doubt that every case of trachoma is accounted for. The cases found in the years 1925 to 1929 numbered 26, 20, 15, 16, and 27, so that for five years on an average roll of 650,000 children there was an average of under 21 cases of trachoma a year, or 0.00032 per cent. When we recall the risks of importation of trachoma through the huge shipping area of the Thames I think you will agree that trachoma is practically extinct in London.

In the United States, according to Webster Fox,¹² there is little trachoma among whites except in some isolated parts of Kentucky, West Virginia, southern Illinois, and Ohio. It is common among the Indians. In 1912 of 39,231 Indians examined in reservations 8,940, or 22.7 per cent., had trachoma. The percentage varied in different places from 68.8 to 0.2. In 1924 the Indians of three reservations were examined to the number of 18,830; trachoma was found in 3,986, or 21.2 per cent.

The foregoing figures are sufficient evidence that there is need for a better control in some countries than exists at the present time, and that no country can relax its vigilance.

Clinical Conditions.

Trachoma means "a roughness," and a roughness of that silkiest of tissues, the conjunctiva. The name is a good one. In typical cases the roughness of the tarsal conjunctiva is uncanny. The term is an old one, and the disease is old. The disease was described, with an accuracy that will be little bettered to-day, in the works of Hippocrates and in the later authors of the Greek school, Aetius, Paulus Aeginetus, and Alexander Trallianus. There is one passage in Celsus which may be cited:

Pejus etiamnum est (genus videlicet lippitudinis), ubi pituita pallida aut livida est, lacrima calida et multa profluit, caput

* Made in opening a discussion in the Section of Ophthalmology at the Annual Meeting of the British Medical Association, Winnipeg, 1930.

calet, a temporibus ad oculos dolor pervenit, nocturna vigilia urget: siquidem sub his oculis plerumque rumpitur; votumque est, ut tantum exulceretur. Intus ruptum oculum febricula juvat: si foras jam ruptus procedit, sine auxilio est. Si de nigro aliquid albidum factum est, diu manet. At si asperum, et crassum est, etiam post curationem vestigium aliquod relinquit. (Lib. VI, cap. vi.)

The characteristic signs of the disease in its early stages are the slight ptosis of the upper lid, and a variable degree of discharge from the conjunctiva. The membrane shows a profuse overgrowth of the tarsal covering, so that it may look like a plush pile, or be grossly studded with enlarged follicles. Many cases are so little acute that there may be no outward symptoms of the disease save the slight ptosis, and in these the inflammatory process is dry and sluggish, and the harsh roughness of the tarsal membrane is marked.

Whether or not corneal involvement is a necessary clinical character of the disease is a moot point. Wilson¹³ of Cairo thinks that it is. Other observers do not admit this. My own experience is that within the first year of the disease in children it is rare, and it may never appear if efficient treatment is begun early; but it is certain to appear in long-standing cases, especially among adults.

The disease is undoubtedly highly contagious. Doctors and nurses have been infected, and inoculation experiments have been done. Perhaps the most dramatic account of an experimental inoculation is that recorded by Treacher Collins¹⁴ in his account of the London ophthalmia schools. Children were loath to leave the lovely country schools to go back to the old-time town barrack schools, and deliberately irritated their eyes to prolong their treatment.

"One child, whose name peculiarly enough was Sly, was admitted with marginal blepharitis and slight conjunctivitis; this was cured and all treatment was stopped preparatory to her leaving the school. She was then caught by the nurse taking discharge from another child's eye who was suffering from trachoma and deliberately putting it into her own. The symptoms of acute muco-purulent ophthalmia rapidly set in, and two months later typical trachoma follicles on the tarsal conjunctiva were recognized. After a year's treatment the trachoma was cured."

The most striking clinical feature of the disease is its chronicity. From six months to two years is its usual duration, and most cases extend to the longer term. So strongly is this impressed upon me that I am critical of my own or of others' diagnosis when a case of suspected trachoma reacts speedily to treatment!

The histological feature of the changes produced by the disease is the extraordinary proliferation of the lymphoid tissue. There is a diffuse lymphocytic infiltration of the conjunctiva with numerous follicles occupying the sub-epithelial layer. A follicle may measure from 0.5 to 2 mm. in diameter. The periphery of a follicle is formed of layers of lymphocytes; in the central area are many large mononuclear cells. All the changes are most marked in the retrotarsal fold, but no part of the conjunctiva is exempt. The beginning of a cure is shown by the breakdown of the centres of follicles and the gradual growth of connective tissue fibrils around the follicles. In advanced stages the fibrosis is so extreme that the follicles are strangled by the shrinkage of the scar tissue. Success in treatment is shown in a fine even spread of the scarring. Failure is shown by a gross unequal scarring and consequent distortions of the lids with all their painful and disabling effects. I am inclined to the view that the worst end-results are sometimes due more to ill-advised severity of treatment than to the effects of the disease.

The Causes of the Disease.

The control of trachoma needs a knowledge of its cause and of the conditions under which it spreads. The primary exciting cause of the disease is as yet uncertain. There is a general agreement that it has the characters of a distinct entity, and such that it may certainly be ascribed to some virus. There is no doubt that its progress is affected by intercurrent infections, but none of these infections, which are common and well known, appears to be the determining cause. From the days of Koch's investigation of the disease in Egypt in 1883 there have been many attempts to identify specific organisms. So far no claim has been established. The most recent work

is that of Noguchi,¹⁵ a piece of experimental investigation of much promise. His *Bacillus granulosis* is described as being present in the affected tissues in extremely small numbers in the vicinity of the small and large mononuclear cells constituting the follicles. It has been isolated in cultures; then it is found to have a single polar flagellum. The cultures have been inoculated into monkeys, and have induced conditions of granular conjunctivitis apparently identical with trachoma in man. Wilson¹³ of Cairo has published the report of an investigation he has made on the lines of Noguchi's work. His results are indefinite.

If the primary cause of the disease is uncertain there can be no doubt of some of the adjuvant causes. These are conditions of life which can be dealt with. Trachoma is rarely found except among people of low standards of living. It is found among squalid people who are herded together. In these conditions there is a common neglect of what we speak of as sanitary rules, but which may be better described as the rules of civilization. The easy communal generosity of the feckless has often been noted. Unfortunately this liberality extends to the use of sanitary articles which in more developed communities are regarded as strictly personal. It is, I believe, to the careless but pernicious generosity of these people that the ready dissemination of eye disease among them is due. When once the distinction of *meum* and *tuum* in regard to toilet articles has been learned there is a distinct rise in the standard of cleanliness, and therewith a lessened risk of communicable disease. I have known outbreaks of acute conjunctivitis in schools coincide with the breach of the rule of separate towels; and in no case have I known an outbreak spread where there was a strict re-enforcement of the rule. Confirmation of this observation may be obtained in the care of the men of the Chinese Labour Corps in France. These men at all times carried about their person a towel which was used for many purposes. It was freely loaned to companions. Lister found it necessary to arrange for a regular sterilization of these towels, and he was certain of the efficacy of this procedure.

London Schools.

In former days the chief breeding places of trachoma in London were the Poor Law schools. The children of destitute families were drafted into huge barrack schools. These schools were ravaged from time to time by epidemics of ophthalmia, which was always endemic. Stephenson,¹⁶ in an historical note, showed that the evil of these schools was known as early as 1848. In 1858 Bowman made recommendations regarding them. Ten years later similar recommendations were made by George Critchett. Nettle-ship in 1874 inspected all these schools, and of one he stated that "not 15 per cent. of the eyes could be described as healthy." A report in 1888 by Litteljohn, the medical officer of one of the schools, in which he said "Children have contracted the disease in the school . . . to an appalling extent," attracted the attention of Parliament. An isolation school for ophthalmia was provided under the care of Sydney Stephenson. From later London reports I find that the separate attempts of the local London Poor Law authorities were amalgamated by the Metropolitan Asylums Board. Two ophthalmia schools were established in the country north and south of London in 1903 and 1904 in charge of Treacher Collins. At the time of the foundation of these isolation schools the average number of children housed in the Poor Law schools was 10,800. The accommodation of the isolation schools was 720. In the first year 625 children were admitted, of whom 292, or 46.7 per cent, were suffering from trachoma. The segregation of affected children was so efficacious that in 1918 there were only 186 entries, so one of the isolation schools was closed. In 1921 there was a risk that the other would be closed too for lack of cases. It was therefore determined to admit children also from the elementary schools. Even with this far wider field from which to gather patients the demand upon the resources of the school at Swanley has been below the accommodation. In January, 1930, only 253 of the 364 beds were occupied. Thirty-nine were pauper children

gathered from the Poor Law schools with a roll of 6,375 children; 12 were cases from outside London; and 152 were elementary school children. Of the total cases 67 were trachomatous, or 26.5 per cent.

A most effective agency in the control of trachoma is the School Medical Service. For the past twenty-five years I have been intimately connected with this work in the County of London. My duties as ophthalmic consultant include work at a consultation centre at the County Hall, to which are referred children whose sight presents special difficulties in education or medical treatment.

By Act of Parliament the education authority is responsible for the medical inspection and treatment of the school children. The schools are visited regularly and all the children examined in specified groups. Those requiring treatment are referred to their home doctors or to school clinics maintained by the authority. Parallel with this arrangement there is the School Attendance Department, which has the duty of investigating the reasons for the absences of children from school. Absences of more than a specified period are reported to the head office for special investigation. This dual organization within and without the schools ensures a very complete supervision of health of the children.

The efficiency of the organization was well demonstrated a few years ago. Early in 1924 an unusual number of absences from school on account of "external eye disease" were reported by the attendance officers in the Thames-side districts of Poplar and Stepney. A batch of the affected children was brought to the consultation centre at the head office. I found them to be suffering from early and acute trachoma. Thereon all absentees and the other children of their families, and also the children of the schools they had attended, were medically inspected. A definite epidemic of trachoma was discovered among the children of a few schools in the poorest quarter close to the docks. Ordinarily cases of trachoma average a score a year for the whole school population of London. In this year, 1924, the numbers seen were: January, none; February, none; March, 17; April, 34; May, 51; June, 36; July, 51; August, 2; September, 4; October, 4; November, 10; December, 6; making a total of 215 cases. The affected children were transferred for treatment to the Swanley Ophthalmia School, now under the direction of Stephen Mayou, with the most satisfactory results. The epidemic was confined to the original area of its outbreak, and ceased at the end of the year. I have heard some hard sayings about the school attendance officer. It has been asserted he is as hard-hearted as the pedagogue of a familiar Pauline argument; but his strictness is an invaluable safeguard to the children, as was demonstrated in this outbreak. Imagine what might have happened in densely populated London if there had been no inquisitorial attendance officer.

War Conditions.

An example of large-scale prevention and treatment is recorded by the ophthalmic surgeons^{4, 5} detailed during the great war for oversight of the Labour Corps. Large numbers of coloured men were brought into France for labour purposes. Trachoma was rife among them. It was recognized that with the proximity in which the individuals of the Labour Corps had to live there was a danger of trachoma becoming universal throughout these units. Had this occurred their capacity for work would have been greatly impaired, and there would have been a risk of the disease spreading to the British troops and to the French population.

The Egyptian labourers were highly affected. At a low estimate 45 per cent. were either suffering from or had had trachoma. Of the South African Cape boys only 3 per cent. were affected. The main problem was with the Chinese, of whom there were roughly 100,000. The incidence among them was 8 per cent.—that is, about 8,000 cases; besides these there were 5,500 cases of suspicious conjunctivitis.

The steps taken to remedy matters were three: (1) instructions were given that no labourers with trachoma should be recruited from abroad, and for those on the voyage sanitary treatment was given; (2) the affected men

were segregated; (3) treatment was given to both the affected and the "clean"; the latter received zinc drops, and their towels were sterilized regularly. The effect of these measures was speedily apparent in the improved condition of the men and of their work.

Conclusions.

The evidence presented in this paper points to two certain conclusions: (1) that trachoma can be controlled; (2) that the control of trachoma is a practical proposition. The measures requisite to this control may be viewed from two points: that of the country where the disease is endemic, and that of the country free from the disease. It will be agreed that the principal condition favourable to the spread of trachoma is squalor, the product of bad social conditions. If we can raise the social status of a community, the risks of communicating trachoma will be reduced until they are small—as in England. Social conditions can rarely be effectively altered by outside influences, but this can be achieved if the influence works from within the community. There is now scarcely a country in the world that does not maintain some sort of system of elementary education for its children. Where there is such a system there is ready to hand the basis upon which an efficient campaign against trachoma can be waged. The recognition that a school for children is a place for the training of the child in the use and care of its body, as much as for the training of its mind, will make the school the most efficient prophylactic against contagious eye disease. Instruction in the care of the body engenders pride of body, and this in its turn fosters a sense of separateness or fastidiousness which is offended by a community of interests in toilet articles. That lesson is, I believe, one of the chief gains of civilization; without it our cities would be pest centres, instead of ranking with health resorts. It would do more to extirpate trachoma than any other measure. It would create in countries where trachoma is rife the demand by teachers and parents for routine examination of the eyes of children on entry to school, at specific intervals, and of suspects at all times. Experience in London shows how readily medical inspection, at first resented, becomes demanded as a safeguard to all parties—the child, its family, and the teacher.

Discovery of disease demands treatment. Isolation ophthalmic schools, such as Swanley, are an economic proposition in countries where the incidence of trachoma is low; where it is high such measures are impossible. But it is possible to provide local dispensaries and travelling hospitals after the type of the beneficent foundation of Sir Ernest Cassel in Egypt. Further, it will be good practice to provide for the issue to the people generally of zinc sulphate drops. Regular and long-continued use of these drops in residential schools I have found safe and of value. There is evidence of their value in the control of trachoma among the coolies of the Labour Corps in France. David¹⁷ in Palestine records that during a local epidemic of ophthalmia the school children were unaffected so long as they used the drops, but they fell victims to the attack when their use was stopped. Maybe there would be a few cases where intraocular inflammations would be injuriously affected by the use of the zinc drops, but even with that risk in view I think the universal use of the drops would be justified in a trachoma-ridden country. Finally, in such countries there should be a rule reserving appointments to posts in the public services to the healthy, and disqualifying candidates with trachoma. There can be no doubt that such a rule would furnish an effective "sanction" in a campaign against trachoma.

In a country where trachoma is rare there will be a justifiable demand for the exclusion of immigrants suffering from the disease. In these days of widespread travel the risk of entry of communicable disease into a clean country is great. Quarantine is no service in the prevention of trachoma. The disease is too enduring. Exclusion is the proper remedy. There have been at various times outcries against the action of some countries in rejecting immigrants for failure to attain standards of health. In my view stringent rules as regards health are wholly justified, both for the safety of the one country and for the improvement of the other. The fact that trachoma will exclude the immigrant in any country will do much to awaken the

authorities of a trachoma-ridden country to the disability under which its nationals labour, and to the necessity for remedial measures.

In conclusion, I would venture to reiterate my belief that the best line of attack is through an efficient school service. Through this we can get an oversight of the children such as no other means will secure. The school also tends to inculcate a sense of personal responsibility that is invaluable to the common health. There is no doubt that if we could keep the children of one generation free from the disease trachoma would be extinct.

BIBLIOGRAPHY.

- ¹ Van Millingen: *Annales d'Oculistique*, September, 1895.
- ² Clemow, F. G.: *Geography of Disease*, Cambridge, 1903, p. 299.
- ³ Thirteenth Annual Report of the Ophthalmic Section, Ministry of the Interior, Egypt, Cairo, 1928.
- ⁴ Lister, W. T.: *Official History of the Great War: Med. Services, Surgery of the War*, 1923, ii, p. 421.
- ⁵ Cunningham and Wharton: *Trans. Ophth. Soc. U.K.*, 1918, xxxviii, p. 18.
- ⁶ Howard, Harvey J.: *Ten Weeks with Chinese Bandits*, London, 1927, p. 106.
- ⁷ Annual Report of the Madras Government Ophthal. Hosp., 1923-1928.
- ⁸ Luttraria, A.: Trachoma in Italy. League of Nations Health Organization. No. C.H.495, 1926.
- ⁹ Jitta, N. M. Josephus: The History of Trachoma in Holland. League of Nations Health Organization. No. C.H.408, 1926.
- ¹⁰ Story, J. B.: *Trans. Ophthal. Soc. U.K.*, 1918, xxxviii, p. 9.
- ¹¹ Causes and Prevention of Blindness. Departmental Committee's Report, Ministry of Health, London, 1922, p. 41.
- ¹² Fox, L. Webster: *Amer. Journ. of Ophthal.*, 1929, xii, p. 457.
- ¹³ Wilson, R. P.: Third Annual Report of the Giza Memorial Ophthal. Lab., Cairo, 1928, p. 74.
- ¹⁴ Collins, E. Treacher: Royal London Ophthal. Hosp. Reports, xviii, Pt. I.
- ¹⁵ Noguchi, H.: *Journ. Exper. Med.*, xlviii, Sup. 2, 1928.
- ¹⁶ Stephenson, Sydney: *Trans. Ophthal. Soc. U.K.*, 1918, xxxviii, p. 11.
- ¹⁷ David, J.: *Presse Méd.*, 1920, p. 829.

SOME IMMUNOLOGICAL PROBLEMS IN SEPTICAEMIA.*

BY

FRED T. CADHAM, M.D.,

PROFESSOR OF BACTERIOLOGY, UNIVERSITY OF MANITOBA MEDICAL
SCHOOL.

WHEN pyogenic micro-organisms overcome all defences of the body, travel freely through, and even on occasion multiply in the blood stream, giving rise to symptoms of a general invasion, the condition is recognized as septicaemia. Any definition of the term, however, is apparently subject to modification; for instance, with the extension and perfection of blood culture methods, micro-organisms may be recovered from the blood in many states, such as typhoid and pneumonia, which are not classed as septicaemia. Then, too, disease entities exist in which the evidence suggests that there is a general invasion of an ultra-microscopic organism or virus. The diagnosis of septicaemia, then, rests not alone on laboratory procedures, but depends also on the clinical evidence. For this discussion I will consider the type of case in which the symptoms of a general bacterial invasion overshadow those of local origin, and which is characterized, clinically, by chills, sweats, irregular temperature, and is associated with the finding in the blood stream of the causative micro-organism, generally a pyogenic coccus, most frequently a streptococcus. In the treatment of such cases the physician turns for help to the immunologist.

The origin and outcome of such a condition depend naturally, on the two interdependent variables—the infective agent and the patient's resistance.

THE INFECTIVE AGENT.

Briefly let us consider the invasive power inherent to the micro-organism. What is the influence of numbers? We know that a measured quantity of a certain microbe may at times be required to induce a septicaemia, yet, clearly, it is not the determining factor, for the few streptococci driven into the tissues and the lymph channels by the prick of a needle may initiate a rapid and fatal type of the disease, while on the other hand a massive infection frequently remains localized. That the power of elective

localization of bacteria has an essential bearing on the question has been clearly demonstrated by Rosenow. Even so, in elective localization the variable factor is in evidence, for a meningococcal infection occasionally exists only as a septicaemia, with no clinical or pathological evidence of any particular involvement of the meninges. Again, the *Streptococcus viridans* may invade the heart valves, which indicates that the microbe passed through the blood stream unaffected by the defences of the body, and possibly without giving rise at the time to clinical manifestations of its presence in the blood; subsequently a septicaemia arises from the endocardial focus.

An overwhelming invasion following the inoculation of a few organisms suggests that the circulatory system may be the elective site, for it is not unusual in some cases to find scant evidence that any particular tissue is involved, even though the micro-organisms may be noted in direct blood smears. Besredka, however, emphasizes the importance of tissue immunity at the primary site of elective localization; according to his theory a general invasion of the staphylococcus or streptococcus indicates a previous cutaneous or mucous area of infection.

The capacity to produce powerful toxins, to multiply rapidly, or to resist destruction is peculiar to certain bacteria. Such factors determine aggressiveness; while just as important, evidently, in favouring a continued bacteraemia, is the inability of the causative organism to incite antibody production.

As a rule bacterial association favours a local infection, but that it is, in septicaemia, an important factor receives slight support; however, a simultaneous general invasion of more than one micro-organism may occur. Further, while one grants that septicaemias may be induced experimentally by the inoculation of a single selected strain of an organism, such as a streptococcus, yet the evidence shows that no single strain is responsible for all streptococcal septicaemias. Here, in carrying out agglutination tests with forty-five strains of streptococci recovered from as many cases of septicaemia, we failed to obtain any common agglutinative type.

Virulence as associated directly with the microbe lacks definition. More recent work, such as that of Falk, stresses the theory that the dynamics of the electro-potential differences of the cells underlie some of these problems. For the further elucidation of the term virulence as related to the micro-organism, Holman suggests more intensive physiological studies of the metabolism of bacteria. These factors are bound up with the structure of the microbe; how infinitely complicated this may be one can judge from the fact, as Cameron illustrates, that a comparable unit, such as a red blood cell, contains approximately a million million molecules and ions.

I have touched only on some of the principal characteristics of the micro-organism which are believed to determine its invasive powers, for aside from preventive measures, the nature of the microbe which infects the patient and produces a septicaemia is the accidental factor over which the physician has no control. The attenuation of the virulence of an infective agent by world-wide measures such as universal vaccine therapy is a problem not yet solved. In Winnipeg the incidence of septicaemia caused by the haemolytic streptococcus shows periodic waves, suggesting the prevalence at intervals of a type or types of this streptococcus favouring such an infection.

THE PATIENT'S RESISTANCE.

The rapid spread of an infection from a small focus indicates primarily an inability of the phagocytes, either leucocytes or clasmatoocytes, to cope with the infective agent. A determination of the opsonic index in such cases frequently shows that the blood is deficient in natural opsonins. These opsonins when present facilitate phagocytosis until such time as the body responds with the production of specific antibodies, including the thermostable opsonins, for the bacteria and their products responsible for the infection.

This weakness in the defence, which allows the extended invasion of some bacteria, particularly the pyogenic cocci, the haematopoietic tissues may attempt to offset by an overproduction of leucocytes. It was characteristic of the cases

* Read in opening a discussion in the Section of Bacteriology, Pathology, Physiology, and Biochemistry at the Annual Meeting of the British Medical Association, Winnipeg, 1930.