THE GERM AS A FRIEND IN THERAPEUTICS.

(NOTES ON THE OPSONIC INDEX.)

(BY EDW. J. ROBERTS, M.B.)

During the last decade, the rapid strides made in surgery are well-known to the general public. It may be that the attention is so centred on that branch of the "Art of Healing" that, in a measure, the researches in medicine have not called forth the notice which they certainly deserve. The important question of immunity is now attracting the attention of the whole medical world, brought to its notice by the workers in hæmatology and bacteriology. In all cases where the unwelcome germ takes a part, the physician and bacteriologist must work together. The busy physician has not the time to complete his investigations of his case further than the clinical aspect of it, nor has he the laboratory, instruments, etc., necessary to the close study of the action of the germs causing that particular disease which he has under his care. The bacteriologist now informs the physician that there is a process by which one is able to pick out the defensive factors of the body, and to estimate their power of destruction over the investing bacilli. Although the process may not be taken over by the physician, yet, with the help of the bacteriologist, he is able to more clearly understand his patient's vital condition. We are indebted to Metchnikoff for pointing out some peculiar properties of certain white corpuscles, or leucocytes in the blood of man. These leucocytes have the power of absorbing or destroying the germs of disease under certain conditions, and it is pointed out that these conditions can be so altered as to effect the destroying property of the leucocytes. These leucocytes, or white corpuscles, are called phagocytes, and the process by which they absorb the bacilli is named phagocytosis. The blood serum has been found to contain certain substances or elements, to which the name "Opsonins" was given—this word "opsonin" is from the Latin verb "opsono," meaning I cater, or prepare. Therefore, the opsonins in the serum prepare the germs in such a manner as to render them an easy prey to the phagocytes. It is supposed, and it is probably the case, that the opsonins act by chemically uniting with the bacilli, so enabling the phagocytes to render them inert. In 1902, Major Leishman published in the "British Medical Journal" an account of a practical method whereby one can estimate the phagocytic power of the white corpuscles of the blood, and in following years Wright and Douglas also wrote. This year, Dr. McFarland and his confreres of Philadelphia published to my mind a much simpler process, which almost brings its usage into the hands of the physician. I will now come to the practical point of estimating the phagocytic power of the leucocytes. To quote Dr. McFarland: "In order to perform the experiment it is necessary to have first the living phagocytic cells; and, secondly, the bacteria they are to take up, and it is necessary to bring these two in contact under invariable conditions, in order that correct deductions concerning their interaction may be drawn." Now, first to secure the cells. Make a small puncture in the finger of the patient at the root of the finger nail, draw a small quantity of the blood that flows in a pipett, made for the purpose, or a capillary tube with even calibre. To prevent coagulation draw up in the same pipett an exactly equal quantity of a solution of citrate of sodium, 1½ per cent. Now blow both fluids on a clean slide, or better, in the depression of the slide. Draw up and blow out several times, until the fluids are thoroughly mixed. Now the blood is ready for the particular germ you wish to experiment with. Now, an exactly similar quantity (as the blood) of a standard emulsion of the bacteria is thoroughly mixed with the solution of blood and citrate of sodium. This mixture of blood, emulsion, and citrate solution is drawn up in a capillary tube, the ends sealed, and the tube placed in an incubator for thirty minutes. The tube is now removed from the incubator, the ends broken off, and the contents spread on a clean slide, and allowed to dry. The smear is then stained and counterstained, dried, and mounted in the usual manner. The field should show the polymorpho nuclear neutrophiles with their nuclei and the bacilli stained according to staining method used. The phagocytes are counted, and the number of bacilli in each also counted, and the average taken. This number gives you the phagocytic index, and, dividing their number by the standard you have chosen, you get the Opsonic Index. This method, I hold, is a much simpler one than that of Wright and Douglas. Wright and Douglas separate the corpuscles with a centrifuge, wash the corpuscles, and use patient's serum. Now, one may well ask, What is the use and value of finding the opsonic index? It is to estimate the amount of the particular vaccine required to increase the patient's opsonic index, thereby increasing his power to resist attacks of bacilli. If the experiment is carried to a successful issue, and if the bacteriologist can place in the hands of the physician a simple workable test, there is no doubt that Pasteur's hope will come to be a fact. Pasteur prophesied that in time to come all infectious diseases would be treated and cured by vaccination, and when we review the past twelve years, we

cannot but be convinced that this will be our method in the near future. I may here briefly describe the method of obtaining the vaccines. The vaccine consists of an emulsion of the particular germ which causes the disease which one is treating. Large growths of young cultures are grown on a medium, principally Agar, and when ready are washed off the agar with warm salt solution. This is now thoroughly shaken up in a test tube to separate the bacilli and to break down the clumps. A centrifuge does the work of separating very quickly; it is a very tedious process to get the emulsion to the proper standard. By comparing the number of red corpuscles with a number of germs in a given quantity of fluid, one can estimate the number of germs very readily. Take a mixture of one part emulsion, one part blood, and three-parts saline solution, and count both corpuscles and germs in a given space. Therefore, supposing there were ten times the number of germs as there were corpuscles, we should have 45,000,000 in one cubic millimetre. Now we come to the method of applying the treatment. First of all, you diagnose the disease, take the opsonic index of your patient, and have your vaccine. The patient is now given his injection of warm vaccine, and his opsonic index watched very carefully. A short time after the injection the opsonic index falls, and this stage is called the "negative phase." After a time, from a few hours to two or three days, the opsonic index rises again, and this stage is called the "positive phase." In time the index diminishes, and another injection is required, but this time the "negative phase" should be much shorter than the first. Then, again, the index rises, and may reach or even go higher than the normal. Repeat the injection until the opsonic index remains at the normal. Never give the vaccine during the "negative phase." What goes on in the patient during this treatment is, first, the opsonins are increased and the phagocytosis is improved, and, secondly, the bacilli are destroyed, and the infection ceases, and a cure is recorded. There is no doubt whatever that performing the experiment is not so easy as one would imagine from merely reading an account of it. The difficulty of standardising the emulsion and the grinding and separating the bacilli require a lot of practice and care. The decalcifying the blood and the mixing of the fluids is simple enough, but it is rather a delicate and difficult job to fix and stain the smear satisfactorily. "Opsonin" is the sauce which is mixed with the bacteria to increase the appetite of the phagocytes. I mentioned immunity in the beginning of these notes. Immunity is really the power of resisting the attacks of any given germ or disease. This immunity may be either natural or may be produced by artificial means. To render my meaning more clear, I will take the disease small-pox, of which we have had quite enough experience in this State. Some persons were naturally immune against this disease, while others readily fell victims to the small-pox bacilli. To prevent the spread of this disease, we artificially rendered people immune by giving them the disease in a very mild form by vaccination. It was not actually the mild disease which we introduce that caused the immunity, but the products of bacterial action formed during its course. So, by these bacterial products, are produced various degrees of immunity without causing any disturbance to the patient in the majority of cases. Of course, an attack of the disease small-pox itself causes a much higher degree of immunity, and is more lasting than that caused by vaccination. It has been discovered that the serum of a highly-immunised animal when injected into a second animal will protect that second animal more or less from an attack of the given bacteria. Now, this serum from the highly-immunised animal is called anti-toxin, and one particular anti-toxin was used only recently in the slight outbreak of diphtheria in this city. Although all the sera have not been so successful as the anti-toxin of diphtheria, yet still I am certain, as the researches continue, we may be sanguine that they will be so. With reference to the phagocytic action of the leucocytes, we endeavour to increase that action by the injection of the bacterial products of the given germ. Let us take a case of consumption or tuberculosis—unhappily, we have not far to go for examples—would it not be a blessing to all if we could destroy the tubercle bacilli by increasing the phagocytic power of the leucocytes by the simple means of injections of a serum? The delicate and most interesting process of finding the opsonic index, which I have endeavoured to explain to you to-night, may be hailed as another fighting factor against the dreadful disease tuberculosis. What physician would dare neglect to give the anti-toxin of diphtheria in a case of diphtheria at the present time if it were procurable? The same question will be asked in the future concerning other anti-toxins. The discovery of the phagocytic power of the leucocytes has caused workers all over the world to endeavour to make the test simple, and give a practical therapeutic value to it. I trust these few remarks will be understood, so that the public will be prepared in some measure for the practical working of this new curative agency.