It is impossible to discuss in detail the thirty-two cases I have placed in this group; but it is certain that the characteristic features of the suprarenal lesion in Addison's disease are not described in any one of them. I must, however, advert to the most recent of these cases, published by Dr. Wickham Legg, in the last volume of the *St. Bartholomew's Hospital Reports*. The patient, a woman aged 37, unquestionably exhibited some of the constitutional symptoms of Addison's disease, for she suffered for eighteen months from debility, shortness of breath, occasional vomiting of food, and constipation, and she died after five weeks' residence in the hospital, of vomiting and exhaustion. But, on the other hand, there was a distinct bilious tendency to explain the vomiting; the appetite was fair, and there was great thirst, with a red fissured tongue, swollen spongy gums, and a temperature above the normal. Moreover, the patient had lost four stones in weight during her illness: an absolutely unprecedented circumstance in Addison's disease, unless when resulting from some serious coexisting wasting disease. The discoloured skin, also, was harsh, dry and warm, instead of being soft and cool, and was not more deeply pigmented in the axillæ or areolæ of the nipples than at other parts. At the *post mortem* examination, the right suprarenal capsule could not be found, its place being filled by a mass of yellow fat; and the left was only represented by a black body as thin as paper. This was a most peculiar and interesting condition of the suprarenal capsules, but it obviously bore no relation whatever to Addison's disease of those organs; nor were the constitutional symptoms and discoloration of skin, taken as a whole, characteristic of that disease. The most difficult point in the case is the absence of any apparent cause of illness and death.

One case remains of the whole number collected, which represents another misconception so remarkable, that it cannot be entirely passed over. The case is related by Dr. Gilliam of the United States, and is that of a man aged 45, who suffered from many of the constitutional symptoms of Addison's disease. Gradually increasing debility, dyspnoea and palpitation on exertion, loss of appetite, and tendency to vomiting, which became more and more obstinate until the patient died of exhaustion—were symptoms which, in the absence of any other discoverable cause might fairly lead to a diagnosis of Addison's disease, although no discoloration of skin was present. But when, after death, not only were the suprarenal capsules found to be healthy, but advanced degeneration and atrophy of the gastric tubules were discovered, which, as the author himself observed, fully accounted for all the symptoms, the diagnosis had clearly been a mistake. From this case, however, Dr. Gilliam concludes, first, that the bronzing of the skin is quite an unimportant feature of Addison's disease; and, secondly, that Addison's disease itself consists, not in a lesion of the suprarenal capsules at all, but in disease of the gastric tubules. The misconception lying at the root of this singular theory seems to be, that the presence of constitutional symptoms resembling those of Addison's disease was, in itself, sufficient evidence of the existence of that disease, and that the lesion which produced them might safely be regarded as the essential lesion constituting Addison's disease. That, in the case referred to, the lesion found in the stomach was the cause of the gastric and other symptoms, is obvious enough, but I trust I have made it equally clear that no symptoms, obviously referable to other morbid conditions can justify any assumption as to the existence of Addison's disease.

The question naturally arises, how misconceptions, so baseless in fact and disproved by such conclusive evidence, can have been so widely propagated and have survived so long. I believe this has been mainly due to the great rarity of the disease, which has prevented all but a small minority of medical men from acquiring even the degree of practical acquaintance with its true characters which the observation of a single typical case would afford.

If, however, the relation between the clinical phenomena and the specific suprarenal lesion in Addison's disease may be considered as proved, the obscure pathological processes involved in that relation, and the equally obscure causes of the suprarenal lesion itself, will still afford ample field for investigation. To these parts of the subject, I must endeavour to address myself in my next lecture, although perfectly conscious of the insurmountable difficulties they present, in the present vague and imperfect state of our knowledge with respect to many essential facts.

ACUTE GLOSSITIS IN SCARLATINA.—An instance of this extremely rare complication has lately been published by Dr. Wm. Moore, of Dublin. It occurred in a young gentleman aged 18, and was the only example Dr. Moore had ever seen in this disease. He strongly advocates the treatment by iron and stimulants, when this complication takes place. A somewhat similar case has been described as occurring in the practice of Dr. Banks, but the complication is unusual.

THE GOULSTONIAN LECTURES ON PUERPERAL FEVER.

Delivered at the Royal College of Physicians, London.

By ROBERT J. LEE, M.D., F.R.C.P.,

Assistant Physician at the Hospital for Sick Children, Great Ormond Street.

LECTURE III.—(Continued.)

WHEN Professor Lister remarks, "We now see it is not essential to assume the existence of a special virus at all, but that organisms common to all the sores in the ward may, for aught we know, assume specific properties in the discharges long putrefying under the dressings" (*Microscopical Journal*, vol. xiii), it is clear that he is indisposed to allow that a poison apart from bacteria can be brought into existence. It is not really because these points, so difficult at present to decide, are of practical importance that I refer to them. But they are interesting, as showing pretty clearly where the various parties of investigation have started from in search of fresh knowledge. We have claimed the privilege of testing all reports thus returned by the rules of general experience, supposing there is any great difference of opinion as to their correctness. There has been little occasion, however, to do this as yet; for the most valuable contributions we have received are the results of the labours of men of practical experience in the clinical phenomena of the disease produced by septic infection. It seems to me that, for this reason, we may accept the conclusions of Virchow, Lister, Billroth, Heiberg, and others, who are quite able for themselves, and are in the habit, of applying to their researches the test of clinical experience.

There is one case, for instance, in which we might find it difficult to explain, by the theory of bacteria, certain morbid phenomena, if we confined ourselves to the limited effect which the particles produce on the tissues: those changes, namely, which we term inflammatory. It is well known that there are cases in which we find no collections of pus, or secondary abscesses, and no well marked pathological alterations, cases usually of the acute form of puerperal fever, and where the constitutional symptoms have been the chief evidence of septic infection. In such instances, morbid anatomy reveals conditions not unlike those which we meet with in certain other contagious diseases: enlargement and softening of the spleen, congestion of the mucous and serous membranes, fluid condition of the blood, and slight general congestion of the pulmonary tissue. It is in these cases that Heiberg felt a difficulty in retaining the use of the term pyæmia; for there is neither a primary focus of purulent matter, nor are there any evidences of the presence of pus in any part of the body.

This is the reason why Professor Billroth uses the term *septhæmia* to signify the resorption of septic stuff, and pyæmia the resorption of pus. We have also septicæmia contrasted with icorrhæmia in some recent German works. These terms are intended to separate cases of acute septic infection from those of longer duration; for, as it is well known, in cases of abortion, retained placenta, and others, where the origin of the decomposing substance is not very doubtful, we observe a series of symptoms which lead to the belief that a slow process of poisoning is going on in the system of the patient. Such a process would be termed *ichorrhæmic*.

If we follow Professor Heiberg, as certainly we are inclined to do, on the grounds of clinical experience, we should regard these puerperal processes, in whatever form they present themselves, and whatever characters the symptoms and pathological changes may assume, as depending on one and the same cause, the action of which on the nervous system, the organs of circulation and respiration, on the temperature, and on the fluids and tissues of the body, may be modified by circumstances similar to those which we know to be capable of modifying the action of poisons generally.

For some reasons, therefore, we might feel disposed to rest satisfied with the old term putridity, which involves no such theory as septicæmia, pyæmia, and others; or we might fall back on the simple classical term sepsis as a convenient one for general use. In the clinical observation of cases in which septic agents are more or less actively at work in the system, whether in simple puerperal fever, in cases of abortion or retained placenta, in carcinoma uteri, or under any other circumstances, we are led to divide our attention between local

and constitutional symptoms; that is, between local pathological changes and general constitutional disturbance.

This evidently becomes necessary for the purposes of treatment. Allowing that the local action of septic agents is the production of those changes of tissue which we term inflammation, the question arises whether there are other causes for the same effects as well as septic material.

This question is answered by some in the following manner. "It is possible that inflammation may be excited by various causes other than the presence of bacteria; and we would distinguish the former from the latter by the term simple traumatic pyæmia and specific traumatic pyæmia, pyæmia being used in the general signification of sepsis. From simple traumatic pyæmia may follow metritis, endometritis, parametritis, perimetritis simplex, or diffuse peritonitis. In surgical cases, this disease assumes the form of erysipelatous rubor around the wound; that is to say, conditions depending on local causes. Phlebitis and thrombosis may also be consequences of simple traumatic pyæmia. The only difference between these and the specific form of pyæmia is the presence of bacteria." These are the views of Billroth, Heiberg, and others.

Now, it does not unfrequently occur that cases present themselves in which we find only those alterations of tissue which are attributed to simple traumatic causes, and yet the history and other circumstances of these cases are the same as those in specific traumatic inflammation. What must always be a difficulty appears to me to be the diagnosis between the one and the other form of inflammation. It is difficult, I think, to obtain a very clear idea of what simple traumatic inflammation is, as distinguished from the other. Does it not seem that we are defining it by negative characters; in fact, that, instead of being simple, it is a very complex expression, for it may be anything; that is, any substance or force except bacteria? If we are to call one simple in its nature, the most definite ought to have the first claim to the title. We are aware that, pathologically considered, there is no difference, as far as we can tell at present, between cellulitis or phlebitis of the thigh, as it occasionally occurs in men, or as we meet with it in the puerperal condition in women; so that, in any particular case, we are obliged to depend upon the history for information as to the origin of the disease, and upon the general symptoms for evidence of septic infection.

This is the clinical aspect which the subject presents, and, regarded in a practical point of view, it appears doubtful whether the division proposed is consistent or useful. We may have cases of metritis which have originated in abortion; but, by active treatment, the decomposition of organic matter within the uterine cavity has been prevented from infecting the system, and no symptoms are present which enable a diagnosis to be made between simple traumatic metritis and specific metritis. It may be remarked, that the difference which is assumed and appears to exist between simple and specific inflammation was present to Cullen's mind when he observed: "Whether there be any belonging to the order of phlegmasia is doubtful." (*Op. cit.*, p. 80.) In speaking of erysipelas, he remarks: "It is doubtful if this disease be properly, in nosology, separated from phlegmasia." (*Op. cit.*, p. 377.) Or, again, "It is probable that an erysipelas is sometimes attended with, or is a symptom of, a putrid fever." (*Op. cit.*, p. 379.) Looking at the question from a common sense point of view, we may reasonably ask whether there is not a danger of making confusion in our views of the symptoms, pathology, and treatment of the disease we are considering by allowing the use of an indefinite or ill-defined word like "traumatic" into the terms of definitions. It sometimes happens than we can discern the flaw in an argument or proposition without much trouble; at other times, we are withheld from consent by a feeling that, though the logical process by which the conclusion is arrived at be correct, there is a certain want of character in it which makes us hesitate. If we take the trouble to examine carefully any proposition of this kind,—and we know how frequently they present themselves to the physiologist and physician,—we shall find that there is some slight incorrectness in the premises of the argument. It is quite open to discussion whether metritis in all its forms, which are said to be traumatic, may not have been occasioned by the influence of an organic poison developed under certain conditions, or of external forces, such as cold, injury, and others. It is not difficult to perceive the direction which such reflections must give and are giving to pathological research. To return, however, to puerperal fever—a disease which, we are induced to believe, is to be explained in all respects by the influence of septic poison—it would appear that, in most cases, we are to search for the focus of decomposition in the cavity of the uterus or the surface of the mucous membranes which are connected with it. Whether we can prove that there is organic substance undergoing decomposition or not, we are to be satisfied by the symptoms which are

present that such is the case. We are also required to admit that, under several conditions, all of which involve the presence of septic substance, symptoms similar to puerperal fever may be developed; and that, whatever differences are observed in the acute or chronic character of such symptoms, we are to refer them to the rate of admission of the poison into the system. We assume that we may explain the peculiarly acute form of puerperal fever with which we are acquainted by the fact of the existence of venous sinuses in the walls of the gravid uterus, and of large lymphatic vessels by which the septic material easily enters the circulating fluids; and, when asked to define what we mean by a septic agent, by sepsis, or by any other term involving the same idea, we may make the basis of our definition the existence of active living organisms resulting from the decomposition of organic matter, having special microscopical characters, producing special effects on the system of man and beast, and the transmission of which is regulated by ascertained principles.

(To be continued.)

ON THE ACTIONS OF PICROTOXINE, AND THE ANTAGONISM BETWEEN PICROTOXINE AND CHLORAL HYDRATE.

By J. CRICHTON BROWNE, M.D., F.R.S.E.,
Medical Director of the West Riding Asylum.

THE admirable report of the Committee of the British Medical Association, appointed to investigate the antagonism of medicines, which we owe to Dr. Hughes Bennett's powers of lucid exposition, suggested to me, when reading it, various instances beyond those which received the attention of the Committee, in which a direct physiological antagonism between the actions of remedies in all probability exists. Of the conjectures which thus occurred to me, I have as yet been able to put one only to the test of actual experiment; but the results which this single investigation has afforded me are so interesting and important as to appear to me to merit early publication.

It was when perusing the description given of the effects of chloral hydrate in reducing the force and frequency of the tetanic convulsions which follow a fatal dose of strychnia, that I began to speculate that, in all likelihood, the same agent might exercise a similar influence over the somewhat analogous symptoms which follow the administration of a fatal dose of picROTOXINE. An inquiry, which I commenced some years ago, into the actions of that substance had satisfied me that, in some respects, its effects upon the living organism resemble those of strychnia. Tonic and clonic spasms of great severity and violence, culminating speedily in death, are induced by large doses of it, and opisthotonos and gasping and respiration are frequently present. The very particular in which the toxic effects of picROTOXINE differs from those of strychnia, in that they are exercised to a greater extent over the cerebral and to a less extent over the spinal centres, seemed to hold out an additional hope that chloral hydrate would effectually counteract them; for chloral hydrate powerfully diminishes the activity of the brain, and so might be expected to mitigate the influence of any agent which irritates that organ and stimulates it to excessive and irregular discharges of energy.

In proceeding to put to trial the theory thus formed as to the antagonism of picROTOXINE and chloral hydrate, it was thought desirable, in the first instance, to arrive at definite notions as to the physiological actions of the former. And these could scarcely be derived from books; for, although *cocculus Indicus*, of which picROTOXINE is the proximate principle, has been recognised as a medicine since the days of the Arabian physicians, by whom it was designated *Maderadsch*, its modes of operation and uses may still be said to be undetermined. Christison says of it, that it was probably first known in Europe as a means of taking fish, which it first throws into violent irregular motion and then stupefies; and that it is an active poison, adequate to occasion death, producing chiefly giddiness, staggering, tetanic convulsions and coma. He adds, that nothing is known of its medicinal properties or actions in small doses, more than that it is beneficial as an external application in scabies, ring-worm, and porrigo. Taylor intimates that it gives rise to nausea, vomiting, and griping pains, followed by stupor and intoxication; and he describes one of the few recorded cases in which it has proved fatal, and in which these symptoms were present, and extended over a period of nineteen days. Dr. Glover describes it as a narcotico-acrid poison that acts on the spinal cord, raises the animal temperature, and causes great congestion at the base of the brain. Dr. Roeber of Berlin, who experimented with picROTOXINE,